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HENRY FORD HEALTH

Henry Ford Health Publication List – December 2024

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health personnel. Searches were conducted in PubMed, Embase, Web of Science, CINAHL, PsycINFO, and Google Books during the month, and then imported into EndNote for formatting. There are 508 unique citations listed this month, including 159 articles, 260 conference abstracts, and 89 books or book chapters.

Articles are listed first, followed by conference abstracts and books and book chapters. Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health authors.

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Articles

Conference Abstracts

Books and Book Chapters

Articles

Allergy and Immunology

Baptist AP, Germain G, Klimek J, Laliberté F, Schell RC, Forero-Schwanhaeuser S, Moore A, Noorduyn SG, and Paczkowski R. Medicare Advantage Population in the United States: Outcomes of Patients with Asthma Treated with ICS/LABA Before and After Initiation with Fluticasone Furoate/Umeclidinium/Vilanterol (FF/UMEC/VI). *Adv Ther* 2024; Epub ahead of print. PMID: 39714547. Full Text

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Global Medical Affairs, General Medicines, GSK, London, UK.
Value Evidence and Outcomes, R&D Global Medical, GSK, Mississauga, ON, Canada.
Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada.
US Value Evidence and Outcomes, GSK, Collegeville, PA, USA.

INTRODUCTION: The clinical benefits of fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) have been demonstrated in clinical trials. There is limited evidence regarding the effectiveness and economic outcomes associated with FF/UMEC/VI use in US clinical practice. This real-world study assessed asthma-related exacerbations, healthcare resource utilization (HRU), and healthcare costs among a Medicare Advantage-insured population before and after initiation of FF/UMEC/VI in patients with asthma previously treated with an inhaled corticosteroid/long-acting β(2)-agonist (ICS/LABA). METHODS: De-identified data were obtained from the Komodo Health database (01/01/2016-12/31/2023) for adults with asthma who received prior ICS/LABA treatment and had ≥ 12 months of continuous Medicare Advantage coverage both pre- and post-FF/UMEC/VI initiation (index date). Rates of asthma-related exacerbations and HRU were compared using rate ratios (RR) from Poisson regressions. Healthcare costs were calculated per patient per year (PPPY) and compared using mean cost differences from generalized linear models. RESULTS: In total, 2598 Medicare Advantage-insured patients who initiated FF/UMEC/VI for asthma were included. The mean ± SD age was 67.9 ± 12.3 years; 75.5% were female. The rate of overall asthma-related exacerbations was 31% lower in the post- versus pre-initiation period (RR 0.69; 95% CI 0.65, 0.73; $p < 0.001$) and included a 24% lower rate of inpatient/emergency department (IP/ED)-defined exacerbations (RR 0.76; 95% CI 0.68, 0.85; $p < 0.001$) and a 34% lower rate of systemic corticosteroid (SCS)-defined exacerbations (RR 0.66; 95% CI 0.61, 0.71; $p < 0.001$). Asthma-related ED visits (RR 0.69; 95% CI 0.60, 0.80; $p < 0.001$) and asthma-related outpatient (OP) visits (RR 0.77; 95% CI 0.71, 0.84; $p < 0.001$) were both lower, and the mean reduction in cost was $411 PPPY (95% CI $575, $248; $p < 0.001$), after FF/UMEC/VI initiation. CONCLUSIONS: Initiation of FF/UMEC/VI after ICS/LABA treatment among Medicare Advantage-insured patients with asthma was associated with reduced rates of asthma-related exacerbations, ED and OP visits, and healthcare costs, highlighting the benefits of therapy escalation among this patient population.

Allergy and Immunology

Brunwasser SM, Gebretsadik T, Satish A, Cole JC, Dupont WD, **Joseph C**, Bendixsen CG, Calatroni A, Arbes SJ, Jr., Fulkerson PC, Sanders J, Bacharier LB, Camargo CA, Jr., **Johnson CC**, Furuta GT, Gruchalla RS, Gupta RS, Khurana Hershey GK, Jackson DJ, Kattan M, Liu A, O'Connor GT, Rivera-Spoljaric K, Phipatanakul W, Rothenberg ME, Seibold MA, Seroogy CM, Teach SJ, **Zoratti EM**, Togias A, and Hartert TV. Caregiver worry about COVID-19 as a predictor of social mitigation behaviours and SARS-CoV-2 infection in a 12-city U.S. surveillance study of households with children. *Prev Med Rep* 2025; 49:102936. PMID: 39697187. Full Text

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OBJECTIVE: Understanding compliance with COVID-19 mitigation recommendations is critical for informing efforts to contain future infectious disease outbreaks. This study tested the hypothesis that higher levels of worry about COVID-19 illness among household caregivers would predict lower (a) levels of overall and discretionary social exposure activities and (b) rates of household SARS-CoV-2 infections. METHODS: Data were drawn from a surveillance study of households with children (N = 1913) recruited from 12 U.S. cities during the initial year of the pandemic and followed for 28 weeks (data collection: 1-May-2020 through 22-Feb-2021). Caregivers rated how much they worried about family members getting COVID-19 and subsequently reported household levels of outside-the-home social activities that could increase risk for SARS-CoV-2 transmission at 14 follow-ups. Caregivers collected household nasal swabs on a fortnightly basis and peripheral blood samples at study conclusion to monitor for SARS-CoV-2 infections by polymerase chain reaction and serology. Primary analyses used generalized linear and generalized mixed-effects modelling. RESULTS: Caregivers with high enrollment levels of worry about COVID-19 illness were more likely to reduce direct social contact outside the household, particularly during the U.S.'s most deadly pandemic wave. Households of caregivers with lower COVID-19 worry had higher odds of (a) reporting discretionary outside-the-home social interaction and (b) SARS-CoV-2 infection. CONCLUSIONS: This was, to our knowledge, the first study showing that caregiver COVID-19 illness worry was predictive of both COVID-19 mitigation compliance and laboratory-determined household infection. Findings should inform studies weighing the adaptive value of worrying about infectious disease outbreaks against established detrimental health effects.

Allergy and Immunology

Greimann E, Freigeh GE, Wettenstein RP, **Nelson B**, Carpenter LM, Mohan A, and **Baptist A**. Mild Asthma- What Matters to Patients and Parents. *Ann Allergy Asthma Immunol* 2024; Epub ahead of print. PMID: 39608675. Full Text

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BACKGROUND: Mild asthma has received less attention despite accounting for the majority of asthma patients. However, asthma complications including hospitalizations and progressive loss of lung function frequently occur in such patients. The priorities of mild asthma patients are unknown, hindering the ability to advance care. OBJECTIVE: To identify patient and parent perspectives on the definition of mild asthma, treatment preferences, concerns and goals of care. METHODS: Participants with self-defined mild/intermittent asthma were recruited using emails distributed through the Allergy & Asthma Network (AAN) and Allergy Foundation of America (AAFA). A demographic survey and measures of asthma control/quality of life were completed. Focus groups consisting of approximately 5 participants and a focus group leader were conducted. RESULTS: A total of 20 patients and 20 parents of children with mild asthma participated. Focus groups revealed significant variability in the definition and treatment preferences. Frequency of symptoms appears to be a key driver in treatment decisions for mild asthma, and those with infrequent symptoms were opposed to the addition of an inhaled corticosteroid to albuterol. Use of recommended asthma monitoring strategies such as asthma action plans or peak flow meters was low among adults. Participants desired more education from their providers regarding asthma remission and long-term complications associated with mild asthma. CONCLUSION: There is significant heterogeneity in the definition and treatment preferences among patients and parents of those with mild asthma. Shared decision making between patients and providers is necessary to personalize medical decisions in those with mild asthma.

Allergy and Immunology

Non AL, Li X, Jones MR, Oken E, Hartert T, Schoettler N, Gold DR, Ramratnam S, Schauberger EM, Tantisira K, Bacharier LB, Conrad DJ, Carroll KN, Nkoy FL, Luttmann-Gibson H, Gilliland FD, Breton CV, Kattan M, Lemanske RF, Jr., Litonjua AA, McEvoy CT, Rivera-Spoljaric K, Rosas-Salazar C, **Joseph CLM**, Palmore M, Ryan PH, **Wegienka G**, **Sitarik AR**, Singh AM, Miller RL, **Zoratti EM**, Ownby D, Camargo CA, Jr., Aschner JL, Stroustrup A, Farzan SF, Karagas MR, Jackson DJ, and Gern JE. Comparison of Race-neutral Versus Race-specific Spirometry Equations for Evaluation of Child Asthma. *Am J Respir Crit Care Med* 2024; Epub ahead of print. PMID: 39642347. Full Text

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RATIONALE: Race-based estimates of pulmonary function in children could influence the evaluation of asthma in children from racial and ethnic minoritized backgrounds. OBJECTIVES: To determine if race-neutral (GLI-Global) versus race-specific (GLI-Race-Specific) reference equations differentially impact spirometry evaluation of childhood asthma. METHODS: The analysis included 8,719 children aged 5 to <12 years from 27 cohorts across the United States grouped by parent-reported race and ethnicity. We analyzed how the equations affected forced expiratory volume in 1 second (FEV(1)), forced vital capacity (FVC), and FEV(1)/FVC z-scores. We used multivariable logistic models to evaluate associations between z-scores calculated with different equations and asthma diagnosis, emergency department (ED) visits, and hospitalization. MEASUREMENTS AND MAIN RESULTS: For Black children, the GLI-Global vs. Race-Specific equations estimated significantly lower z-scores for FEV(1) and FVC but similar values for FEV(1)/FVC, thus increasing the proportion of children classified with low FEV(1) by 14%. While both equations yielded strong inverse relationships between FEV(1) and FEV(1)/FVC z-scores and asthma outcomes, these relationships varied across racial and ethnic groups ($p<0.05$). For any given FEV(1) or FEV(1)/FVC z-score, asthma diagnosis and ED visits were higher among Black and Hispanic versus White children ($p<0.05$). For FEV(1), GLI-Global equations estimated asthma outcomes that were more uniform across racial and ethnic groups. CONCLUSIONS: Parent-reported race and ethnicity influenced relationships between lung function and asthma outcomes. Our data show no advantage to race-specific equations for evaluating childhood asthma, and the potential for race-specific equations to obscure lung impairment in disadvantaged children strongly supports using race-neutral equations.

Anesthesiology

Attali A, **Vander Woude T**, Fayed M, and **Nowak K**. Microbial Safety Assessment of Gebauer's Pain Ease®Spray on Invasive Procedural Sites. *J Vasc Access* 2024; 29(1):57-63. PMID: Not assigned.
Request Article

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Aim: This study aimed to investigate the impact of Gebauer's Pain Ease® (Gebauer Company, Cleveland, OH) topical refrigerant spray on the disinfection of skin sites, focusing on the volar wrist and lower back. The primary objective was to determine whether the application of Pain Ease would compromise the disinfection of these sites, potentially making it a suitable alternative to injectable lidocaine for invasive medical procedures. Methods: This prospective, blinded, controlled study was conducted at Henry Ford Hospital in Detroit, MI. Healthy adult hospital employees were recruited, and written consent was obtained. Swabs were taken from the volar wrist and lower back sites before and after treatment with ChloraPrep™ (BD, Franklin Lakes, NJ) and Pain Ease. Microbial cultures were performed, and microbial growth levels were assessed and categorized. Data analysis included comparisons of microbial growth between untreated samples, ChloraPrep-Treated samples, and ChloraPrep + Pain Ease-Treated

samples. Results: Data were collected from 72 participants, with 6 samples per participant (2 locations, 3 treatments each). For wrist samples, there were no statistically significant differences in microbial growth between ChloraPrep and ChloraPrep + Pain Ease. Similarly, for lower-back samples, microbial growth did not significantly differ between these 2 treatment groups. Conclusions: This study demonstrates that the application of Gebauer's Pain Ease to ChloraPrep disinfected skin areas does not negatively affect the reduction of the bacterial load, supporting its potential as an alternative to injectable lidocaine and other superficial anesthetics for vascular access or invasive medical procedures. However, further research is warranted to explore the application of Pain Ease in various clinical scenarios and optimize patient comfort during longer and more invasive procedures. ©

Anesthesiology

Chang C, Laird-Fick HS, **Mitchell JD**, Parker C, and Solomon D. Assessing the impact of clerkships on the growth of clinical knowledge. *Ann Med* 2025; 57(1):2443812. PMID: 39731632. Full Text

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PURPOSE: This study quantified the impact of clinical clerkships on medical students' disciplinary knowledge using the Comprehensive Clinical Science Examination (CCSE) as a formative assessment tool. METHODS: This study involved 155 third-year medical students in the College of Human Medicine at Michigan State University who matriculated in 2016. Disciplinary scores on their individual Comprehensive Clinical Science Examination reports were extracted by digitizing the bar charts using image processing techniques. Segmented regression analysis was used to quantify the differences in disciplinary knowledge before, during, and after clerkships in five disciplines: surgery, internal medicine, psychiatry, pediatrics, and obstetrics and gynecology (ob/gyn). RESULTS: A comparison of the regression intercepts before and during their clerkships revealed that, on average, the participants improved the most in ob/gyn ($\beta = 11.193$, $p < .0001$), followed by psychiatry ($\beta = 10.005$, $p < .001$), pediatrics ($\beta = 6.238$, $p < .0001$), internal medicine ($\beta = 1.638$, $p = .30$), and improved the least in surgery ($\beta = -2.332$, $p = .10$). The regression intercepts of knowledge during their clerkships and after them, on the other hand, suggested that students' average scores improved the most in psychiatry ($\beta = 7.649$, $p = .008$), followed by ob/gyn ($\beta = 4.175$, $p = .06$), surgery ($\beta = 4.106$, $p = .007$), and pediatrics ($\beta = 1.732$, $p = .32$). CONCLUSIONS: These findings highlight how clerkships influence the acquisition of disciplinary knowledge, offering valuable insights for curriculum design and assessment. This approach can be adapted to evaluate the effectiveness of other curricular activities, such as tutoring or intersessions. The results have significant implications for educators revising clerkship content and for students preparing for the United States Medical Licensing Examination Step 2.

Anesthesiology

Volquez LME, **Haddad R**, and **Patel N**. Cephalad Migration of Spinal Cord Stimulator Lead: A Case Report. *Pain Med Case Reps* 2024; 8(7):273-277. PMID: Not assigned. Full Text

L.M.E. Volquez, Henry Ford Hospital, Detroit, MI, United States

Background: Case Report: Conclusions: Since the introduction of neuromodulation, significant advances in technology and safety have been achieved. Despite these improvements, complications are frequently observed. Among these complications, lead migration has been reported as the most common, with significant cephalad displacement being among the rarest for this type. We present a case of a 69-year-old woman with chronic low back pain that experienced lead migration from T8 to T3 during the trial period, leading to an unsuccessful trial. Although rare, drastic displacement in the cephalad direction of a

spinal cord stimulator lead has been reported in the literature and warrants recognition. There are multiple potential etiologies that could explain this movement. There is a need to further study its mechanism, how the current methods for securing the lead perform, and developing better options for securing the device.

Anesthesiology
Volquez LME, **Kanuri SH**, and **Haddad R**. Tibial Nerve Mononeuropathy Post-COVID-19 and Successful Management with Peripheral Nerve Stimulation: A Case Report. *Pain Med Case Reps* 2024; 8(7):249-252. PMID: Not assigned. Full Text

L.M.E. Volquez, Henry Ford Hospital, Detroit, MI, United States

Background: Case Report: Conclusions: Infection with COVID-19 has evolved from a novel health crisis into an entity with a myriad of increasingly recognized sequelae. Among these, peripheral neuropathy is often an underrecognized and underdiagnosed complication. Neuropathic pain can be challenging to treat with many cases being refractory to conservative management, often requiring advanced techniques. Neuromodulation has become an important tool for the treatment of the refractory cases. We present a case of a 43-year-old woman with refractory right tibial mononeuropathy secondary to COVID-19 infection who was treated successfully using peripheral nerve stimulation. The use of peripheral neuromodulation represents a pivotal strategy for the management of difficult cases. Our case highlights the first use of neuromodulation to treat neuropathic pain secondary to CO-VID-19 infection. We hope that this case sparks further research on the topic, which could lead to better clarification of this condition and potential expansion of treatment strategies.

Anesthesiology
Zorrilla-Vaca A, Grant MC, **Mendez-Pino L**, Rehman MJ, Sarin P, Nasra S, and Varelmann D. Preoperative Multivariable Model for Risk Stratification of Hypoxemia During One-Lung Ventilation. *Anesth Analg* 2024. PMID: Not assigned. Full Text

A. Zorrilla-Vaca, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, 75 Francis St, Boston, MA, United States

BACKGROUND: Hypoxemia occurs with relative frequency during one-lung ventilation (OLV) despite advances in airway management. Lung perfusion scans are thought to be one of the most accurate methods to predict hypoxemia during OLV, but their complexity and costs are well-known limitations. There is a lack of preoperative stratification models to estimate the risk of intraoperative hypoxemia among patients undergoing thoracic surgery. Our primary objective was to develop a risk stratification model for hypoxemia during OLV based on preoperative clinical variables. METHODS: This is a single-center, retrospective cohort study including 3228 patients who underwent lung resections with OLV from 2017 to 2022, at a tertiary academic health care center in the United States. Vital signs and ventilator settings were retrieved minute by minute. Intraoperative hypoxemia was defined as an episode of oxygen desaturation (Spo2 <90%) for at least 5 minutes. Demographic and clinical characteristics were included in a stepwise logistic regression, which was used for the selection of predictors of the risk score model. All patients included in this cohort underwent elective lung surgery in lateral decubitus position, with double lumen tube and placement confirmation with fiberoptic bronchoscopy. Our model was validated internally using area under the receiver operating curves (AUC) with bootstrapping correction. RESULTS: The incidence of hypoxemia during OLV was 8.9% (95% confidence interval [CI], 8.0-10.0). Multivariable logistic regression identified 9 risk factors with their corresponding scoring: preoperative Spo2 <92% (15 points), hemoglobin <10 g/dL (6 points), age >60 years old (4 points), male sex (4 points), body mass index >30 kg/m2 (8 points), diabetes mellitus (4 points), congestive heart failure (7 points), hypertension (3 points), and right-sided surgery (3 points). The AUC of the model after bootstrap correction was 0.708 (95% CI, 0.676-0.74). Based on the highest Youden index, the optimal score for predicting intraoperative hypoxemia was 13. The risk of hypoxemia increased from 4.7% in the first quartile of scores (0-13 points), to 32% in the third quartile (27-39 points), and 83.3% in the fourth quartile (>39 points). At scores of 20 or greater, the specificity of the model exceeded 90% and reached a positive predictive value of 80%. CONCLUSIONS: The risk of hypoxemia during OLV can be stratified preoperatively using accessible clinical variables. Our risk model is well calibrated but showed moderate discrimination for predicting

intraoperative hypoxemia. The accuracy of preoperative models for risk stratification of hypoxemia during OLV should be explored in prospective studies.

Behavioral Health Services/Psychiatry/Neuropsychology
Miller-Matero LR, **Yeh HH**, **Ma L**, Jones RA, Nadolsky S, Medcalf A, Foster GD, and Cardel MI. Alcohol Use and Antiobesity Medication Treatment. *JAMA Netw Open* 2024; 7(11):e2447644. PMID: 39589745. Full Text

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This cohort study examines the association of antiobesity medication use and alcohol use among participants enrolled in a weigh loss program.
eng

Behavioral Health Services/Psychiatry/Neuropsychology
Pearl ES, **Murray MF**, **Haley EN**, **Snodgrass M**, **Braciszewski JM**, **Carlin AM**, and **Miller-Matero LR**. Weight and shape overvaluation and its relation to anxiety, depression, and maladaptive eating symptoms for patients up to 4 years after bariatric surgery. *Surg Obes Relat Dis* 2024; Epub ahead of print. PMID: 39710526. Full Text

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BACKGROUND: Weight and shape overvaluation (WSO; undue influence of weight and shape on self-evaluation) is common among individuals undergoing bariatric surgery. Little is known about how WSO relates to poorer outcomes for patients remote from surgery. OBJECTIVES: To examine associations between WSO with anxiety and depression symptoms and various maladaptive eating behaviors in patients up to 4 years post-bariatric surgery. SETTING: Henry Ford Health, United States. METHODS: Patients who underwent surgery between 2018 and 2021 were invited to complete the study between 2021 and 2022. Participants (N = 765) completed anxiety and depression symptom and eating behavior measures. RESULTS: Participants endorsed moderate WSO (M = 3.62, standard deviation = 1.87), which was positively related to anxiety (r = .37) and depression (r = .20) symptoms; eating in response to anger/frustration (r = .26), anxiety (r = .28), and depression (r = .31); and addictive eating behaviors (r = .26); and was significantly associated with the presence of loss-of-control (odds ratio [OR] = 1.39), binge (OR = 1.39), and graze (OR = 1.24) eating. WSO also was related to more frequent grazing (r = .23) but not loss-of-control or binge eating frequency for participants who endorsed behavior presence. CONCLUSIONS: Findings underscore that links between WSO, psychiatric distress, and maladaptive eating behaviors persist up to 4 years after bariatric surgery. These domains should be assessed at bariatric follow-ups, and assessment of WSO may help providers identify patients at risk for poorer outcomes. Findings should be used to inform temporal modeling of how WSO may predispose patients to poorer bariatric outcomes.

Behavioral Health Services/Psychiatry/Neuropsychology
Shippen NA, **Felton JW**, Stevens AE, Khaireddin M, Lejuez CW, Chronis-Tuscano A, and Meinzer MC. Longitudinal Association of Adolescent ADHD Symptoms in the Trajectory of Maternal Depression Symptoms. *J Psychopathol Behav Assess* 2024; 46(4):888-899. PMID: Not assigned. Full Text

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Maternal depression is a common mental health condition that can have adverse impacts on both mothers and their offspring. Research is growing on what factors are related to maternal depression longitudinally, specifically on transactional framings of how both maternal and child mental health symptoms may potentially impact mothers. Attention-deficit/hyperactivity disorder (ADHD) is a common childhood disorder, characterized by symptoms of inattention, hyperactivity, and/or impulsivity with impacts across the lifespan. Research has demonstrated the effects of youth ADHD on caregiver well-being and how race and sex may have a potential influence on experiences of families of youth with ADHD. Less is known about how adolescent ADHD symptoms longitudinally relate to maternal depressive symptoms. The current study draws from a community sample of adolescents and their mothers. Children in the sample were approximately 12-year-olds (M = 12.07 years, SD = 0.90) at the start of study and 18 at the end (M = 18.05, SD = 0.96). Mothers completed a measure of their child's ADHD symptoms at approximately age 12 and a measure of their own depressive symptoms annually over seven years. Latent growth modeling was used to examine the intercept and slope of mothers' depression symptoms throughout their child's adolescence. The slope of maternal depressive symptoms was flat across adolescence. ADHD symptoms of hyperactivity/impulsivity (but not inattention) were significantly associated with the intercept of maternal depressive symptoms, with higher levels of hyperactivity/impulsivity symptoms predicting a higher intercept of maternal depressive symptoms, but not the slope of maternal depressive symptoms, across adolescence. The results of this study highlight associations between ADHD symptoms and maternal mental health and the longevity of its effects. Future directions and clinical implications are discussed.

Cardiology/Cardiovascular Research
Alrifai N, Puttur A, Ghanem F, Dhital Y, **Jabri A**, Al-Abdouh A, and Alhuneafat L. Maternal and fetal outcomes in those with autoimmune connective tissue disease. *Clin Rheumatol* 2024; Epub ahead of print. PMID: 39616303. Full Text

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INTRODUCTION: Autoimmune CTDs like systematic lupus erythematosus (SLE), systemic sclerosis (SSc), and rheumatoid arthritis (RA)predominantly affect women during reproductive years and are linked to maternal and fetal complications. METHODS: We conducted a population-based, retrospective cohort study using the national inpatient data sample to compare maternal and fetal outcomes in patients with and without CTD delivering between October 2015 and December 2020. Regression analysis was performed and adjusted for multiple patient characteristics to compare outcomes. RESULTS: Our study comprised of 18,866,050 deliveries, of which 50,450 (0.02%) had autoimmune CTD, including 25,340 with SLE, 23,945 with RA, and 1,165 with SSc. Patients with CTDs had significantly higher odds of maternal death (aOR 3.898; 95% CI: 1.462-10.389, p = 0.007), hypertensive disorders (aOR 1.554; 95% CI: 1.456-1.659, p < 0.001), acute kidney injury (aOR 4.886; 95% CI: 3.934-6.069, p < 0.001), blood transfusions (aOR 1.853; 95% CI: 1.628-2.109, p < 0.001), peripartum cardiomyopathy (aOR 2.709; 95% CI: 1.492-4.917, p = 0.001), sepsis (aOR 2.112; 95% CI: 1.430-3.119, p < 0.001), and ARDS (aOR 1.623; 95% CI: 1.076-2.449, p = 0.021). Fetal outcomes were also worse, with higher odds of small for gestational age fetuses (aOR 1.926; 95% CI: 1.779-2.086, p < 0.001), stillbirth (aOR 1.644; 95% CI: 1.352-2.000, p < 0.001), and preterm labor (aOR 1.702; 95% CI: 1.574-1.841, p < 0.001). Patients with

RA, SS, and SLE experience varying degrees of complications. CONCLUSION: Our study shows that pregnant patients with autoimmune CTDs have worse maternal and fetal outcomes compared to those without CTDs. The rates of adverse outcomes varies among CTD subtypes. Comprehensive preconception counseling and tailored management strategies are essential for optimizing outcomes in these patients. Key Points • Increased Maternal Complications: Patients with autoimmune CTDs had significantly higher odds of maternal death, hypertensive disorders, acute kidney injury, blood transfusions, peripartum cardiomyopathy, sepsis, and ARDS. • Adverse Fetal Outcomes: Higher odds of small for gestational age fetuses, stillbirth, and preterm labor were observed in patients with CTDs compared to those without. • CTD Subtype Variations: Complication rates varied among CTD subtypes, with SLE, RA, and SSc each presenting varying risks and outcomes.

Cardiology/Cardiovascular Research

Bamford P, Henry TD, **O'Neill WW**, and Grines CL. The Revolution of STEMI Care: A Story of Resilience, Persistence, and Success. *J Soc Cardiovasc Angiogr Interv* 2024; 3(11):102395. PMID: 39649828. Full Text

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Cardiology/Cardiovascular Research

Bauer TM, Janda AM, Wu X, Ling C, Shook DC, Querejeta-Roca G, Shann KG, Smith T, Mathis MR, Kaneko T, Sundt TM, 3rd, Schonberger RB, **Harrington SD**, Dias RD, Pagani FD, Likosky DS, and Yule S. Multicenter Analysis of the Relationship Between Operative Team Familiarity and Safety and Efficiency Outcomes in Cardiac Surgery. *Circ Cardiovasc Qual Outcomes* 2024; 17(12):e011065. PMID: 39689169. Full Text

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BACKGROUND: Safety in cardiac surgical procedures is predicated on effective team dynamics. This study associated operative team familiarity (ie, the extent of clinical collaboration among surgical team members) with procedural efficiency and Society of Thoracic Surgeons (STS) adjudicated patient outcomes. METHODS: Institutional STS adult cardiac surgery registry and electronic health record data from 2014 to 2021 were evaluated across 3 quaternary hospitals. Team familiarity was defined as the mean number of cardiac operations performed by surgeon-anesthesiologist, surgeon-perfusionist, and anesthesiologist-perfusionist dyads within 1 year of the operation. The primary outcomes were (1) safety, measured by the STS' composite major morbidity and operative mortality measure, and (2) procedural efficiency, assessed by cardiopulmonary bypass duration. Team familiarity was stratified by terciles (low, moderate, and high) for crude analyses and analyzed continuously for adjusted analyses. Multivariable logistic and linear regression models were used to assess the association between team familiarity and

outcomes. RESULTS: Team familiarity was calculated for 13 581 operations. The median (interquartile range) patient age was 64 (55-72) years, and 31.9% (4328/13 581) were women. Terciles of team familiarity were defined as low (<6.00 average shared operations), moderate (6.00-9.67), and high (>9.67). Teams in lower terciles had higher observed STS morbidity and mortality rates (low, 17.9%; moderate, 18.0%; high, 16.0%; P=0.02) and longer median cardiopulmonary bypass duration (low, 137 minutes; moderate, 131 minutes; high, 118 minutes; P<0.001). After risk adjustment, team familiarity was not significantly associated with STS morbidity and mortality (estimate, -0.001 [95% CI, -0.998 to 0.997]) but was inversely associated with cardiopulmonary bypass duration (estimate, -2.02 minutes per 1 unit increase in team familiarity [95% CI, -2.30 to -1.75]). CONCLUSIONS: Increased team familiarity was not associated with STS morbidity and mortality but was inversely correlated with cardiopulmonary bypass duration, demonstrating potential benefit. Interventions aimed at improving team familiarity among operative teams may increase procedural efficiency.

Cardiology/Cardiovascular Research
Cascino TM, Ling C, Likosky DS, Pagani FD, and **Cowger J**. A gift of life, not immortality: Evaluation of a strategy of heart transplant listing in the older patient with advanced heart failure. *J Heart Lung Transplant* 2024; Epub ahead of print. PMID: 39642950. Full Text

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Patients 65 years of age or older represent the fastest-growing demographic group added to the U.S. heart transplant (HT) list. While post-HT outcomes appear acceptable, immortal time bias is introduced if adverse outcomes that occur while waiting for HT are not considered. Recent durable left ventricular assist device (dLVAD) technological innovations have engendered the question of whether this patient subgroup would achieve equivalent survival from a strategy of primary dLVAD implant as opposed to HT listing. We identified adults ≥65 years of age listed for HT between 2018-2021, excluding persons with dLVAD support and/or multi-organ listing. Among 1176 patients, 2-year survival from HT listing was 78.4 ± 1.2%, similar to the 71% to 75% reported in The Society of Thoracic Surgeons (STS) Intermacs National Database for older adults. Linkage of the Scientific Registry of Transplant Recipients with STS Intermacs would enable comparative effectiveness analyses of surgical heart failure therapeutic strategies in high-risk patient cohorts.

Cardiology/Cardiovascular Research
Fang JX, **Fram G**, **Wang DD**, **Villablanca PA**, **O'Neill BP**, **Frisoli TM**, **Giustino G**, **Lee JC**, **O'Neill WW**, and **Engel Gonzalez P**. Subaortic Membrane and Cardiac Catheterization-Beware of Diagnostic Pitfall. *J Soc Cardiovasc Angiogr Interv* 2024; 3(11):102284. PMID: 39649826. Full Text

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Cardiology/Cardiovascular Research
Jabri A, **Alameh A**, **Giustino G**, **Gonzalez PE**, O'Neill B, Bagur R, Cox P, **Frisoli T**, **Lee J**, **Wang DD**, **O'Neill WW**, and **Villablanca P**. Transcatheter Aortic Valve Replacement is Ready for Most Low-risk Patients: A Systematic Review of the Literature. *Card Fail Rev* 2024; 10:e11. PMID: 39386082. Full Text

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Transcatheter aortic valve replacement (TAVR) has undergone rapid expansion, emerging as a viable therapeutic option for low-risk patients in lieu of surgical aortic valve replacement. This paper aims to provide a review of the scientific evidence concerning TAVR in low-risk patients, encompassing both observational and clinical trial data. Furthermore, a substantial proportion of low-risk patients possesses a

bicuspid aortic valve, necessitating careful examination of the pertinent anatomic and clinical considerations to TAVR that is highlighted in this review. Additionally, the review expands upon some of the unique challenges associated with alternate access in low-risk patients evaluated for TAVR. Last, this review outlines the pivotal role of a multidisciplinary heart team approach in the execution of all TAVR procedures and the authors' vision of 'minimalist TAVR' as a new era in low-risk TAVR.

Cardiology/Cardiovascular Research
Jain V, **Gupta K**, Bhatia NK, El-Chami MF, Tamirisa KP, Volgman AS, and Merchant FM. Outcomes of pregnancy-related hospitalizations in women with pacemakers and defibrillators. *Heart Rhythm O2* 2024. PMID: Not assigned. Full Text

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Background: There is limited information on pregnancy outcomes in women who have previously undergone implantation of cardiac implantable electronic devices (CIEDs). Objective: The study sought to describe outcomes of pregnancy related hospitalizations in women with CIEDs. Methods: The National Inpatient Sample database was analyzed to identify pregnancy-related hospitalizations between 2016 and 2021. Results: We identified 23,611,200 weighted pregnancy-related hospitalizations, of which 11,220 (0.05%) had a history of CIED implantation. Of these, 5105 had permanent pacemakers (PPMs) and 6115 had implantable cardioverter-defibrillators (ICDs). The mortality rate during pregnancy-related hospitalization was significantly higher among women with ICDs (0.9%) compared with those without CIEDs (0.01%). Of note, there were no in-hospital deaths among pregnant women with PPMs. After adjusting for covariates, the excess mortality risk in women with ICDs was no longer noted. However, pregnant women with ICDs remained at higher risk of cardiogenic shock (odds ratio 3.06, 95% confidence interval 2.17–4.30) and need for mechanical circulatory support (odds ratio 2.37, 95% confidence interval 1.48–3.80). Conclusion: In a nationwide cohort of pregnancy-related hospitalizations, a history of CIED implantation was rare, occurring in about 0.05% of women. In-hospital mortality was significantly higher among pregnant women with ICDs. However, after adjustment for covariates, the excess mortality risk was no longer observed. Pregnant women with ICDs remain at increased risk of cardiogenic shock and need for mechanical circulatory support, even after adjusting for covariates. Outcomes for pregnant women with PPMs are generally excellent and comparable to those without CIEDs.

Cardiology/Cardiovascular Research
Jamil D, **Fadel R**, **Kollman P**, and **Swanson B**. A Case of an Interventricular Septum Pseudoaneurysm With Perforation Mimicking a Ventricular Septal Defect. *Cureus* 2024; 16(11):e73080. PMID: 39640109. Request Article

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Ventricular pseudoaneurysm (PSA) is a ventricular outpouching contained by adherent pericardium or myocardial scar tissue and represents a rare but potentially fatal complication of acute myocardial infarction (AMI). The vast majority of cases involve the left ventricular apex, in the area of infarct. It is extremely rare to see PSA formation within the interventricular septum (IVS). We present a case of ventricular PSA of the IVS, with contained perforation into the right ventricle, mimicking a ventricular septal defect (VSD) in a patient presenting with ST-elevation myocardial infarction (STEMI). This case underscores the importance of maintaining a high index of clinical suspicion and reviews the pathophysiological mechanisms and treatment options for these life-threatening mechanical complications.

Cardiology/Cardiovascular Research

Krittanawong C, Castillo Rodriguez B, Ang SP, **Qadeer YK**, Wang Z, Alam M, Sharma S, and Jneid H. Conservative Approach versus Percutaneous Coronary Intervention in Patients with Spontaneous Coronary Artery Dissection from a National Population-Based Cohort Study. *Rev Cardiovasc Med* 2024; 25(11):404. PMID: 39618857. Full Text

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BACKGROUND: Spontaneous coronary artery dissection (SCAD) is a rare and often underdiagnosed cause of acute coronary syndrome (ACS), predominantly affecting younger women without traditional cardiovascular risk factors. The management of SCAD remains a subject of debate, likely secondary to inconclusive evidence. This study aims to compare the clinical outcomes of SCAD patients treated with optimal medical therapy (OMT) versus those who underwent percutaneous coronary intervention (PCI) using a national population-based cohort. METHODS: We conducted a retrospective analysis using the National Inpatient Sample (NIS) database from 2016 to 2020. The study included patients identified with SCAD using the ICD-10-CM (the International Classification of Diseases, Tenth Revision, Clinical Modification) code I25.42. We excluded individuals who did not receive PCI or coronary angiography, those who underwent coronary artery bypass grafting, and patients with incomplete records. The primary outcome was in-hospital mortality, while secondary outcomes included acute kidney injury, cardiac arrest, cardiogenic shock, use of temporary mechanical circulatory support, cost of hospitalization, and length of stay. National estimates were obtained using discharge weights, and statistical comparisons were performed using chi-square tests and linear regression. Multivariate logistic regression was employed to identify predictors of mortality and other outcomes. RESULTS: A total of 31,105 SCAD patients were included in the study, with 10,480 receiving OMT and 20,625 undergoing PCI. Patients in the PCI group were older (mean age 64 vs. 54 years) and had higher comorbidities compared to those in the OMT group. The proportion of SCAD patients receiving PCI declined from 72% in 2016 to 60% in 2020. In multivariable analysis, PCI was associated with increased in-hospital mortality (odds ratio (OR) 1.89, 95% confidence interval (CI) 1.24-2.90, $p = 0.0003$), cardiogenic shock (OR 2.29, 95% CI 1.71-3.07, $p < 0.0001$), use of a left ventricular assist device (LVAD) (OR 3.97, 95% CI 2.42-6.53, $p < 0.0001$), and an intra-aortic balloon pump (IABP) (OR 2.24, 95% CI 1.63-3.09, $p < 0.0001$). Trends also suggested an association between PCI and cardiac arrest, extracorporeal membrane oxygenation (ECMO), and acute kidney injury (AKI). The PCI group had significantly higher hospitalization costs and longer lengths of stay compared to the OMT group (both $p < 0.001$). CONCLUSIONS: In this large, national cohort study, SCAD patients who underwent PCI had significantly higher risks of adverse in-hospital outcomes, including mortality, compared to those treated with OMT. These findings underscore the importance of careful patient selection and the potential advantages of conservative management in SCAD, particularly in patients without severe or unstable presentations. Further research is needed to develop evidence-based guidelines for the optimal management of SCAD.

Cardiology/Cardiovascular Research

Llamocca EN, **Bossick AS**, **Perkins DW**, **Ahmedani BK**, **Behrendt R**, **Bloemen A**, **Murphy A**, **Kulkarni A**, and **Lockhart E**. Health-related social needs screening, reporting, and assistance in a large health system. *Prev Med* 2024; 190:108182. PMID: 39586330. Full Text

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BACKGROUND: National mandates require screening for and addressing health-related social needs (HRSNs) in healthcare settings. However, differences in HRSN screening process (i.e., completed screenings, screening results, documented offer of assistance, documented assistance request) have been reported by population subgroup. Knowledge of the most effective HRSN screening and intervention methods is limited. We sought to describe differences in completed HRSN screenings, screening results, and assistance request rates across patient and healthcare visit characteristics. METHODS: We examined data from all patients aged ≥18 years and residing in the US receiving services at a large, Midwestern healthcare system with a goal to screen all patients for HRSN at least once annually between July 2021-June 2023 (n = 1,190,488). We examined the proportion of patients with any HRSN screening, with any reported HRSN, asked whether they wanted assistance, or who requested assistance for a reported HRSN stratified by patient demographics and healthcare visit characteristics (i.e., payer, screening location, who completed the screening). RESULTS: Less than half of eligible patients (47.0 %) were screened for HRSNs. About one-sixth (16.9 %) reported any HRSN. Although most patients reporting HRSNs were asked whether they wanted assistance, only about one-quarter (26.8 %) responded affirmatively. Proportions included in each step of the HRSN screening process significantly differed by patient and healthcare visit characteristics. DISCUSSION: This study is one of the first to investigate various steps of a population-wide HRSN screening program. Our findings suggest that examining differences in HRSN screening process by population subgroup is key to addressing HRSNs through a health equity lens.

Cardiology/Cardiovascular Research

Mansoor T, Rao BH, **Gupta K**, **Parikh SS**, Abramov D, Mehta A, Al Rifai M, Virani SS, Nambi V, Minhas AMK, and Koshy SKG. Inclisiran as a siRNA Inhibitor of Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9); Past, Present, and Future. *Am J Cardiovasc Drugs* 2024; Epub ahead of print. PMID: 39707142. Request Article

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Reducing low-density lipoprotein cholesterol (LDL-C) levels has been shown to reduce the risk of developing atherosclerotic cardiovascular disease (ASCVD). Statins are the foundation of LDL-C lowering therapy with other non-statin agents used in circumstances where goal LDL-C levels are not reached or owing to intolerance to adverse effects of statins. In 2003, the discovery of the role of the proprotein convertase subtilisin/kexin type 9 (PCSK9) system in promoting elevated LDL-C levels led to new avenues of drug development to achieve target LDL-C. In 2021, inclisiran, a small interfering ribonucleic acid (siRNA) molecule targeting PCSK9 was approved by the Food and Drug Administration (FDA). Inclisiran has demonstrated effective reductions of LDL-C, such as in the large phase-3 ORION-9, ORION-10, and ORION-11 trials in which it achieved LDL-C reductions of 39.7%, 52.3%, and 49.9%, respectively. This review discusses the current clinical evidence and ongoing clinical studies of inclisiran as well as analyzes other areas of PCSK9 inhibition development.

Cardiology/Cardiovascular Research
O'Neill WW. Expandable Transvalvular Flow Pumps: "It's the Flow, Dummy". *JACC Cardiovasc Interv* 2024; 17(24):2863-2865. PMID: 39722268. Full Text

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Cardiology/Cardiovascular Research
O'Neill WW. Routine Usage of Impella for High-Risk Percutaneous Coronary Intervention. *Am J Cardiol* 2024; 239:18-19. PMID: 39694082. Full Text

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Cardiology/Cardiovascular Research
Pack QR, Keys T, Priya A, Pekow PS, **Keteyian SJ**, Thompson MP, D'Aunno T, Lindenauer PK, and Lagu T. Is 70% Achievable? Hospital-Level Variation in Rates of Cardiac Rehabilitation Use Among Medicare Beneficiaries. *JACC Adv* 2024; 3(11):101275. PMID: 39741644. Full Text

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BACKGROUND: Despite national goals to enroll 70% of cardiac rehabilitation (CR)-eligible patients, enrollment remains low. OBJECTIVES: The purpose of this study was to evaluate how the treating hospital influences CR enrollment nationally. METHODS: We included Fee-for-Service Medicare beneficiaries aged ≥66 years who were hospitalized for acute myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention, or heart valve repair/replacement. We examined: 1) a risk-standardized model to assess comparative hospital rates; 2) a linear regression model to identify hospital factors associated with rates of risk-standardized CR; and 3) a hierarchical generalized linear model to calculate the hospital median OR. RESULTS: At 3,420 hospitals, we identified 264,970 eligible patients. A minority of hospitals (n = 1,446; 38%) performed cardiac surgery, but these hospitals cared for the majority (n = 242,875; 92%) of all eligible patients. Subsequent analyses were limited to these hospitals. The median risk-standardized CR enrollment rate was low (22%) and varied 10-fold across hospitals (10th, 90th percentile: 3%, 42%). Factors associated with higher hospital performance were Midwest location, higher number of hospital beds, directly affiliated CR program, and <1 mile distance

between the hospital and closest CR facility. The national hospital median OR was 2.1. CONCLUSIONS: The treating hospital plays a key role in facilitating CR enrollment after discharge. Fewer than 1% of U.S. hospitals achieved a risk-standardized CR enrollment rate of >70%. Hospitals with cardiac surgery capability care for more than 90% of all CR-eligible patients and may be a logical place to focus improvement efforts.

Cardiology/Cardiovascular Research
Pollack LM, Chang A, Thompson MP, **Keteyian SJ**, Stolp H, Wall HK, Sperling LS, and Jackson SL. Hospital-level variation in cardiac rehabilitation metrics. *Am Heart J* 2024; Epub ahead of print. PMID: 39675500. Full Text

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BACKGROUND: To inform the delivery of cardiac rehabilitation (CR) care nationwide at the hospital level, we described hospital-level variation in CR metrics, overall and stratified by the hospital's tier of cardiac care provided. METHODS: This retrospective cohort analysis used Medicare fee-for-service (FFS) data (2018-2020), Parts A and B, and American Hospital Association (AHA) data (2018). We included beneficiaries with an acute myocardial infarction (AMI), percutaneous coronary intervention (PCI), or coronary artery bypass graft (CABG) in 2018, aged ≥65 years, and continuously enrolled in a FFS plan. We calculated hospital-level metrics for hospitals with ≥20 CR-qualifying events, which were identified using diagnostic/procedure codes. Claims for CR were identified by Healthcare Common Procedure Coding System (HCPCS) codes. We used multi-level models to examine patient- and hospital-level factors associated with CR metrics. Hospitals were stratified by tier of cardiac care provided (comprehensive, AMI/PCI, AMI-only care). RESULTS: Across the US, 2,212 hospitals treated individuals aged ≥65 years with a CR-qualifying event in 2018. By tier of cardiac care, 44.4% of hospitals provided comprehensive care, 31.2% provided AMI/PCI care, and 24.4% provided AMI-only care. Across all hospitals, there was substantial variation in CR enrollment (median 19.6%, interquartile range [IQR]=7.0%, 32.8%). Among hospitals with enrollment (n=1,866), median time to enrollment was 55.0 days (IQR=41.0, 71.0), median number of CR sessions was 26.0 (IQR=23.0, 29.0), and median percent completion was 26.0% (IQR=10.5%, 41.2%). There was also substantial variation in CR performance metrics among hospitals within each tier of cardiac care (e.g., median percent CR enrollment was 30.7% [IQR=20.7%-41.3%] among comprehensive care hospitals, 18.6% [IQR=9.5%-27.7%] among AMI/PCI hospitals, and 0.0% [IQR=0.0%-7.7%] among AMI-only hospitals). In adjusted analyses, characteristics associated with lower odds of CR enrollment included patient-level factors (older age, female sex, non-White race or ethnicity), and hospital-level factors (for-profit ownership, regions other than the Midwest, rural location, medium/large hospital size). CONCLUSIONS: This is the first national, hospital-level analysis of CR metrics among Medicare beneficiaries. Substantial variation across hospitals, including peer hospitals within the same tier of cardiac care, indicates opportunities for hospital-level quality improvement strategies to improve CR referral and participation metrics.

Cardiology/Cardiovascular Research
Shoji S, Kaltenbach L, Granger BB, Fonarow GC, Al-Khalidi HR, Albert NM, Butler J, Allen LA, **Lanfear DE**, Thibodeau JT, Chapman BM, Oliver-McNeil SM, Felker GM, Pina IL, Granger CB, Hernandez AF, and DeVore AD. Guideline-Directed Medical Therapy After Hospitalization for Acute Heart Failure: Insights From the CONNECT-HF. *J Am Heart Assoc* 2024; 13(24):e036998. PMID: 39655748. Full Text

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BACKGROUND: Significant gap remains in the implementation of guideline-directed medical therapy (GDMT) in patients with heart failure after a hospitalization. We aimed to evaluate the use and titration of GDMT at discharge and over a 12-month period after hospital discharge and to identify factors associated with GDMT use and titration. METHODS AND RESULTS: The CONNECT-HF (Care Optimization Through Patient and Hospital Engagement Clinical Trial for Heart Failure) trial evaluated the effect of a hospital and postdischarge quality improvement intervention in participants with heart failure with reduced ejection fraction. In this secondary analysis, we examined use and titration to at least 50% of the target dose of GDMTs at hospital discharge and over time. Among 4646 participants (mean age 63 years, 34% women), GDMT use did not numerically improve from discharge to 12 months: beta blockers (84%-78%), angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers/angiotensin receptor-neprilysin inhibitors (73%-65%), mineralocorticoid receptor antagonists (39%-36%), and sodium-glucose cotransporter 2 inhibitors (1.5%-2.1%). Achieving ≥50% of the target dose also showed little change over 12 months: beta blockers (35%-32%), angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers/angiotensin receptor-neprilysin inhibitors (28%-25%). For all medications, use of GDMT at discharge was associated with the use and achieving ≥50% of the target dose at 12 months. CONCLUSIONS: Following a hospitalization for heart failure, GDMT use remained low and did not numerically improve over 12 months. Use of GDMT at discharge was significantly associated with the use of GDMT over time, highlighting the importance of initiating GDMT during hospitalization.

Cardiology/Cardiovascular Research
Steinberg RS, Wang J, **Cowger JA**, Morris AA, Hall SA, Nohria A, and Nayak A. The Association of Provider-Assessed Psychosocial Risk With Outcomes in Destination Therapy Left Ventricular Assist Device Patients: An Intermacs Registry Analysis. *ASAIO J* 2024; Epub ahead of print. PMID: 39666453. Full Text

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Cardiology/Cardiovascular Research
Strepkos D, Alexandrou M, Mutlu D, Carvalho PEP, Bahbah A, Choi JW, Gorgulu S, Jaffer FA, Chandwaney R, **Alaswad K**, **Basir MB**, Azzalini L, Rangan BV, Mastrodemos OC, Voudris K, Al-Ogaili A, Burke MN, Sandoval Y, Brilakis ES, and Ybarra LF. Impact of the COVID-19 pandemic on CTO PCI: analysis from the PROGRESS-CTO registry. *Hellenic J Cardiol* 2024; Epub ahead of print. PMID: 39586352. Full Text

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Cardiology/Cardiovascular Research

Strepkos D, Rempakos A, Alexandrou M, Mutlu D, Carvalho PEP, Bahbah A, Kontantinis S, Choi JW, Gorgulu S, Jaffer FA, Chandwaney R, **Alaswad K**, **Basir MB**, Azzalini L, Ozdemir R, Uluganyan M, Khatri J, Young L, Poommipanit P, Aygul N, Davies R, Krestyaninov O, Khelimskii D, Goktekin O, Tuner H, Rafeh NA, Elguindy A, Rangan BV, Mastrodemos OC, Voudris K, Al-Ogaili A, Burke MN, Sandoval Y, and Brilakis ES. Association of Proximal Vessel Tortuosity with Technical Success and Clinical Outcomes: Analysis From the Progress-CTO Registry. *Catheter Cardiovasc Interv* 2024; 105(1):1-10. PMID: 39660868. Full Text

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BACKGROUND: Proximal vessel tortuosity can hinder wiring and equipment delivery during chronic total occlusion (CTO) percutaneous coronary intervention (PCI). AIMS: We sought to examine the association of proximal vessel tortuosity with the short and long-term outcomes of patients undergoing CTO PCI. METHODS: We examined the association of proximal vessel tortuosity with clinical outcomes in patients who underwent CTO PCI at 50 US and non-US centers between 2012 and 2024. RESULTS: Of 14,141 patients, 3,974 (28.1%) had moderate or severe proximal vessel tortuosity. Patients with moderate or severe proximal vessel tortuosity had more comorbidities and more complex angiographic characteristics, such as longer lesion length and higher prevalence of side branch at the proximal cap. Lesions with moderate or severe proximal tortuosity required greater procedure and fluoroscopy time. On unadjusted analyses, moderate/severe proximal vessel tortuosity was associated with lower technical success and higher incidence of major adverse cardiac events (MACE). In multivariable analysis, moderate/severe proximal vessel tortuosity was associated with lower technical success (odds ratio [OR]: 0.77; 95% confidence intervals [CI]: 0.67, 0.89) but similar MACE (OR: 1.26; 95% CI: 0.91, 1.73). Higher operator volume (≥ 30 CTO PCI cases per year) was associated with higher technical (85.2% vs. 75.6%, $p < 0.001$) and procedural success (83.6% vs. 74.5%, $p < 0.001$) but also higher risk of perforation (6.49% vs.

3.57%, p < 0.001) but not pericardiocentesis, in lesions with moderate/severe proximal vessel tortuosity. CONCLUSIONS: Moderate or severe proximal vessel tortuosity is independently associated with lower technical success in CTO PCI but not with MACE. High-volume operators are more likely to successfully perform CTO PCI in lesions with moderate/severe tortuosity at the cost of higher risk of perforation, without higher MACE.

Cardiology/Cardiovascular Research
Ungureanu C, Avran A, Brilakis ES, Mashayekhi K, **Alaswad K**, Agostoni P, Gasparini G, Colletti G, Cocoi M, Achim A, Wu EB, Novotný V, Kovacic M, Rathore S, La Manna A, Noterdaeme T, Gach O, Bozinovic N, Novelli L, and Leibundgut G. Comprehensive Overview of Retrograde-Antegrade Connection Techniques Without Externalization in Chronic Total Occlusion PCI: The Portal Techniques. *Catheter Cardiovasc Interv* 2024; 105(1):11-22. PMID: 39665265. Full Text

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BACKGROUND: Advancing the retrograde microcatheter (MC) into the antegrade guide catheter during retrograde chronic total occlusion (CTO) percutaneous coronary intervention (PCI) can be challenging or impossible, preventing guidewire externalization. OBJECTIVES: To detail and evaluate all the techniques focused on wiring to achieve intubation of the distal tip of a microcatheter, balloon, or stent with an antegrade or retrograde guidewire, aiming to reduce complications by minimizing tension on fragile collaterals during externalization and enabling rapid antegrade conversion in various clinical scenarios. METHODS: We describe the two main techniques, tip-in and rendezvous, and their derivatives such a facilitated tip-in, manual MC-tip modification, tip-in the balloon, tip-in the stent, deep dive rendezvous, catch-it and antegrade microcatheter probing. We provide case studies that demonstrate the effectiveness of these techniques in complex scenarios involving extreme vessel angulation, severe calcification, fragile collaterals, and challenging retrograde MC crossing without externalization. CONCLUSION: The development of advanced variants along with traditional techniques to establish retrograde guidewire connection and antegrade conversion has led to the establishment of a cohesive group of methods known as portal techniques. These approaches serve as strategic advantages in retrograde CTO-PCI, providing a valuable and feasible alternative to conventional retrograde connection techniques, particularly when those techniques fail. Their ability to avoid the externalization process reduces potential damage to collateral channels and the ostium of the donor artery, potentially leading to a reduction in complication rates.

Cardiology/Cardiovascular Research
Weinberg I, **Aronow H**, Kim E, Sharma A, and Ratchford E. SVM Communications: Message from the Society for Vascular Medicine Executive Committee. *Vasc Med (United Kingdom)* 2024; 29(1):103-104. PMID: Not assigned. Full Text

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Cardiology/Cardiovascular Research
Yau RM, Mitchell R, Afzal A, George TJ, Siddiqullah S, Bharadwaj AS, Truesdell AG, Rosner C, **Basir MB**, Fisher R, Dupont A, Alviar CL, Chweich H, Kapur NK, Patel RAG, Silvestry S, Patel SM, and Abraham J. Blueprint for Building and Sustaining a Cardiogenic Shock Program: Qualitative Survey of 12 US Programs. *J Soc Cardiovasc Angiogr Interv* 2024; 3(11):102288. PMID: 39649821. Full Text

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BACKGROUND: Multidisciplinary cardiogenic shock (CS) programs have been associated with improved outcomes, yet practical guidance for developing a CS program is lacking. METHODS: A survey on CS program development and operational best practices was administered to 12 institutions in diverse sociogeographic regions and practice settings. Common steps in program development were identified. RESULTS: Key steps for program development were identified: measuring baseline outcomes; identifying subspecialty champions; gaining leadership and team buy-in; developing institution-specific CS protocols; educating staff and referring providers; consulting with external experts; and developing quality assessment and process improvement. CONCLUSIONS: An assessment of 12 US CS programs highlights a blueprint for establishing and maintaining a successful, multidisciplinary shock program.

Cardiology/Cardiovascular Research
Zordok M, Etiwy M, Abdelazeem M, Dani SS, Tawadros M, Lichaa HT, Kerrigan JL, **Basir B**, **Alaswad K**, Miedema M, Brilakis ES, and Megaly M. Gender disparity in morbidity and mortality among patients with ST-elevation myocardial infarction due to spontaneous coronary artery dissection complicated by cardiogenic shock. *Cardiovasc Revasc Med* 2024; Epub ahead of print. PMID: 39609239. Full Text

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BACKGROUND: There is limited data on gender differences among patients with spontaneous coronary artery dissection (SCAD) who present as ST-elevation myocardial infarction (STEMI) and develop cardiogenic shock (CS). OBJECTIVES: To describe outcomes of SCAD patients presenting with STEMI and CS and outline the differences between men and women. METHODS: We queried the US Nationwide Readmissions Database (NRD) from January 2016 to December 2020 to identify patients with SCAD presenting with STEMI who developed CS. We compared the characteristics, trends, and outcomes between men and women in this cohort. RESULTS: Out of 582,633 hospitalizations with STEMI, 0.2 % (1176 patients) had SCAD, of which 346 (29.4 %) had CS. There was no difference in median age between men and women (64 years (IQR 57-71) vs. 63 years (IQR 49-72), p = 0.181). Men had a higher prevalence of prior myocardial infarction (MI) (14.2 % vs. 6.2 %, p = 0.021). The overall mortality rate of SCAD patients with AMI-CS was 28.2 %, with no difference between men and women. Patients with SCAD who had CS and underwent CABG had a mortality of 20.3 %. ECMO was used in 6.1 % of SCAD patients presenting with STEMI and CS, with a survival rate of 49.9 %. CONCLUSION: There were no differences in the baseline characteristics, rates of revascularization, or in-hospital mortality between men and women who had SCAD complicated by CS (SCAD-CS). Patients with SCAD-CS patients who underwent CABG had around 80 % in-hospital survival. CABG should be considered as a method of revascularization in this patient cohort.

Center for Health Policy and Health Services Research

Chaker AN, **Melhem M**, **Kagithala D**, **Telemi E**, **Mansour TR**, Simo L, **Springer K**, **Schultz L**, **Jarabek K**, **Rademacher AF**, **Brennan M**, **Kim E**, **Nerenz DR**, Khalil JG, Easton R, Perez-Cruet M, Aleem I, Park P, Soo T, Tong D, **Abdulhak M**, **Schwalb JM**, and **Chang V**. A propensity score-matched comparison between single-stage and multistage anterior/posterior lumbar fusion surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2024; 1-8. Epub ahead of print. PMID: 39705706. Full Text

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OBJECTIVE: Patients undergoing anterior/posterior lumbar fusion surgery can undergo either a single-stage or multistage operation, depending on surgeon preference. The goal of this study was to assess different patient outcomes between single-stage and multistage lumbar fusion procedures in a multicenter setting. METHODS: The Michigan Spine Surgery Improvement Collaborative database was queried for anterior/posterior lumbar fusion surgeries between July 2018 and January 2022. Patients who underwent either single-stage or multistage procedures were included. For multistage procedures, the first surgery included both anterior lumbar interbody fusions and lateral lumbar interbody fusions. Primary outcomes included postoperative complications and improvement in patient-reported outcomes: Patient-Reported Outcomes Measurement Information System Physical Function, EQ-5D, and satisfaction. The two cohorts were propensity score matched, while Poisson generalized estimating equation models were used for multivariate analyses. RESULTS: After one-to-one propensity score matching, 355 patients were identified in the single-stage and multistage cohorts. Single-stage procedures were associated with a lower risk of complications (p = 0.024), fewer emergency department visits (p = 0.029), and higher patient satisfaction after 1 year (p = 0.026) and 2 years (p = 0.007), compared with multistage procedures. After

adjusting for baseline patient and operative characteristics, patients undergoing multistage procedures had a higher risk of complications (relative risk [RR] 1.17, 95% CI 1.02-1.34; p = 0.026), were less likely to be satisfied after 1 year (RR 0.83, 95% CI 0.74-0.93; p < 0.001), and were less likely to experience improvement in back pain after 90 days (RR 0.86, 95% CI 0.75-0.99; p = 0.039) and 2 years (RR 0.76, 95% CI 0.60-0.96; p = 0.023). CONCLUSIONS: The authors observed that patients who undergo lumbar fusion surgery using a multistage approach have higher postoperative complication rates and are less likely to report satisfaction compared with a matched, single-stage procedure cohort.

Center for Health Policy and Health Services Research
Farmer ML, Hoffman J, **Vance A**, Li Y, and Bell TR. Examining Shift Length and Fatigue: A National Study of Neonatal Advanced Practice Providers. *Adv Neonatal Care* 2024; Epub ahead of print. PMID: 39724563. Full Text

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BACKGROUND: Neonatal advanced practice providers (APPs) often work prolonged hours in high-acuity neonatal intensive care units (NICUs). It is imperative to understand how fatigue affects the APP's ability to react quickly following long shifts. There is a lack of data on the effects of shift length and fatigue on neonatal APP job performance and clinical decision-making. PURPOSE: The purpose of this study was to describe the variation in shift length, knowledge-based competency, personal well-being, and behavioral alertness for neonatal APPs. METHODS: This study evaluated neonatal APPs before and after a clinical shift. Provider well-being was assessed during the pre-survey. Pretest-posttest surveys evaluated neonatal APP's psychomotor vigilance skills and knowledge. Participants completed an online, anonymous questionnaire to answer a series of knowledge-based questions before and after their shift, along with a psychomotor vigilance test (PVT). A paired t test analysis evaluated the pre- and post-shift PVT values and knowledge-based test scores. RESULTS: Overall, 61 pre-surveys and 42 post-surveys were completed; 36 were matched by participants pre- to post-survey. The mean between pre- and post-knowledge-based questions was statistically significant, with higher posttest scores. There was no statistical difference noted in the paired t test analysis of the PVT values. IMPLICATIONS FOR PRACTICE AND RESEARCH: The small sample size may limit the generalizability of findings, but these results may indicate that shift length does not affect psychomotor vigilance or knowledge-based competency. It is vital that future work assess the associations between APP shift length, fatigue, and critical decision-making.

Center for Health Policy and Health Services Research
Ijaz N, Nader M, Ponticiello M, **Vance AJ**, van de Water BJ, Funaro MC, Abbas Q, Adabie Appiah J, Chisti MJ, Commerell W, Elvis Dzelamunyuy S, Martinez Fernandez R, Gonzalez AL, Johnston C, Luckson Kaiwe E, Kaur M, Lang HJ, McCollum ED, Marcos González Moraga J, Muralidharan J, Renning K, Tan HL, Alejandra Vélez Ruiz Gaitán L, González-Dambrauskas S, Wilson PT, Morrow BM, and Davis JL. Contextual factors influencing bubble continuous positive airway pressure implementation for paediatric respiratory distress in low-income and middle-income countries: a realist review. *Lancet Glob Health* 2024; Epub ahead of print. PMID: 39675373. Full Text

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BACKGROUND: Bubble continuous positive airway pressure (bCPAP) is a low-cost, non-invasive respiratory support therapy for children with respiratory distress, but its effectiveness is dependent on the context. We aimed to understand contextual factors influencing bCPAP implementation for children aged 1-59 months in low-income and middle-income countries (LMICs) and to develop a theory explaining how these factors influence implementation outcomes. METHODS: In this realist review, we generated an initial programme theory comprising candidate context-mechanism-outcome configurations (CMOCs) via review of key references and team discussion. On July 25, 2023, we conducted a search for peer-reviewed and grey literature, without date restrictions, describing bCPAP use for paediatric respiratory distress in LMICs. We included references describing related contexts, mechanisms, or outcomes. We coded statements from the literature supporting each CMOC, iteratively revising and adding CMOCs using inductive and deductive logic. We assembled an international, interdisciplinary panel of 22 bCPAP stakeholders to refine CMOCs using iterative surveys, focus groups, and interviews until we reached thematic saturation. This realist review is registered with PROSPERO (CRD42023403584). FINDINGS: Of 1640 peer-reviewed references and eight grey literature references retrieved, 38 peer-reviewed articles and two grey literature documents were deemed eligible for inclusion after removal of duplicates and screening. After four rounds of expert surveys and three focus groups, we identified 18 CMOCs. CMOCs were synthesised into a final programme theory operating at five levels to influence implementation feasibility, fidelity, and sustainability: (1) the bCPAP device, (2) local partnerships and infrastructure, (3) clinical and technical teams, (4) caregivers and the community, and (5) institutional practices. INTERPRETATION: Using realist methods with a diverse, international stakeholder panel, we generated a theory that could explain how bCPAP therapy works in different contexts. This theory could be leveraged to enhance the rigour of future bCPAP implementation trials. FUNDING: Yale National Clinician Scholars Program, US National Center for Advancing Translational Science (TL1TR001864), and National Heart, Lung, and Blood Institute (T32HL155000).

Center for Health Policy and Health Services Research

Johannes CB, Ziemiecki R, **Pladevall-Vila M**, Ebert N, Kovesdy CP, Thomsen RW, Baak BN, García-Sempere A, Kanegae H, Coleman CI, Walsh M, Andersen IT, Rodríguez Bernal C, Robles Cabaniñas C, Christiansen CF, Farjat AE, Gay A, Gee P, Herings RMC, Hurtado I, Kashihara N, Kristensen FPB, Liu F, Okami S, Overbeek JA, Penning-van Beest FJA, Yamashita S, Yano Y, Layton JB, Vizcaya D, and Oberprieler NG. Clinical Profile and Treatment Adherence in Patients with Type 2 Diabetes and Chronic Kidney Disease Who Initiate an SGLT2 Inhibitor: A Multi-cohort Study. *Diabetes Ther* 2024; Epub ahead of print. PMID: 39688776. Full Text

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INTRODUCTION: The clinical landscape for the treatment of patients with chronic kidney disease (CKD) and type 2 diabetes (T2D) is rapidly evolving. As part of the FOUNTAIN platform (NCT05526157; EUPAS48148), we described and compared cohorts of adult patients with CKD and T2D initiating a sodium-glucose cotransporter 2 inhibitor (SGLT2i) before the launch of finerenone in Europe, Japan, and the United States (US). METHODS: This was a multinational, multi-cohort study of patients with T2D in five data sources: the Danish National Health Registers (DNHR) (Denmark), PHARMO Data Network (The Netherlands), Valencia Health System Integrated Database (VID) (Spain), Japan Chronic Kidney Disease Database Extension (J-CKD-DB-Ex) (Japan), and Optum's de-identified Clinformatics(®) Data Mart Database (CDM) (US). Eligible patients had CKD (based on either diagnosis codes, eGFR values, and/or urine ACR) and initiated an SGLT2i between 2012 and 2021. Baseline demographic, lifestyle, and clinical characteristics were analyzed, and drug utilization patterns were described. RESULTS: The final cohorts included 21,739 patients in DNHR, 381 in PHARMO, 31,785 in VID, 1157 in J-CKD-DB-Ex, and 56,219 in CDM. Across data sources, approximately 41-70% had CKD stage 1 or 2 at baseline; severe CKD (stage 4) was uncommon (1.6-6.7%). The median duration of SGLT2i therapy ranged from 7.5 months in PHARMO to 17.0 months in VID. At least 50% of patients were currently receiving SGLT2i treatment at 1 year after initiation. CONCLUSIONS: At a 1-year follow-up, at least half of the patients with CKD and T2D were receiving SGLT2i treatment across the data sources. In patients initiating SGLT2i, treatment options for T2D and CKD were heterogeneous and dynamic within and among data sources.

Center for Health Policy and Health Services Research
Llamocca EN, **Bossick AS**, **Perkins DW**, **Ahmedani BK**, **Behrendt R**, **Bloemen A**, **Murphy A**, **Kulkarni A**, and **Lockhart E**. Health-related social needs screening, reporting, and assistance in a large health system. *Prev Med* 2024; 190:108182. PMID: 39586330. Full Text

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BACKGROUND: National mandates require screening for and addressing health-related social needs (HRSNs) in healthcare settings. However, differences in HRSN screening process (i.e., completed screenings, screening results, documented offer of assistance, documented assistance request) have been reported by population subgroup. Knowledge of the most effective HRSN screening and intervention methods is limited. We sought to describe differences in completed HRSN screenings, screening results, and assistance request rates across patient and healthcare visit characteristics. METHODS: We examined data from all patients aged ≥18 years and residing in the US receiving services at a large, Midwestern healthcare system with a goal to screen all patients for HRSN at least once annually between July 2021-June 2023 (n = 1,190,488). We examined the proportion of patients with any HRSN screening, with any reported HRSN, asked whether they wanted assistance, or who requested assistance for a reported HRSN stratified by patient demographics and healthcare visit characteristics (i.e., payer, screening location, who completed the screening). RESULTS: Less than half of eligible patients (47.0 %) were screened for HRSNs. About one-sixth (16.9 %) reported any HRSN. Although most patients reporting HRSNs were asked whether they wanted assistance, only about one-quarter (26.8 %) responded affirmatively. Proportions included in each step of the HRSN screening process significantly differed by patient and healthcare visit characteristics. DISCUSSION: This study is one of the first to investigate various steps of a population-wide HRSN screening program. Our findings suggest that examining differences in HRSN screening process by population subgroup is key to addressing HRSNs through a health equity lens.

Center for Health Policy and Health Services Research
Lockhart E, **Gootee J**, **Copeland L**, and Turner D. Willingness to Be Contacted via a Patient Portal for Health Screening, Research Recruitment, and at-Home Self-Test Kits for Health Monitoring: Pilot Quantitative Survey. *JMIR Form Res* 2024; 8:e59837. PMID: 39584575. Full Text

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BACKGROUND: Patient portals are being increasingly used by health systems in the United States. Although some patients use portals for clinical use, patient perspectives on using portals for research-related activities, to complete health screenings, and to request at-home self-test kits are unclear. OBJECTIVE: We aimed to understand patient perspectives on using electronic health portals for research; health-related screenings; and patient-initiated, home-based self-testing. METHODS: Patients (N=105) from the Patient Engaged Research Center at a large, urban, midwestern health system completed a 23-item web-based survey on patient portal (MyChart) use and willingness to use the patient portal for research, risk assessments, and self-test kits. Frequencies and percentages were generated. RESULTS: Almost all participants (102/105, 97.1%) had accessed MyChart at least once, with most (44/102, 43.1%) indicating they logged in at least once per month. Participants indicated logging into MyChart to check laboratory results or other health data (89/105, 84.8%), because they received a message to log in (85/105, 81%), and to message their health care professional (83/105, 79%). Fewer participants logged in to see what medications they had been prescribed (16/105, 15.2%) and to learn

more about their health conditions (29/105, 27.6%). Most participants indicated logging into MyChart on a computer via a website (70/105, 66.7%) or on a smartphone via an app (54/105, 51.4%). When asked about how likely they would be to participate in different types of research if contacted via MyChart, most (90/105, 85.7%) said they would be likely to answer a survey, fill out a health assessment (87/105, 82.9%), or watch a video (86/105, 81.9%). Finally, participants would be willing to answer risk assessment questions on MyChart regarding sleep (74/101, 73.3%), stress (65/105, 61.9%), diabetes (60/105, 57.1%), anxiety (59/105, 56.2%), and depression (54/105, 51.4%) and would be interested in receiving an at-home self-test kit for COVID-19 (66/105, 62.9%), cholesterol (63/105, 60%), colon cancer (62/105, 59%), and allergies (56/105, 53.3%). There were no significant demographic differences for any results (all P values were >.05). CONCLUSIONS: Patient portals may be used for research recruitment; sending research-related information; and engaging patients to answer risk assessments, read about health information, and complete other clinical tasks. The lack of significant findings based on race and gender suggests that patient portals may be acceptable tools for recruiting research participants and conducting research. Allowing patients to request self-test kits and complete risk assessments in portals may help patients to take agency over their health care. Future research should examine if patient portal recruitment may help address persistent biases in clinical trial recruitment to increase enrollment of women and racial minority groups.

Center for Health Policy and Health Services Research
Miller-Matero LR, **Yeh HH**, **Ma L**, Jones RA, Nadolsky S, Medcalf A, Foster GD, and Cardel MI. Alcohol Use and Antiobesity Medication Treatment. *JAMA Netw Open* 2024; 7(11):e2447644. PMID: 39589745. Full Text

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This cohort study examines the association of antiobesity medication use and alcohol use among participants enrolled in a weigh loss program.
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Center for Health Policy and Health Services Research
Pearl ES, **Murray MF**, **Haley EN**, **Snodgrass M**, **Braciszewski JM**, **Carlin AM**, and **Miller-Matero LR**. Weight and shape overvaluation and its relation to anxiety, depression, and maladaptive eating symptoms for patients up to 4 years after bariatric surgery. *Surg Obes Relat Dis* 2024; Epub ahead of print. PMID: 39710526. Full Text

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BACKGROUND: Weight and shape overvaluation (WSO; undue influence of weight and shape on self-evaluation) is common among individuals undergoing bariatric surgery. Little is known about how WSO relates to poorer outcomes for patients remote from surgery. OBJECTIVES: To examine associations between WSO with anxiety and depression symptoms and various maladaptive eating behaviors in patients up to 4 years post-bariatric surgery. SETTING: Henry Ford Health, United States. METHODS: Patients who underwent surgery between 2018 and 2021 were invited to complete the study between

2021 and 2022. Participants (N = 765) completed anxiety and depression symptom and eating behavior measures. RESULTS: Participants endorsed moderate WSO (M = 3.62, standard deviation = 1.87), which was positively related to anxiety (r = .37) and depression (r = .20) symptoms; eating in response to anger/frustration (r = .26), anxiety (r = .28), and depression (r = .31); and addictive eating behaviors (r = .26); and was significantly associated with the presence of loss-of-control (odds ratio [OR] = 1.39), binge (OR = 1.39), and graze (OR = 1.24) eating. WSO also was related to more frequent grazing (r = .23) but not loss-of-control or binge eating frequency for participants who endorsed behavior presence. CONCLUSIONS: Findings underscore that links between WSO, psychiatric distress, and maladaptive eating behaviors persist up to 4 years after bariatric surgery. These domains should be assessed at bariatric follow-ups, and assessment of WSO may help providers identify patients at risk for poorer outcomes. Findings should be used to inform temporal modeling of how WSO may predispose patients to poorer bariatric outcomes.

Dermatology

Burshtein J, Armstrong A, Chow M, DeBusk L, Glick B, Gottlieb AB, **Gold LS**, Korman NJ, Lio P, Merola J, Rosmarin D, Rosenberg A, Van Voorhees A, and Lebwohl M. The Association between Obesity and Efficacy of Psoriasis Therapies: An Expert Consensus Panel. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 39709077. Full Text

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BACKGROUND: Psoriasis is a chronic inflammatory skin disease often associated with obesity. Psoriasis therapies may be less effective in obese patients. The purpose of this expert consensus panel is to evaluate the relationship between obesity and efficacy of psoriasis therapies, thereby optimizing patient care. METHODS: A comprehensive literature search was completed on July 19, 2024, using the keywords "psoriasis," "obesity," "efficacy," "treatments," and "therapies". A panel of 11 dermatologists with significant expertise in treatment of psoriasis gathered to review the articles and create consensus statements. A modified Delphi process was used to approve each statement and a strength of recommendation was assigned. RESULTS: The literature search produced 500 articles. A screening of the studies resulted in 22 articles that met criteria. The panel unanimously voted to adopt 10 consensus statements and recommendations, six were given a strength of "A", two were given a strength of "B", and two was given a strength of "C". CONCLUSION: Psoriasis and obesity have a strong association. Obesity decreases efficacy of biologics and may decrease efficacy and potentiate side effects of conventional therapies. It also impacts drug survival. Weight control is a vital component of caring for psoriasis patients and the number of therapeutic options available is rising.

Dermatology

El Gemayel M, Hawat T, Cahn BA, **Nadir U**, Yi MD, Tsoukas M, and Haber R. Adult-Onset Acquired Ichthyosis Revealing an Underlying Colon Adenocarcinoma. *Cureus* 2024; 16(11):e73045. PMID: 39640179. Request Article

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Acquired ichthyosis is an uncommon dermatologic disorder that presents in adulthood and is often associated with systemic conditions, including malignancies. We report the case of a 38-year-old male patient who developed diffuse scaling characterized by rhomboidal, fish-like scales predominantly affecting the trunk and limb extensors, with sparing of the flexures, palms, and soles. Initial therapeutic interventions with emollients and corticosteroids were unsuccessful. A skin biopsy confirmed the diagnosis of acquired ichthyosis, and subsequent diagnostic imaging revealed an underlying colon adenocarcinoma. Notably, the patient's family history was significant for his mother's colon adenocarcinoma, suggesting a potential genetic predisposition. This case highlights the critical importance of conducting a comprehensive diagnostic evaluation for underlying malignancies upon the diagnosis of acquired ichthyosis, particularly in patients with pertinent familial cancer histories. Although the patient was lost to follow-up, this case underscores the role of acquired ichthyosis as a potential paraneoplastic marker, emphasizing the need for early detection and management of associated malignancies.

Dermatology
Gao DX, **Ozog DM**, **Maghfour J**, **Mi QS**, and **Veenstra J**. Cost-efficiency of excision and non-excision-based keratoacanthoma treatment modalities. *Int J Dermatol* 2024; Epub ahead of print. PMID: 39609945. Full Text

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Dermatology
Grant GJ, **Lim HW**, and **Mohammad TF**. A review of ultraviolet filters and their impact on aquatic environments. *Photochem Photobiol Sci* 2024; Epub ahead of print. PMID: 39704908. Request Article

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Numerous anthropogenic ultraviolet filters (UVF) have been detected in aquatic environments and concerns have arisen regarding their potential impacts on aquatic organisms. This manuscript reviews the environmental concentrations and potential toxicity of various UVF. The highest concentrations of UVF are typically observed near frequently visited recreational areas and during peak water-activity periods, which suggests that sunscreen application correlates with noticeable alterations in UVF concentrations. Aquatic concentrations of certain filters have sporadically exceeded 10 µg/L, although most measurements remain below 1 µg/L, which is below commonly reported toxicity levels. UVF have also been detected in aquatic organisms, typically ranging from nondetectable levels to a few hundred ng/g, depending on the species. The toxic effects from UVF, such as coral bleaching and diminished growth, have been observed in laboratory settings, however, toxicity tends to manifest only at significantly higher levels than what is typically detected in aquatic environments. Further research is imperative to provide consumers with improved guidance on selecting sunscreen containing UVF that poses the least environmental risk.

Dermatology
Harris JE, Pandya AG, Lebwohl M, **Hamzavi IH**, Grimes P, Gottlieb AB, Sofen HL, Moore AY, Wang M, Kornacki D, Butler K, and Rosmarin D. Safety and efficacy of ruxolitinib cream for the treatment of vitiligo: A randomised controlled trial secondary analysis at 3 years. *Skin Health Dis* 2024; 4(6):e404. PMID: 39624731. Full Text

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Dermatology
Holbrook RK, **Bardhi R**, **Pandher K**, **Okoli T**, **Jacobsen G**, and **Kohen L**. Assessing the risk of subcutaneous nodules: a retrospective cohort study. *Arch Dermatol Res* 2024; 317(1):140. PMID: 39704817. Full Text

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Dermatology
Lamberg O, **Pandher K**, and **Matthews NH**. Nivolumab-induced hidradenitis suppurativa: a case report. *Dermatol Online J* 2024; 30(4). PMID: 39644467. Full Text

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We present a 44-year-old man with metastatic clear cell renal cell cancer undergoing treatment with nivolumab immunotherapy. Three months post-initiation, he developed symmetric recurrent nodules and boils in intertriginous areas, diagnosed as stage II hidradenitis suppurativa of the groin and gluteal cleft. The progressive course, lesion symmetry and location, worsening with nivolumab infusions, and biopsy findings supported the diagnosis. Hidradenitis suppurativa pathogenesis involves immune dysregulation marked by elevated IL17 and neutrophil-dominated inflammation [1]. Immune checkpoint inhibitors, including anti-PD1 agents like nivolumab, are linked to immune-related adverse events related to widespread T cell activation, potentially increasing IL17 signaling associated with HS [2,3]. Clinicians should be aware of, and observant for anti-PD1-induced HS, a rare immune-related adverse event, in patients undergoing immune checkpoint inhibitor therapy.

Dermatology
Lamberg O, **Pandher K**, Troost JP, and **Lim HW**. Long-term adverse event risks of oral JAK inhibitors versus immunomodulators: a literature review. *Arch Dermatol Res* 2024; 317(1):109. PMID: 39666160. Full Text

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The long-term adverse event risks associated with oral Janus kinase (JAK) inhibitors compared to broader immunomodulators are poorly understood, with limited comparative studies available. This study aims to assess the long-term adverse event risks of oral JAK inhibitors compared to broader immunomodulators in dermatology. A PubMed search included terms such as specific drug names and "adverse events," "long-term safety," "malignancy," "cardiovascular events," and/or "infections." Included were studies with over one year of medication exposure reporting adverse events. A total of 25 studies were included, comprising 19 clinical trials and 6 cohort studies, representing greater than 100,000 patient years of data. We found comparable long-term incidence rates of malignancy (excluding non-melanoma skin cancer (NMSC)), venous thromboembolism (VTE), and serious infections between oral JAK inhibitors and broader immunomodulators. Oral JAK inhibitors demonstrated lower incidence rates of NMSC and major adverse cardiovascular events (MACE), but higher rates of herpes zoster virus (HZV) infections compared to non-JAK medications. Study limitations include variations in underlying diseases, age, and comorbidities between studies introducing patient population heterogeneity. Overall, oral JAK inhibitors may be viable long-term treatment options given their comparable safety profile to broader immunomodulators currently used in dermatology. However, monitoring for HZV infections may be warranted. These findings aid clinicians in making informed treatment decisions and prioritizing patient safety.

Dermatology

Levin AM, **Okifo O**, **Buhl K**, **Ouchi T**, **Parker B**, **Tan J**, **Datta I**, **Dai X**, **Chen Y**, **Palanisamy N**, **Veenstra J**, **Carskadon S**, **Li J**, **Ozog D**, **Keller CE**, **Chitale D**, **Bobbitt KR**, **Crawford HC**, **Steele N**, **Mi QS**, and **Jones LR**. Higher expression of mir-31-5p is associated with reduced risk of head and neck keloid recurrence following surgical resection. *Laryngoscope Investig Otolaryngol* 2024; 9(6):e70040. PMID: 39664781. Full Text

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OBJECTIVE: In this study, we aimed to evaluate mir-31-5p as a prognostic biomarker of keloid disease (KD) recurrence using a retrospective, treatment naïve, surgical cohort of head and neck KD cases from Henry Ford Health. METHODS: Using a tissue microarray, mir-31-5p expression was measured with miRNAscope, and mir-31-5p cell positivity was determined with QuPath. Logistic regression was used to test the association between mir-31-5p positive cells and KD recurrence at 1 year. In an independent dataset, associations between mir-31-5p and messenger RNA (mRNA) expression were assessed. Ingenuity Pathway Analysis identified target genes and pathways impacted by mir-31-5p. RESULTS: Of the 58 KD patients, 42 (72%) received adjuvant triamcinolone injections, and 8 recurred (14%). mir-31-5p was expressed in 48 (83%) specimens. Increasing mir-31-5p expression was associated with decreased risk of recurrence (p = .031), with an odds ratio of 0.86 (95% CI 0.75-0.98) for each 20% increase in mir-31-5p cellular positivity. This effect persisted with triamcinolone treatment (odds ratio 0.82; 95% CI 0.71-0.95; p = .015). mir-31-5p correlated with gene expression enriched in KD pathways, including mRNA splicing and autophagy. CONCLUSION: Taken together, our data supports the association between mir-31-5p expression and KD recurrence. Its potential as a prognostic biomarker should be further investigated. LEVEL OF EVIDENCE: Level 2.

Dermatology

Linz ME, Xiong M, Lanser HC, **Young AT**, and James M. Analysis of intestinal ostomy content on TikTok: The role of social media in countering fear and stigma. *Am J Surg* 2024; 241:116136. PMID: 39689619. Full Text

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BACKGROUND: Ostomates suffer from multiple comorbidities and social stigma, which can be especially debilitating in young patients. TikTok has become a popular platform for this population to establish a community and gain resources. This study aims to characterize intestinal ostomy videos on TikTok. METHODS: The top 50 videos for search terms "ileostomy," "colostomy," "ostomy," and "stoma" were queried on TikTok. Information was compiled regarding the videos' creators, content type, overall sentiment, and viewer engagement. RESULTS: A total of 113 videos amongst 38 creators garnered 52,021,700 likes and 370,983 comments. Most videos focused on education (45.5%) and personal stories (22.7%). Creators were predominantly young females (82.0%), with minimal input from healthcare professionals (3% of videos). Sixty-nine (61%) of videos had responses with further questions. CONCLUSIONS: Our study reveals a gap between interest and availability of professional educational material regarding intestinal ostomies. Addressing this deficiency may improve patient acceptance, bystander understanding, and its negative stigma.

Dermatology

Ma L, Digby M, Wright K, Germain MA, McClure EM, Kartono F, Rahman S, **Friedman SD**, Osborne C, and Desai A. The Impact of Socioeconomic Status and Comorbidities on Non-Melanoma Skin Cancer Recurrence After Image-Guided Superficial Radiation Therapy. *Cancers (Basel)* 2024; 16(23). PMID: 39682223. Full Text

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BACKGROUND: Non-melanoma skin cancers (NMSCs) are the most common cancers in the United States. Image-guided superficial radiation therapy (IGSRT) is an effective treatment for NMSCs. Patient comorbidities and socioeconomic status (SES) are known contributors to health disparities. However, the impact of comorbidities or SES on the outcomes of IGSRT-treated NMSCs has not yet been studied. This study evaluated freedom from recurrence in IGSRT-treated NMSCs stratified by SES and the number of comorbidities. METHODS: This large retrospective cohort study evaluated associations between SES (via Area Deprivation Index (ADI)) or comorbidity (via Charlson Comorbidity Index (CCI)) and 2-, 4-, and 6-year year freedom from recurrence in patients with IGSRT-treated NMSC (n = 19,988 lesions). RESULTS: Freedom from recurrence in less (ADI ≤ 50) vs. more (ADI > 50) deprived neighborhoods was 99.47% vs. 99.61% at 6 years, respectively (p = 0.2). Freedom from recurrence in patients with a CCI of 0 (low comorbidity burden) vs. a CCI of ≥7 (high comorbidity burden) was 99.67% vs. 99.27% at 6 years, respectively (p = 0.9). CONCLUSIONS: This study demonstrates that there are no significant effects of SES or comorbidity burden on freedom from recurrence in patients with IGSRT-treated NMSC. This supports the expansion of IGSRT in deprived neighborhoods to increase access to care, and IGSRT should be a consideration even in patients with a complex comorbidity status.

Dermatology
Mokhtari M, **Alkhouri F**, **Jafry M**, and **Mohammad TF**. Over-the-counter dermatology supplements- a practical guide to authenticity labels and reputable sources. *Arch Dermatol Res* 2024; 317(1):73. PMID: 39636426. Full Text

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Over-the-counter (OTC) oral supplements are increasingly used by consumers and recommended by dermatologists for managing various dermatologic conditions. Despite their popularity, these supplements often lack standardized regulation, potentially posing risks to both patients and clinicians. This review examines the importance of evaluating OTC oral supplements in dermatology, focusing on the prevalence and consequences of adulterated products and the implications of different authenticity labels for consumer education and clinical practice. Various authenticity labels are discussed, such as USP, NSF, ConsumerLab.com, and UL, which aim to verify supplement quality and safety. However, these labels have different criteria and methods for testing, leading to further confusion about their meanings and comparisons. This review provides practical guidance on evaluating OTC oral supplements and interpreting authenticity labels, aiming to help dermatologists and consumers make informed decisions and improve outcomes.

Dermatology
Quiñonez RL, **Ziglar J**, **Mpyisi LFM**, **Mohammad TF**, **Hamzavi I**, and **Lim HW**. The ethics behind treating scars in skin of color research subjects. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 39736357. Full Text

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Dermatology
Szeto MD, Alhanshali L, Rundle CW, Adelman M, Hook Sobotka M, Woolhiser E, Wu J, Presley CL, **Maghfour J**, Meisenheimer J, Anderson JB, and Dellavalle RP. Dermatologic Data From the Global Burden of Disease Study 2019 and the PatientsLikeMe Online Support Community: Comparative Analysis. *JMIR Dermatol* 2024; 7:e50449. PMID: 39661989. Full Text

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The Global Burden of Disease (GBD) study aims to characterize the worldwide prevalence and morbidity of major diseases, while PatientsLikeMe (PLM) is an online community providing patient-generated insights into lived experiences; for dermatologic conditions, quantitative comparisons of GBD and PLM data revealed expected demographic differences but also notable correlations, highlighting their potential as complementary data sources elucidating unmet patient needs and priorities.

Dermatology
Veenstra J, **Loveless I**, **Dimitrion P**, **Adrianto I**, **Ozog D**, and **Mi QS**. Unveiling intratumoral heterogeneity in high-risk cutaneous squamous cell carcinoma using single-cell spatial enhanced resolution omics-sequencing (Stereo-seq). *J Dermatol Sci* 2024; Epub ahead of print. PMID: 39643570. Full Text

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Dermatology
Yamaguchi Y, Peeva E, Adiri R, Ghosh P, Napatalung L, **Hamzavi I**, Pandya AG, Shore RN, Ezzedine K, and Guttman-Yassky E. Response to ritlecitinib with or without narrow-band UVB add-on therapy in patients with active nonsegmental vitiligo: results from a phase 2b extension study. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 39709084. Full Text

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BACKGROUND: Ritlecitinib demonstrated efficacy in a phase 2b trial of nonsegmental vitiligo. OBJECTIVE: To evaluate the efficacy and tolerability of ritlecitinib with add-on narrow-band UVB (nbUVB) phototherapy in patients with nonsegmental vitiligo. METHODS: Following a 24-week, placebo-controlled, dose-ranging period, patients received ritlecitinib 200mg for 4 weeks then 50mg for 20 weeks, with or without nbUVB phototherapy 2x/week. Missing data were handled using last observation carried forward (LOCF) and observed case (OC). RESULTS: Forty-three patients received ritlecitinib+nbUVB and 187

received ritlecitinib-monotherapy. Nine patients receiving ritlecitinib+nbUVB discontinued due to nbUVB group-specific efficacy criteria requiring >10% improvement in %change from baseline (%CFB) in Total-Vitiligo Area Scoring Index (T-VASI) at week 12. At week 24, mean %CFB in Facial-VASI score was -57.0 vs -51.5 (LOCF; P=0.158) and -69.6 vs -55.1 (OC; P=0.009), for ritlecitinib+nbUVB vs ritlecitinib-monotherapy, respectively. Mean %CFB in T-VASI at week 24 was -29.4 vs -21.2 (LOCF; P=0.043) and -46.8 vs -24.5 (OC; P<0.001), respectively. nbUVB addition to ritlecitinib was well-tolerated with no new safety signals. LIMITATIONS: Exploratory analysis; discontinuation criterion applied only to the ritlecitinib+nbUVB group; small sample size. CONCLUSION: Ritlecitinib alone and with nbUVB therapy improved facial and total body repigmentation and was well-tolerated. Adding nbUVB may improve ritlecitinib efficacy.

Dermatology

Young KZ, **Loveless I**, **Su WK**, **Veenstra J**, **Yin C**, **Dimitrion P**, **Krevh R**, **Zhou L**, **She R**, **Pan M**, **Levin AM**, **Young A**, **Samir E**, **Dai A**, **Ge J**, **Huggins RH**, **de Guzman Strong C**, **Lim HW**, **Ozog DM**, **Hamzavi I**, **Adrianto I**, and **Mi QS**. A diverse hidradenitis suppurativa cohort: A retrospective cross-sectional study of 13,130 patients from a large US health care system database from 1995 to 2022. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 39532232. Full Text

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BACKGROUND: Most epidemiological studies of hidradenitis suppurativa (HS) have described homogeneous patient populations. OBJECTIVE: To characterize demographics, modifiable health behaviors, and comorbidities of HS patients within a diverse cohort. METHODS: A retrospective cross-sectional study of 13,130 HS patients within a health care system was conducted. RESULTS: A female sex bias of ~3:1 in all racial/ethnic subgroups was observed. Black/African American (AA) patients had a lower age at HS diagnosis than White patients (37.1 years vs 39.4 years, P < .001). A higher proportion of Black/AA females than White females with HS had body mass index in the obese range (69.9% vs 56.5%; P = .03). In contrast, fewer Black/AA males with HS had a body mass index in the obese range compared to White males (51.4% vs 61.0%; P < .001). More Black/AA patients than White patients with HS had congestive heart failure (odds ratio (OR) = 2.10, confidence interval (CI) = 1.19-3.78; P < .05), chronic pulmonary disease (OR = 1.34; CI = 1.02-1.78; P < .05), diabetes with chronic complication (OR = 1.73; CI = 1.16-2.60; P < .05), renal disease (OR = 2.66; CI = 1.67-4.34; P < .05), and Charlson comorbidity index score ≥4 (OR = 1.67; CI = 1.09-2.58; P < .05). Furthermore, male patients were more likely than female patients to have renal disease (OR = 2.62; CI = 1.66-4.14; P < .05). LIMITATIONS: A single-center study. CONCLUSION: Subgroups of HS patients had significant differences in demographics, risk factors, and comorbid conditions.

Diagnostic Radiology

Akbari H, Bakas S, Sako C, Fathi Kazerooni A, Villanueva-Meyer J, Garcia JA, Mamourian E, Liu F, Cao Q, Shinohara RT, Baid U, Getka A, Pati S, Singh A, Calabrese E, Chang S, Rudie J, Sotiras A, LaMontagne P, Marcus DS, Milchenko M, Nazeri A, Balana C, Capellades J, Puig J, Badve C, Barnholtz-Sloan JS, Sloan AE, Vadmal V, Waite K, Ak M, Colen RR, Park YW, Ahn SS, Chang JH, Choi YS, Lee SK, Alexander GS, Ali AS, Dicker AP, Flanders AE, Liem S, Lombardo J, Shi W, Shukla G, **Griffith B**, **Poisson LM**, **Rogers LR**, Kotrotsou A, Booth TC, Jain R, Lee M, Mahajan A, Chakravarti A, Palmer JD, DiCostanzo D, Fathallah-Shaykh H, Cepeda S, Santonocito OS, Di Stefano AL, Wiestler B, Melhem ER, Woodworth GF, Tiwari P, Valdes P, Matsumoto Y, Otani Y, Imoto R, Aboian M, Koizumi S, Kurozumi K, Kawakatsu T, Alexander K, Satgunaseelan L, Rulseh AM, Bagley SJ, Bilello M, Binder ZA, Brem S, Desai AS, Lustig RA, Maloney E, Prior T, Amankulor N, Nasrallah MLP, O'Rourke DM, Mohan S, and Davatzikos C. Machine Learning-based Prognostic Subgrouping of Glioblastoma: A Multi-center Study. *Neuro Oncol* 2024; Epub ahead of print. PMID: 39665363. Full Text

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BACKGROUND: Glioblastoma is the most aggressive adult primary brain cancer, characterized by significant heterogeneity, posing challenges for patient management, treatment planning, and clinical trial stratification. METHODS: We developed a highly reproducible, personalized prognostication and clinical subgrouping system using machine learning (ML) on routine clinical data, MRI, and molecular measures from 2,838 demographically diverse patients across 22 institutions and 3 continents. Patients were stratified into favorable, intermediate, and poor prognostic subgroups (I, II, III) using Kaplan-Meier analysis (Cox proportional model and hazard ratios [HR]). RESULTS: The ML model stratified patients into distinct prognostic subgroups with HRs between subgroups I-II and I-III of 1.62 (95%CI: 1.43-1.84, p<0.001) and 3.48 (95%CI: 2.94-4.11, p<0.001), respectively. Analysis of imaging features revealed several tumor properties contributing unique prognostic value, supporting the feasibility of a generalizable prognostic classification system in a diverse cohort. CONCLUSIONS: Our ML model demonstrates extensive reproducibility and online accessibility, utilizing routine imaging data rather than complex imaging protocols. This platform offers a unique approach for personalized patient management and clinical trial stratification in glioblastoma.

Diagnostic Radiology

Kelly BP, **Patel SC**, **Marin HL**, **Corrigan JJ**, **Mitsias PD**, and **Griffith B**. Autoimmune Encephalitis: Pathophysiology and Imaging Review of an Overlooked Diagnosis. *AJNR Am J Neuroradiol* 2024; 45(12):S55-s63. PMID: 39653432. Full Text

Emergency Medicine

Hassan W, Nila SA, Ahmed M, Okello DO, Maqbool M, Dabas MM, **Nour M**, Khan SM, Ansari F, Anum N, and Pervaiz S. Comparative Efficacy and Long-Term Outcomes of Beta-Blockers Alone or in Combination With Angiotensin-Converting Enzyme (ACE) Inhibitors in Chronic Heart Failure: A Systematic Review. *Cureus* 2024; 16(11):e74329. PMID: 39720381. Request Article

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This systematic review provides a comprehensive comparison of beta-blockers and angiotensin-converting enzyme (ACE) inhibitors in the management of chronic heart failure (CHF), with a focus on their long-term efficacy and safety profiles. By synthesizing evidence from randomized controlled trials (RCTs) and clinical studies, the review highlights the significant benefits of both drug classes in reducing mortality and hospital readmissions, and improving patient outcomes. Beta-blockers, such as bisoprolol and carvedilol, demonstrated superior efficacy in reducing sudden cardiac death, particularly in patients with heart failure with reduced ejection fraction (HFrEF). Angiotensin-converting enzyme (ACE) inhibitors, including enalapril and lisinopril, effectively lowered overall cardiovascular mortality by targeting the renin-angiotensin-aldosterone system (RAAS) and preventing further cardiac remodeling. The findings of this review underscore the importance of utilizing these therapies, either alone or in combination, for optimal heart failure management. Combining beta-blockers and ACE inhibitors, or integrating them with newer agents such as angiotensin receptor-neprilysin inhibitors (ARNIs) and mineralocorticoid receptor antagonists (MRAs), provides an additive benefit, improving long-term survival and reducing heart failure-related hospitalizations. The review also identifies gaps in the current literature, suggesting that future research should focus on personalized treatment approaches, longer follow-up periods, and exploring novel therapeutic combinations for diverse heart failure populations. This evidence reinforces the role of beta-blockers and ACE inhibitors as foundational therapies in CHF and offers actionable insights for clinicians to enhance patient care.

Emergency Medicine

Kaur G, **Morton T**, **Khairy M**, **Foy M**, and **Gardner-Gray J**. Invasive Arterial BP Measurements in the Emergency Department-When, if Ever, is it Indicated? *Curr Hypertens Rep* 2024; 27(1):3. PMID: 39656394. Full Text

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PURPOSE OF REVIEW: Extremes of blood pressure (BP) are common among patients that visit emergency departments. In this review article, we discuss the specific indications for invasive blood pressure monitoring in the ED, particularly in the context of undifferentiated shock and hypertensive emergencies. RECENT FINDINGS: In most cases, non-invasive techniques suffice for blood pressure monitoring, however, in certain patient presentations intermittent automated oscillometry bears significant drawbacks. The most evident drawback is the extended intervals between measurements. Invasive BP (IBP) monitoring offers a pivotal tool for patients with critical illness who require accurate, timely, blood

pressure monitoring and indirectly monitors for complications involving vital organ systems. In the management of patients with critical illness or at risk for end organ injury, invasive methods that directly measure BP via arterial cannulation continues to be an established standard. Overall, evaluating patients on an individual basis, with the understanding that patients who present with extreme blood pressure values need closer monitoring, should prompt consideration of invasive methods of blood pressure monitoring.

Emergency Medicine

Kropf CW, Haidar DA, Tucker RV, Peterson W, **Khanna N**, Huang RD, Fung CM, and Theyyunni N. ● Education ● Outcomes and impact of an advanced clinical ultrasound track in an emergency medicine residency. *World J Emerg Med* 2024; 15(6):486-489. PMID: 39600811. Full Text

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Emergency Medicine

Santos JLC, Harnett NG, van Rooij SJH, Ely TD, Jovanovic T, Lebois LAM, Beaudoin FL, An X, Neylan TC, Linnstaedt SD, Germine LT, Bollen KA, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Pascual JL, Seamon MJ, Harris E, Pearson C, Peak DA, Merchant RC, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Bruce SE, Pizzagalli DA, Harte SE, Ressler KJ, Koenen KC, McLean SA, and Stevens JS. Social Buffering of PTSD: Longitudinal Effects and Neural Mediators. *Biol Psychiatry Cogn Neurosci Neuroimaging* 2024; Epub ahead of print. PMID: 39603414. Full Text

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BACKGROUND: Post-traumatic stress disorder (PTSD) is a well characterized psychiatric disorder featuring changes in mood and arousal following traumatic events. Prior animal and human studies on social support in the peri-traumatic window demonstrate a buffering effect with regards to acute biological and psychological stress symptoms. Fewer studies have explored the magnitude and mechanism on how early, post-trauma social support can reduce longitudinal PTSD severity. METHODS: In this study we investigated the beneficial impact of social support on longitudinal PTSD symptoms, and probed brain regions sensitive to this buffering phenomenon, such as the amygdala and ventromedial prefrontal cortex. In the multi-site AURORA study, n=315 participants reported PTSD symptoms (PCL-5) and perceived emotional support (PROMIS) at 2-weeks, 8-weeks, 3-months, and 6-months post-ED visit. Additionally, neuroimaging data was collected at 2 weeks post trauma. RESULTS: We hypothesized that early, post-trauma social support would be linked with greater fractional anisotropic (FA) values in white matter tracts that have known connectivity between the amygdala and prefrontal cortex and would predict reduced neural reactivity to social threat cues in the amygdala. Interestingly, while we observed greater FA in the bilateral cingulum and bilateral uncinate fasciculus as a function of early post-trauma emotional support, we also identified greater threat reactivity in the precuneus/posterior cingulate, a component of the default mode network. CONCLUSION: Our findings suggest that the neurocircuitry underlying the response to social threat cues are facilitated through broader pathways that involve the posterior hub of the default mode network.

Emergency Medicine

Van Der Pol B, Avery A, Taylor SN, **Miller J**, Emery CL, English A, Lazenby GB, Lillis R, Ruth J, Young D, Young S, Chavoustie S, Crane L, Reid V, Wall G, and Johnson S. Multicenter Clinical Performance Evaluation of the NeuMoDx™ CT/NG Assay 2.0. *Sex Transm Dis* 2024; Epub ahead of print. PMID: 39629837. Full Text

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BACKGROUND: Given the continued increases in rates of both Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) infection, additional diagnostic assays may be useful in increasing access to testing for these sexually transmitted infections. We evaluated the performance of the NeuMoDx™ CT/NG Assay 2.0 on the NeuMoDx-96 and NeuMoDx-288 Molecular Systems. METHODS: The clinical sensitivity and specificity of the assay was assessed when used with: 1) endocervical swabs; 2) self-, and clinician-collected vaginal swabs; and 3) first-catch urine specimens (female and male). Results were compared to a patient infection status based on US Food and Drug Administration (FDA)-cleared assays. RESULTS: The NeuMoDx CT/NG Assay 2.0 demonstrated high sensitivity and specificity in both symptomatic and asymptomatic participants. All specimen types other than endocervical swabs had >95% sensitivity and > 99% specificity for both pathogens. For endocervical samples, sensitivity was 93.2% and 93.3% for CT and NG, respectively. There was no difference in performance based on platform. The frequency of invalid results was low (<1%). CONCLUSIONS: The NeuMoDx CT/NG Assay 2.0 demonstrated performance similar to currently FDA-cleared assays, with the added choice of a moderate- (96-sample) or a high-throughput (288-sample) platform. The system therefore offers solutions to laboratories running lower volumes of testing that may obviate the need for outsourcing to larger reference laboratories.

Endocrinology and Metabolism

Yadav RN, **Oravec DJ**, **Cushman T**, **Rao SD**, and **Yeni YN**. Strength and strain distributions obtained from digital wrist tomosynthesis discriminate patients with and without a history of fragility fracture. *Bone* 2024; 192:117368. PMID: 39672218. Full Text

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Bone fractures due to osteoporosis are a significant problem. Limited accuracy of standard bone mineral density (BMD) for fracture risk assessment, combined with low adherence to bone health screening

precludes identification of those at risk of fracture. Because of the wide availability of digital breast tomosynthesis (DBT) imaging, bone screening using a DBT scanner at the time of breast screening has been proposed. Earlier studies have shown that BMD, microstructure, and stiffness of the distal radius can be calculated using digital tomosynthesis imaging of the wrist (DWT). However, strength and stress/strain parameters, which are more relevant to structural failure, and have the potential to enhance the utility of DWT, were not examined previously. Therefore, this study aimed to examine the ability of DWT to discriminate patients with and without fragility fracture using DWT based finite element (DWT-FE) derived strength and stress/strain distribution properties, and to determine in vivo repeatability of these biomechanical properties. Twenty-two postmenopausal women with any fragility fracture (included spine, hip, distal radius, humerus and tibia fractures) and 68 without were recruited. Each participant's nondominant arm (dominant arm if history of fracture in the nondominant arm) was scanned with DWT and compressive loading was simulated using FE modeling. Six additional patients were DWT-scanned thrice, with repositioning, to determine the repeatability of the study variables. Age and T-score were not different between fracture and nonfracture groups ($p > 0.1$), but strength and stress/strain parameters were significant predictors of fracture status (AUC = 0.64-0.74). Standard deviation of tensile strain was the most discriminatory variable for fracture status (AUC = 0.74) and was independent from stiffness. Repeatability error of DWT biomechanical properties was 0.7 % to 5.8 %. This study demonstrated that DWT-FE based strength and standard deviation of tensile strain were reproducible and predict fracture status independent from BMD and stiffness. The results suggest that the accuracy of fracture risk screening can be improved in the highly accessible environment of mammographic imaging.

Family Medicine

Kaljee L, **Antwi S**, **Dankerlui D**, Harris D, Israel B, **White-Perkins D**, **Aboah VO**, Aduse-Poku L, **Larrious-Lartey H**, Brush B, Coombe C, Patman L, Cawthorne N, Chue S, Rowe Z, **Mills C**, **Fernando K**, Daniels G, **Walker EM**, and **Jiagge E**. Cancer Clinical Trial Participation: A Qualitative Study of Black/African American Communities' and Patient/Survivors' Recommendations. *JNCI Cancer Spectr* 2024; Epub ahead of print. PMID: 39585656. Full Text

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BACKGROUND: Black/African Americans experience a disproportionate cancer burden and mortality rates. Racial/ethnic variation in cancer burden reflects systemic and healthcare inequities, cancer risk factors, and heredity and genomic diversity. Multiple systemic, socio-cultural, economic, and individual factors also contribute to disproportionately low Black/African American participation in cancer clinical trials. METHODS: The Participatory Action for Access to Clinical Trials project utilized a community-based participatory research (CBPR) approach inclusive of Black/African American community-based organizations (CBOs), Henry Ford Health (HFH), and the University of Michigan Urban Research Center. The project aims were to understand Black/African Americans' behavioral intentions to participate in cancer clinical trials and to obtain recommendations for improving participation. Audio-recorded focus group data were transcribed, coded, and searches were conducted to identify themes and subthemes. Representative text was extracted from the transcripts. RESULTS: Six community focus group discussions (70 participants) and six HFH patient/survivor focus group discussions (29 participants) were completed. General themes related to trial participation were identified including: 1) systemic issues related to racism, health disparities, and trust in government, health systems, and clinical research; 2) firsthand experiences with healthcare and health systems; 3) perceived and experienced advantages and disadvantages of clinical trial participation; and 4) recruitment procedures and personal decision-making

processes. Specific recommendations on how to address barriers were obtained. CONCLUSIONS: CBPR is effective in bringing communities equitably to the table. To build trust, health systems must provide opportunities for patients and communities to jointly identify factors affecting cancer clinical trial participation, implement recommendations, and address health disparities.

Family Medicine

Llamocca EN, **Bossick AS**, **Perkins DW**, **Ahmedani BK**, **Behrendt R**, **Bloemen A**, **Murphy A**, **Kulkarni A**, and **Lockhart E**. Health-related social needs screening, reporting, and assistance in a large health system. *Prev Med* 2024; 190:108182. PMID: 39586330. Full Text

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BACKGROUND: National mandates require screening for and addressing health-related social needs (HRSNs) in healthcare settings. However, differences in HRSN screening process (i.e., completed screenings, screening results, documented offer of assistance, documented assistance request) have been reported by population subgroup. Knowledge of the most effective HRSN screening and intervention methods is limited. We sought to describe differences in completed HRSN screenings, screening results, and assistance request rates across patient and healthcare visit characteristics. METHODS: We examined data from all patients aged ≥18 years and residing in the US receiving services at a large, Midwestern healthcare system with a goal to screen all patients for HRSN at least once annually between July 2021-June 2023 (n = 1,190,488). We examined the proportion of patients with any HRSN screening, with any reported HRSN, asked whether they wanted assistance, or who requested assistance for a reported HRSN stratified by patient demographics and healthcare visit characteristics (i.e., payer, screening location, who completed the screening). RESULTS: Less than half of eligible patients (47.0 %) were screened for HRSNs. About one-sixth (16.9 %) reported any HRSN. Although most patients reporting HRSNs were asked whether they wanted assistance, only about one-quarter (26.8 %) responded affirmatively. Proportions included in each step of the HRSN screening process significantly differed by patient and healthcare visit characteristics. DISCUSSION: This study is one of the first to investigate various steps of a population-wide HRSN screening program. Our findings suggest that examining differences in HRSN screening process by population subgroup is key to addressing HRSNs through a health equity lens.

Family Medicine

Perkins K, **Anderi E**, **Costandi M**, **Passalacqua KD**, and **Budzynska K**. A Rare Case of Recurrent Renal Infarcts With Unique Etiologies in Different Kidneys Occurring Six Years Apart. *Case Rep Nephrol* 2024; 2024:8233593. PMID: 39664047. Full Text

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Renal infarcts are uncommon, difficult to diagnose, and can lead to long-term kidney disease. Because they have numerous etiologies and patients may present with nonspecific symptoms, renal infarcts may be mistaken for other common conditions. A 50-year-old woman presented to the emergency department (ED) with flank pain, nausea, and vomiting. Computed tomography (CT) revealed multiple right kidney infarcts, transthoracic echocardiography revealed mitral valve stenosis with no evidence of atrial fibrillation, and hypercoagulability tests were negative. High-intensity anticoagulation therapy resolved the infarcts and she was discharged on warfarin. Six years later, at the age of 56, the woman again presented to the ED with back pain, nausea, vomiting, and fever. She had undergone valvuloplasty to repair the mitral valve stenosis 1 month before this ED visit, and warfarin had been discontinued shortly after the procedure. CT imaging and ultrasonography showed no evidence of infarcts and electrocardiogram was normal. Although urinalysis was negative for infection, pyelonephritis was suspected per CT results. However, renal function and leukocytosis did not improve after 2 days of antibiotic therapy. Radioisotope renal scan then revealed infarcts in the left kidney. Anticoagulation therapy again led to recovery, and the patient was discharged back on warfarin. After the recurrent infarct, monitoring and cardiac care have led to adequate long-term management, and no evidence of atrial fibrillation has ever been observed. This case illustrates the challenging diagnosis of an unusual presentation of recurrent renal infarct, where each infarct was suspected to have a unique and independent etiology: mitral valve stenosis in the first and hypercoagulability from withdrawal of warfarin in the second. Because no clear risk or symptom profiles exist for renal infarcts, this unusual condition should be considered when patients do not respond to treatment for other renal problems, especially those with cardiovascular disease.

Gastroenterology
Abusuliman M, Aboeldahb M, Olimy A, **Abbas O**, Abusuliman A, **Jamali T**, **Gavidia Rosario A**, **Yuan L**, and **Pompa R**. Rare Thymoma With Solitary Liver Metastasis. *ACG Case Rep J* 2024; 11(12):e01562. PMID: 39624200. Full Text

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Thymomas are rare, malignant, epithelial tumors of the thymus gland. Extrathoracic metastasis of thymoma is exceedingly rare, particularly when isolated to the liver. We report an 89-year-old man who presented with urinary retention. Exploratory computed tomography imaging revealed a heterogeneous mass in the aortopulmonary window and a 1.9 cm lesion in the left hepatic lobe. Results from magnetic resonance imaging, positron emission tomography-computed tomography, and histopathological analysis of biopsy samples collectively supported a diagnosis of metastatic type B2 thymoma. To the best of our knowledge, this is the oldest patient to be diagnosed with metastatic type B2 thymoma. Metastatic thymoma is difficult to identify, and patients with mediastinal mass identified after any presentation should be evaluated for malignant spread.

Gastroenterology
Abusuliman M, **Jamali T**, and **El-Nachef N**. Rare Presentation of Cytomegalovirus Colitis Mimicking Colonic Neoplasm. *ACG Case Rep J* 2024; 11(12):e01572. PMID: 39717065. Full Text

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Gastroenterology

Baik I, **Jantz A**, **Poparad-Stezar A**, **Venkat D**, **Khoury N**, **Samaniego-Picota M**, **Gonzalez HC**, and **Fitzmaurice MG**. Evaluating the use of glucagon-like peptide-1 receptor agonists in a matched cohort of kidney and liver transplant recipients. *J Pharm Pract Res* 2024. PMID: Not assigned. Full Text

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Background: Diabetes mellitus (DM) and obesity are common among solid organ transplant recipients, but are associated with an increased risk of graft failure. Aim: Although glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are effective for managing both conditions in the general population, there is limited evidence regarding their use among transplant recipients. Method: The effect of GLP-1 RAs on post-transplant glucose control (defined as haemoglobin A1c [HbA1c]) among 37 liver and kidney transplant patients was compared to a control cohort. Secondary outcomes included change in total daily insulin requirements and oral DM agents, estimated glomerular filtration rate (eGFR), weight, and body mass index (BMI). Adverse events attributed to GLP-1 RAs, hypoglycaemia, incidence of pancreatitis, biopsy-proven acute rejection, graft loss, and death were assessed. Ethical approval was granted by the Henry Ford Health Institutional Review Board (Reference no: 15959) and the study conforms with the US Federal Policy for the Protection of Human Subjects. Results: We observed that patients receiving GLP-1 RAs had a median reduction in HbA1c of 0.5% and reduction in insulin and oral anti-DM agents compared to the control group without GLP-1 RAs. There were statistically significant reductions in both weight and BMI in the GLP-1 RA group. Our observed incidence of adverse events was similar to previous literature. Unlike other smaller studies, a decline in eGFR was observed in the GLP-1 RA group. There were no differences in incidence of biopsy-proven acute rejection, graft loss, or death. Conclusion: When compared to patients without GLP-1 RA therapy, GLP-1 RAs modestly reduced HbA1c and insulin requirements and statistically reduced weight/BMI review at 6 months. GLP-1 RAs, even if initiated early post-transplant, were seemingly safe and effective. Larger, prospective studies are warranted to evaluate the safety and efficacy of GLP-1 RAs in this population.

Gastroenterology

Dawod S, and **Brown K**. Non-invasive testing in metabolic dysfunction-associated steatotic liver disease. *Front Med (Lausanne)* 2024; 11:1499013. PMID: 39606621. Full Text

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Metabolic dysfunction-associated steatotic liver disease (MASLD), previously referred to as non-alcoholic fatty liver disease (NAFLD), is a leading cause of chronic liver disease, affecting up to 30% of the global population. MASLD is strongly associated with metabolic risk factors such as obesity and type 2 diabetes, and can progress to advanced stages including cirrhosis and hepatocellular carcinoma. Early diagnosis and accurate staging of fibrosis are critical in managing the disease and preventing complications. While liver biopsy has long been considered the gold standard for assessing fibrosis, it is invasive and carries associated risks. In response, non-invasive tests (NITs) have emerged as essential alternatives for the diagnosis and monitoring of MASLD. Key methods include blood-based biomarkers such as the Fibrosis-4 (FIB-4) score, NAFLD Fibrosis Score (NFS), and Enhanced Liver Fibrosis (ELF) test, as well as imaging modalities like vibration-controlled transient elastography (VCTE) and magnetic resonance elastography (MRE). These tests provide safer, more accessible methods for identifying liver fibrosis and guiding clinical management. They are integral in assessing disease severity, guiding treatment decisions, and monitoring disease progression, particularly in light of emerging therapies. NITs have become increasingly recommended by clinical guidelines as they reduce the need for invasive procedures like liver biopsy, improving patient care and outcomes. In conclusion, non-invasive testing plays a crucial role in the effective management of MASLD, offering reliable alternatives for diagnosis and monitoring while minimizing risks associated with traditional invasive methods.

Gastroenterology

Francis A, **Chaudhary AJ**, Sohail A, Tarar ZI, Jaan A, **Cavataio JP**, **Farooqui S**, **Varma A**, and **Jafri SM**. Impact of Immunosuppressive Therapy, Vaccination, and Monoclonal Antibody Use With Outcomes in Liver and Kidney Transplant Recipients With COVID-19: A Retrospective Study. *JGH Open* 2024; 8(12):e70072. PMID: 39639985. Full Text

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BACKGROUND AND AIM: Patients who have undergone solid organ transplantation are at an elevated risk of severe coronavirus disease (COVID-19) because of post-transplantation immunosuppressive therapy. However, optimization of vaccination, modification of immunosuppression, and implementation of monoclonal antibody (mAb) therapy in transplant recipients with COVID-19 is uncertain. METHODS: A retrospective cross-sectional study was conducted on patients who underwent liver or kidney transplants and were diagnosed with COVID-19. The association of several vaccine doses, mycophenolate therapy, and mAB therapy with mortality outcomes after COVID-19 diagnosis (3 and 6 months), hospitalization, and length of hospital stay were assessed. RESULTS: This study included 255 patients with a median age of 59 (23-89) were included. Many COVID-19 vaccine doses were not associated with any outcome; however, patients with a liver transplanted with mycophenolate had higher 3-month (19% vs. 0%; $p = 0.02$) and 6-month (21% vs. 0%; $p = 0.01$) mortality rates than those who did not. In addition, transplant recipients who received mAb therapy for COVID-19 were less likely to be hospitalized (37% vs. 68%; $p < 0.001$). CONCLUSIONS: For organ transplant recipients with COVID-19, vaccination alone may not be an optimal strategy for preventing serious outcomes. Rather, the types of organ transplant, immunosuppressive therapy (particularly mycophenolate), and COVID-19 treatment strategy should be synergistically considered to promote an optimal therapeutic dynamic for a vulnerable population.

Gastroenterology

Hartgerink C, **Toiv A**, **Sarowar A**, **Todd E**, **Nagai S**, **Muszkat Y**, **Beltran N**, and **Jafri SM**. Safety and Efficacy of Everolimus Use to Preserve Renal Function in Intestinal and Multivisceral Transplantation Patients. *Transplant Proc* 2024; 56(10):2250-2254. PMID: 39603963. Full Text

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BACKGROUND: As calcineurin inhibitors are associated with renal impairment post intestinal transplant, use of everolimus (EVR) may provide renal-sparing benefits. METHODS: We performed a retrospective analysis focused on EVR use and renal function after intestinal or multivisceral transplant. No prisoners were used in the study. This study is compliant with the Helsinki Congress and the Declaration of Istanbul. RESULTS: A total of 28 patients, 18 patients who underwent isolated intestinal transplant, and 10 patients who underwent multivisceral transplant, were included in this study. For 13 patients that never received EVR, the average change in estimated glomerular filtration rate (eGFR) compared to baseline at the time of transplant were as follows: 1 year post-transplant = -18.1%; 2 years = -43.7%; 3 years = -44.1; and 5 years = -43.3%. For 15 patients who received EVR after transplant, average duration of EVR therapy was (579.60 ± 784.15) days with 87% of patients ultimately removed from medication due to side effects. In the EVR group, the average change in eGFR compared to baseline were as follows: 1 year post-transplant = -37.5%; 2 years = -43.5%; 3 years = -54.2%; and 5 years = -42.9%. After the initiation of EVR, the average change in eGFR compared to eGFR at time of EVR initiation was as follows: 1 year = +5.9%; 2 years = -1.57%; 3 years = -5.01%; and 5 years = -1.79%. CONCLUSIONS: This study suggests that EVR can play an important role in preserving renal function in intestinal and multivisceral transplant recipients, but tolerance of EVR is highly variable in this patient population.

Gastroenterology
Manivannan A, Pillai A, Liapakis A, Parikh ND, Kumar V, Verna EC, **Salgia R**, **Wu T**, **Lu M**, and **Jesse MT**. Influence of Acuity Circles on Hepatocellular Carcinoma and the Interaction of Gender and Race in Liver Transplantation. *Clin Transplant* 2024; 38(12):e70045. PMID: 39620868. Full Text

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The impact of liver transplant allocation policy using acuity circles (ACs) on interactions between race and gender on waitlist mortality or receipt of deceased donor liver transplant (DDLT) is unknown. Using data from the United Network for Organ Sharing (UNOS), we examined adults listed for DDLT from April 3, 2017, to October 4, 2022 (30 months pre- and post-AC). Fine-Gray sub-distribution hazard model explored AC indicators by race and gender interactions and their effect on receipt of DDLT or waitlist mortality. Also explored was AC's impact on hepatocellular carcinoma (HCC) diagnosis and receipt of DDLT or waitlist mortality. 59 592 patients (30 202 pre-AC, 29 390 post-AC) included. For both receipt of DDLT and waitlist mortality, there were no 3-way (AC by race by gender) interactions, indicating that the effects of race and gender on DDLT or waitlist mortality were consistent pre- and post-AC. Irrespective of AC implementation, Black and Hispanic women were less likely to receive DDLT and had an increased risk of waitlist mortality compared to White women. White, Black, and Hispanic men had lower waitlist mortality risk and greater likelihood of receiving DDLT compared to their female race/ethnic counterparts. Patients with HCC had a significantly greater chance for DDLT than non-HCC, although post-AC this effect was attenuated. Patients with HCC were also at greater risk of waitlist mortality pre- and post-AC compared to those without HCC however, the waitlist mortality post-AC was attenuated only for those patients without HCC. To our knowledge, this is the first study to show the interaction of gender and race on waitlist mortality and access to transplantation since the implementation of AC, showing continued disparate outcomes for women both within and across racial groups.

Gastroenterology
Sengupta S, and **Mellinger JL**. Salt of the earth: Predicting and treating alcohol relapse in high-risk patients after liver transplantation. *Liver Transpl* 2024; 30(12):1214-1216. PMID: 39133051. Full Text

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Gastroenterology
Shahzil M, **Chaudhary AJ**, Kashif T, Qureshi AA, Muhammad A, Khan F, **Faisal MS**, Khaqan MA, Ali H, **Dababneh Y**, and **Moonka D**. Switching to Tenofovir Therapy Versus Continuation of Entecavir for Patients With Hepatitis B Virus Infection: A Systematic Review and Meta-Analysis. *JGH Open* 2024; 8(11):e70055. PMID: 39588267. Full Text

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BACKGROUND: Hepatitis B virus (HBV) infection causes liver disease, including hepatocellular carcinoma. Controlling viral activity is crucial to reducing complications. Tenofovir may offer benefits over entecavir, but it is unclear if switching from entecavir to tenofovir improves outcomes. This study assesses the clinical impact of switching to tenofovir therapy for chronic HBV infection. METHODS: Following the PRISMA guidelines, we conducted a literature search within the Cochrane Library, PubMed, MEDLINE, Embase, and Scopus for studies of patients with HBV infection who were switched to tenofovir from entecavir or were maintained on entecavir. Both formulations of tenofovir, that is, tenofovir disoproxil fumarate and tenofovir alafenamide were included and analyzed in subgroup analysis. Meta-analyses were performed with RevMan 5.4 using a random-effects model, with statistical significance set at $p < 0.05$. RESULTS: A total of eight studies, comprising 833 patients, were included in the meta-analysis. Tenofovir showed a significantly higher likelihood of achieving complete virological response (RR 5.60; 95% CI 3.51-8.94; $p < 0.00001$) and a greater reduction in HBV DNA levels (MD -1.03 log IU/mL; 95% CI -1.69 to -0.36; $p = 0.002$) compared to entecavir. However, there was no significant difference in HBsAg reduction or HBeAg seroconversion between the two groups. ALT reductions were not statistically significant overall, although entecavir showed better outcomes in subgroup analysis. CONCLUSION: Switching from entecavir to tenofovir improves virological response and reduces HBV DNA levels, but shows no significant advantage in HBsAg reduction, HBeAg seroconversion, or overall, ALT reduction.

Gastroenterology
Shahzil M, **Chaudhary AJ**, Qureshi AA, Hasan F, **Faisal MS**, Sohail A, Khaqan MA, **Jamali T**, **Khan MZ**, **Alsheik E**, and **Zuchelli T**. Endoscopic Full-Thickness Plication for the Treatment of Gastroesophageal Reflux Disease: A Systematic Review and Meta-Analysis of Randomized Sham Controlled Trials. *JGH Open* 2024; 8(11):e70056. PMID: 39605898. Full Text

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INTRODUCTION: Gastroesophageal reflux disease (GERD) affects approximately 20% of adults in the United States. Proton pump inhibitors are the first-line treatment but are associated with long-term side effects. Endoscopic full-thickness plication (EFTP) is a minimally invasive alternative that improves the valvular mechanism of the gastroesophageal junction. This meta-analysis compared EFTP to a sham procedure for the treatment of refractory GERD. MATERIALS AND METHODS: This meta-analysis followed the Cochrane guidelines and PRISMA standards and was registered with PROSPERO (CRD42023485506). We searched MEDLINE, Embase, SCOPUS, and Cochrane Library through December 2023. Inclusion criteria targeted Randomized controlled trials comparing EFTP with sham procedures for GERD were included. Statistical analyses utilized RevMan with a random-effects model, and the results were considered significant at $p < 0.05$. RESULTS: Of the 2144 screened studies, three RCTs with 272 patients with GERD were included: 136 patients underwent EFTP and 136 underwent sham procedures. Primary outcomes showed a significant reduction in PPI usage (RR 0.51; 95% CI 0.35-0.73; $p < 0.01$) and more than 50% improvement in GERD-HRQL scores at 3 months (RR 15.81; 95% CI 1.40-178.71; $p = 0.03$). No significant difference was found in the DeMeester scores (MD: 12.57; 95% CI -35.12 to 9.98; $p = 0.27$). Secondary outcomes showed no significant difference in time with esophageal pH < 4, but a significant reduction in total reflux episodes. CONCLUSIONS: EFTP significantly reduced PPI usage, improved GERD-HRQL scores, and decreased total reflux episodes compared with sham procedures, highlighting its potential as a minimally invasive treatment. Further research is needed to compare EFTP with other minimally invasive techniques to determine the most effective treatment option.

Global Health Initiative

Kaljee L, **Antwi S**, **Dankerlui D**, Harris D, Israel B, **White-Perkins D**, **Aboah VO**, Aduse-Poku L, **Larrious-Lartey H**, Brush B, Coombe C, Patman L, Cawthorne N, Chue S, Rowe Z, **Mills C**, **Fernando K**, Daniels G, **Walker EM**, and **Jiagge E**. Cancer Clinical Trial Participation: A Qualitative Study of Black/African American Communities' and Patient/Survivors' Recommendations. *JNCI Cancer Spectr* 2024; Epub ahead of print. PMID: 39585656. Full Text

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Friends of Parkside, Detroit, MI, USA.
Institute for Population Health, Detroit, MI, USA.

BACKGROUND: Black/African Americans experience a disproportionate cancer burden and mortality rates. Racial/ethnic variation in cancer burden reflects systemic and healthcare inequities, cancer risk factors, and heredity and genomic diversity. Multiple systemic, socio-cultural, economic, and individual factors also contribute to disproportionately low Black/African American participation in cancer clinical trials. METHODS: The Participatory Action for Access to Clinical Trials project utilized a community-based participatory research (CBPR) approach inclusive of Black/African American community-based organizations (CBOs), Henry Ford Health (HFH), and the University of Michigan Urban Research Center. The project aims were to understand Black/African Americans' behavioral intentions to participate in cancer clinical trials and to obtain recommendations for improving participation. Audio-recorded focus group data were transcribed, coded, and searches were conducted to identify themes and subthemes. Representative text was extracted from the transcripts. RESULTS: Six community focus group discussions (70 participants) and six HFH patient/survivor focus group discussions (29 participants) were completed. General themes related to trial participation were identified including: 1) systemic issues related to racism, health disparities, and trust in government, health systems, and clinical research; 2) firsthand experiences with healthcare and health systems; 3) perceived and experienced advantages and disadvantages of clinical trial participation; and 4) recruitment procedures and personal decision-making processes. Specific recommendations on how to address barriers were obtained. CONCLUSIONS: CBPR is effective in bringing communities equitably to the table. To build trust, health systems must provide opportunities for patients and communities to jointly identify factors affecting cancer clinical trial participation, implement recommendations, and address health disparities.

Graduate Medical Education

Perkins K, **Anderi E**, **Costandi M**, **Passalacqua KD**, and **Budzynska K**. A Rare Case of Recurrent Renal Infarcts With Unique Etiologies in Different Kidneys Occurring Six Years Apart. *Case Rep Nephrol* 2024; 2024:8233593. PMID: 39664047. Full Text

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Renal infarcts are uncommon, difficult to diagnose, and can lead to long-term kidney disease. Because they have numerous etiologies and patients may present with nonspecific symptoms, renal infarcts may be mistaken for other common conditions. A 50-year-old woman presented to the emergency department (ED) with flank pain, nausea, and vomiting. Computed tomography (CT) revealed multiple right kidney infarcts, transthoracic echocardiography revealed mitral valve stenosis with no evidence of atrial fibrillation, and hypercoagulability tests were negative. High-intensity anticoagulation therapy resolved the infarcts and she was discharged on warfarin. Six years later, at the age of 56, the woman again presented to the ED with back pain, nausea, vomiting, and fever. She had undergone valvuloplasty to

repair the mitral valve stenosis 1 month before this ED visit, and warfarin had been discontinued shortly after the procedure. CT imaging and ultrasonography showed no evidence of infarcts and electrocardiogram was normal. Although urinalysis was negative for infection, pyelonephritis was suspected per CT results. However, renal function and leukocytosis did not improve after 2 days of antibiotic therapy. Radioisotope renal scan then revealed infarcts in the left kidney. Anticoagulation therapy again led to recovery, and the patient was discharged back on warfarin. After the recurrent infarct, monitoring and cardiac care have led to adequate long-term management, and no evidence of atrial fibrillation has ever been observed. This case illustrates the challenging diagnosis of an unusual presentation of recurrent renal infarct, where each infarct was suspected to have a unique and independent etiology: mitral valve stenosis in the first and hypercoagulability from withdrawal of warfarin in the second. Because no clear risk or symptom profiles exist for renal infarcts, this unusual condition should be considered when patients do not respond to treatment for other renal problems, especially those with cardiovascular disease.

Hematology-Oncology

Afrah A, Finkel MA, Fonseca C, Asato MT, Jay MS, **Pappas A**, **Gowda SB**, and **Jay A**. Demineralization of Osseous Structures as Presentation of a Rare Genetic Disorder That Is Associated With a High Rate of Mortality. *Case Rep Endocrinol* 2024; 2024:6063059. PMID: 39703927. Full Text

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Objectives: Describe the details of the clinical presentation, diagnostic challenges, and management of a female neonate with neonatal severe hyperparathyroidism (NSHPT). Methods: This case report was developed from a retrospective chart review. The female infant was born to consanguineous parents-first cousins, with multiple prenatal concerns, including gestational diabetes, intrauterine growth restriction, polyhydramnios, and suspicion of a hypoplastic left atrium on prenatal echocardiogram (ECHO). Following a planned C-section at 37 weeks gestation, the neonate exhibited moderate respiratory distress with subcostal retractions. On physical examination, craniotabes, a bell-shaped chest, and a continuous machinery-type murmur were noted. Results: Evaluation at birth revealed a large Patent Ductus Arteriosus and significant demineralization of skeletal structures with atypical rib morphology. Lab work at 24 h of life (HOL) showed elevated serum calcium level (14.3 mg/dL), ionized calcium-iCal (2.32 mmol/L), and normal 25-OH Vitamin D (54.2 ng/mL). A comprehensive skeletal survey uncovered generalized osteopenia, metaphyseal lucencies, and evidence of healing fractures. Repeat lab work at 43 HOL, showed serum calcium of 18.0 mg/dL, iCal 2.67 mmol/L, and elevated parathyroid hormone (PTH) of 2116 pg/mL. Diagnosis of NSHPT was established based on laboratory findings. Molecular testing confirmed a homozygous variant (c.1744T >A; p.Cys582Ser) in the calcium-sensing receptor (CaSR) gene which confirmed the diagnosis of NSHPT. NSHPT, a rare genetic disorder associated with high mortality rates, is often caused by inactivating CaSR gene variants. The patient's family history revealed a strong correlation with familial hypocalciuric hypercalcemia (FHH), a benign condition associated with asymptomatic hypercalcemia, normal to minimally elevated parathyroid level, and hypocalciuria, it is caused by heterozygous inactivating mutations in the CaSR gene. Treatment of NSHPT typically involves total or subtotal parathyroidectomy; however, initial medical intervention is often necessary. In this case, the neonate underwent medical treatment with calcitonin, furosemide to help facilitate renal clearance of calcium, and intravenous fluids before a successful parathyroidectomy. Conclusions: This case accentuates the importance of considering rare genetic disorders in neonates with complex clinical presentations and affirms the need for comprehensive counseling and education, particularly in consanguineous parents, to address familial implications and guide appropriate interventions.

Hematology-Oncology

Bockorny B, Muthuswamy L, **Huang L**, Hadisurya M, Maria Lim C, Tsai LL, Gill RR, Wei JL, Bullock AJ, Grossman JE, Besaw RJ, Narasimhan S, Tao WA, Perea S, Sawhney MS, Freedman SD, Hildago M, Iliuk A, and Muthuswamy SK. A large-scale proteomics resource of circulating extracellular vesicles for biomarker discovery in pancreatic cancer. *Elife* 2024; 12. PMID: 39693144. Full Text

Division of Medical Oncology, Beth Israel Deaconess Medical Center, Boston, United States.
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National Cancer Institute, Bethesda, United States.

Pancreatic cancer has the worst prognosis of all common tumors. Earlier cancer diagnosis could increase survival rates and better assessment of metastatic disease could improve patient care. As such, there is an urgent need to develop biomarkers to diagnose this deadly malignancy. Analyzing circulating extracellular vesicles (cEVs) using 'liquid biopsies' offers an attractive approach to diagnose and monitor disease status. However, it is important to differentiate EV-associated proteins enriched in patients with pancreatic ductal adenocarcinoma (PDAC) from those with benign pancreatic diseases such as chronic pancreatitis and intraductal papillary mucinous neoplasm (IPMN). To meet this need, we combined the novel EVtrap method for highly efficient isolation of EVs from plasma and conducted proteomics analysis of samples from 124 individuals, including patients with PDAC, benign pancreatic diseases and controls. On average, 912 EV proteins were identified per 100 µL of plasma. EVs containing high levels of PDCD6IP, SERPINA12, and RUVBL2 were associated with PDAC compared to the benign diseases in both discovery and validation cohorts. EVs with PSMB4, RUVBL2, and ANKAR were associated with metastasis, and those with CRP, RALB, and CD55 correlated with poor clinical prognosis. Finally, we validated a seven EV protein PDAC signature against a background of benign pancreatic diseases that yielded an 89% prediction accuracy for the diagnosis of PDAC. To our knowledge, our study represents the largest proteomics profiling of circulating EVs ever conducted in pancreatic cancer and provides a valuable open-source atlas to the scientific community with a comprehensive catalogue of novel cEVs that may assist in the development of biomarkers and improve the outcomes of patients with PDAC.

Hematology-Oncology

Cloyd JM, Sarna A, Arango MJ, Bates SE, Bhutani MS, Bloomston M, Chung V, Dotan E, Ferrone CR, Gambino PF, Goenka AH, Goodman KA, Hall WA, He J, Hogg ME, Jayaraman S, Kambadakone A, Katz MHG, Khorana AA, Ko AH, Koay EJ, Kooby DA, Krishna SG, Larsson LK, Lee RT, Maitra A, Massarweh NN, Mikhail S, Muzaffar M, O'Reilly EM, Palta M, Petzel MQB, **Philip PA**, Reyngold M, Santa Mina D, Sohal DPS, Sundaresan TK, Tsai S, Turner KL, Vreeland TJ, Walston S, Washington MK, Williams TM, Wo JY, and Snyder RA. Best Practices for Delivering Neoadjuvant Therapy in Pancreatic Ductal Adenocarcinoma. *JAMA Surg* 2024; Epub ahead of print. PMID: 39630427. Full Text

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Fox Chase Cancer Center, Philadelphia, Pennsylvania.

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Abramson Cancer Center, University of Pennsylvania, Philadelphia.
Mayo Clinic, Rochester, Minnesota.
Icahn School of Medicine at Mount Sinai, New York, New York.
Medical College of Wisconsin, Milwaukee.
Johns Hopkins University School of Medicine, Baltimore, Maryland.
NorthShore University HealthSystem, Chicago, Illinois.
St Joseph's Health Centre Toronto, University of Toronto, Toronto, Ontario, Canada.
Massachusetts General Hospital, Boston.
Cleveland Clinic and Case Comprehensive Cancer Center, Cleveland, Ohio.
University of California San Francisco.
Emory University, Atlanta, Georgia.
City of Hope, Orange County, California.
Joseph M Cleland Atlanta VA Health Care System, Decature, Georgia.
Zangmeister Center, American Oncology Network, Columbus, Ohio.
East Carolina University, Greenville, North Carolina.
Memorial Sloan Kettering Cancer Center, New York, New York.
Duke University, Durham, North Carolina.
Wayne State University, Henry Ford Health, Detroit, Michigan.
University of Cincinnati, Cincinnati, Ohio.
Kaiser Permanente, San Francisco, California.
Moffitt Cancer Center, Tampa, Florida.
Brooke Army Medical Center, San Antonio, Texas.
The Ohio State University Wexner Medical Center, Wooster.
Vanderbilt University Medical Center, Nashville, Tennessee.

IMPORTANCE: Neoadjuvant therapy (NT) is an increasingly used treatment strategy for patients with localized pancreatic ductal adenocarcinoma (PDAC). Little research has been conducted on cancer care delivery during NT, and the standards for optimal delivery of NT have not been defined. OBJECTIVE: To develop consensus best practices for delivering NT to patients with localized PDAC. DESIGN, SETTING, AND PARTICIPANTS: This study used a modified Delphi approach consisting of 2 rounds of voting, and a series of virtual conferences (from October to December 2023) to reach expert consensus on candidate best practice statements generated from a systematic review of the literature and expert opinion. An interdisciplinary panel was formed including 47 North American experts from surgical, medical, and radiation oncology, radiology, pathology, gastroenterology, integrative oncology, anesthesia, pharmacy, nursing, cancer care delivery research, and nutrition as well as patient and caregiver stakeholders. MAIN OUTCOME AND MEASURES: Statements that reached 75% agreement or greater were included in final consensus statements. RESULTS: Of the 47 participating panel members, 27 (57.64%) were male, and the mean (SD) age was 47.6 (8.2) years. Physicians reported completing training a mean (SD) 14.6 (8.6) years prior and seeing a mean (SD) 110.6 (38.4) patients with PDAC annually; 35 (77.7%) were in academic practice. Final consensus was reached on 82 best practices for delivering NT. Of these, 38 statements focused on pre-NT practices, including diagnosis and staging (n = 15), evaluation and optimization (n = 20), and decision-making (n = 3); 29 statements defined best practices during NT, including initiation (n = 3), delivery of therapy (n = 8), restaging practices (n = 12), and management of complications during NT (n = 6); and 15 best practices were identified to guide treatment post-NT, focusing on surgery (n = 7), pathology (n = 4), and follow-up (n = 3). CONCLUSIONS: Using a modified Delphi consensus technique, best practice guidelines were developed focusing on the optimal standards for delivering NT to patients with localized PDAC. Given the prognostic importance of completing multimodality therapy, efforts to standardize and optimize the delivery of NT represent an immediate opportunity to decrease care variation and improve outcomes for patients with PDAC. Future research should focus on validating and implementing best practice standards into clinical practice.

Hematology-Oncology

Desai R, **Huang L**, Gonzalez RS, and Muthuswamy SK. Oncogenic GNAS Uses PKA-Dependent and Independent Mechanisms to Induce Cell Proliferation in Human Pancreatic Ductal and Acinar Organoids. *Mol Cancer Res* 2024; 22(5):440-451. PMID: 38319286. Full Text

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The study identifies an opportunity to discover a PKA-independent pathway downstream of oncogene GNAS for managing IPMN lesions and their progression to PDAC.

Hematology-Oncology
Jamil M, **Nasser Z**, **Jamil D**, and **Sheqwara JZ**. Unmasking Vitamin B12 Deficiency Misdiagnosed as Myelodysplastic Syndrome. *Case Rep Hematol* 2024; 2024:3258227. PMID: 39655186. Full Text

Department of Internal Medicine, Henry Ford Health System, Detroit, Michigan, USA.
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Background: Pancytopenia is characterized by a decrease in all three types of blood cells. Instead of being a standalone disease, it acts as a common outcome resulting from various factors, including infections, autoimmune disorders, genetic issues, nutritional deficiencies, and malignancies. Pinpointing the root cause of pancytopenia poses a challenge but is essential for devising an effective treatment plan and predicting the likely prognosis. Vitamin B12 deficiency is a common cause of megaloblastic anemia, pancytopenia, and various neuropsychiatric symptoms. However, diagnosing vitamin B12 deficiency lacks a definitive gold standard. Case Presentation: We present two cases where patients initially exhibited pancytopenia with seemingly normal vitamin B12 levels. Based on a bone marrow biopsy, they were initially diagnosed with myelodysplastic syndrome (MDS). Subsequent investigations revealed elevated serum methylmalonic acid (MMA) levels, leading to a revised diagnosis of vitamin B12 deficiency. Both patients showed positive responses to adequate vitamin B12 supplementation. Conclusion: Our case series highlights the importance of ruling out alternative causes of dysplasia in MDS when solely morphological abnormalities are observed on a bone marrow biopsy. It also underscores the crucial aspect of assessing MMA and homocysteine levels in individuals with normal vitamin B12 levels when there is a high clinical suspicion of B12 deficiency.

Hematology-Oncology
Kaljee L, **Antwi S**, **Dankerlui D**, Harris D, Israel B, **White-Perkins D**, **Aboah VO**, Aduse-Poku L, **Larrious-Lartey H**, Brush B, Coombe C, Patman L, Cawthorne N, Chue S, Rowe Z, **Mills C**, **Fernando K**, Daniels G, **Walker EM**, and **Jiagge E**. Cancer Clinical Trial Participation: A Qualitative Study of Black/African American Communities' and Patient/Survivors' Recommendations. *JNCI Cancer Spectr* 2024; Epub ahead of print. PMID: 39585656. Full Text

Henry Ford Health, Global Health Initiative, Detroit, MI, USA.
Henry Ford Cancer Institute, Detroit, MI, USA.
Grace Learning Center, Detroit, MI, USA.
University of Michigan Detroit Urban Research Center, Ann Arbor, MI, USA.
Henry Ford Department of Family Medicine and MSU, USA.
University of Florida, Gainesville, FL, USA.
Our Wellness Hub, Detroit, MI, USA.
Eastside Community Network, Detroit, MI, USA.
Caribbean Community Service Center, Detroit, MI, USA.
Friends of Parkside, Detroit, MI, USA.
Institute for Population Health, Detroit, MI, USA.

BACKGROUND: Black/African Americans experience a disproportionate cancer burden and mortality rates. Racial/ethnic variation in cancer burden reflects systemic and healthcare inequities, cancer risk factors, and heredity and genomic diversity. Multiple systemic, socio-cultural, economic, and individual factors also contribute to disproportionately low Black/African American participation in cancer clinical trials. METHODS: The Participatory Action for Access to Clinical Trials project utilized a community-based participatory research (CBPR) approach inclusive of Black/African American community-based

organizations (CBOs), Henry Ford Health (HFH), and the University of Michigan Urban Research Center. The project aims were to understand Black/African Americans' behavioral intentions to participate in cancer clinical trials and to obtain recommendations for improving participation. Audio-recorded focus group data were transcribed, coded, and searches were conducted to identify themes and subthemes. Representative text was extracted from the transcripts. RESULTS: Six community focus group discussions (70 participants) and six HFH patient/survivor focus group discussions (29 participants) were completed. General themes related to trial participation were identified including: 1) systemic issues related to racism, health disparities, and trust in government, health systems, and clinical research; 2) firsthand experiences with healthcare and health systems; 3) perceived and experienced advantages and disadvantages of clinical trial participation; and 4) recruitment procedures and personal decision-making processes. Specific recommendations on how to address barriers were obtained. CONCLUSIONS: CBPR is effective in bringing communities equitably to the table. To build trust, health systems must provide opportunities for patients and communities to jointly identify factors affecting cancer clinical trial participation, implement recommendations, and address health disparities.

Hematology-Oncology

Lakhani NJ, Papadopoulos KP, Johnson ML, Park H, **Wang D**, Yap TA, Dowlati A, Maki RG, Ulahannan S, Lynce F, Kelly K, Williamson S, Malhotra J, Chen S, Gonzalez Ortiz A, Jankovic V, Paccaly A, Masinde S, Mani J, Lowy I, Gullo G, Sims T, and Kroog G. First-in-Human Dose-Escalation Study of Fianlimab, an Antilymphocyte Activation Gene-3 Antibody, with Cemiplimab in Patients with Advanced Malignancies. *Clin Cancer Res* 2024; 30(24):5601-5611. PMID: 39422598. Full Text

START Midwest, Grand Rapids, Michigan.
START San Antonio, San Antonio, Texas.
Sarah Cannon Research Institute, Tennessee Oncology, PLLC, Nashville, Tennessee.
Washington University School of Medicine, St. Louis, Missouri.
Henry Ford Hospital, Detroit, Michigan.
University of Texas MD Anderson Cancer Center, Houston, Texas.
Case Comprehensive Cancer Center, Case Western Reserve University, Cleveland, Ohio.
Cold Spring Harbor Laboratory, Cold Spring Harbor, New York.
Abramson Cancer Center, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania.
Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma.
Lombardi Comprehensive Cancer Center, MedStar Georgetown University Hospital, Washington, DC.
UC Davis Comprehensive Cancer Center, UC Davis Health, Sacramento, California.
University of Kansas Medical Center, Fairway, Kansas.
Rutgers Cancer Institute of New Jersey, New Brunswick, New Jersey.
Regeneron Pharmaceuticals, Inc., Tarrytown, New York.

PURPOSE: Preclinical data indicate that fianlimab (antilymphocyte activation gene-3) plus cemiplimab (anti-PD-1) enhances antitumor activity. Here, we report prespecified final analyses of the dose-escalation part of a first-in-human, phase 1 study (NCT03005782) of fianlimab as monotherapy and in combination with cemiplimab in patients with advanced malignancies. PATIENTS AND METHODS: Adult patients received 1 to 40 mg/kg of fianlimab plus 350 mg of cemiplimab every 3 weeks (Q3W) across various dose-escalation schedules. Primary objectives were the rate of dose-limiting toxicities, adverse events (including immune mediated), deaths, laboratory abnormalities, and pharmacokinetics. Secondary outcomes were objective response rate, best overall response, duration of response, and antidrug antibody variables. RESULTS: Seventy-eight patients were enrolled (fianlimab + cemiplimab, n = 47; fianlimab monotherapy, n = 31). One patient treated with 3 mg/kg fianlimab + cemiplimab experienced dose-limiting toxicities, including increased blood creatine phosphokinase and myasthenic syndrome. No maximum tolerated dose was reached. Any-grade treatment-emergent adverse events occurred in 90% of patients with fianlimab monotherapy, in 87% of patients with fianlimab + cemiplimab, and in 87% of patients who transitioned from monotherapy to combination therapy. Fianlimab pharmacokinetics were dose proportional and similar in monotherapy and combination therapy. Across patients who received fianlimab + cemiplimab, five achieved a partial response, three of whom experienced a response after transitioning from monotherapy to combination therapy. Fianlimab 1,600 mg Q3W (20 mg/kg in an 80-kg

individual) is the selected dose for phase 2 and phase 3 studies. CONCLUSIONS: Fianlimab as monotherapy and in combination with cemiplimab demonstrated acceptable safety and preliminary antitumor activity, which is generally consistent with previous reports of cemiplimab.

Hematology-Oncology
Levin AM, **Okifo O**, **Buhl K**, **Ouchi T**, **Parker B**, **Tan J**, **Datta I**, **Dai X**, **Chen Y**, **Palanisamy N**, **Veenstra J**, **Carskadon S**, **Li J**, **Ozog D**, **Keller CE**, **Chitale D**, **Bobbitt KR**, **Crawford HC**, **Steele N**, **Mi QS**, and **Jones LR**. Higher expression of mir-31-5p is associated with reduced risk of head and neck keloid recurrence following surgical resection. *Laryngoscope Investig Otolaryngol* 2024; 9(6):e70040. PMID: 39664781. Full Text

Department of Public Health Science Henry Ford Health Detroit Michigan USA.
Center for Bioinformatics Henry Ford Health Detroit Michigan USA.
Department of Otolaryngology Henry Ford Hospital Detroit Michigan USA.
Department of Pathology Henry Ford Hospital Detroit Michigan USA.
Department of Urology Henry Ford Hospital Detroit Michigan USA.
Department of Dermatology Henry Ford Hospital Detroit Michigan USA.
Henry Ford Cancer Institute Detroit Michigan USA.

OBJECTIVE: In this study, we aimed to evaluate mir-31-5p as a prognostic biomarker of keloid disease (KD) recurrence using a retrospective, treatment naïve, surgical cohort of head and neck KD cases from Henry Ford Health. METHODS: Using a tissue microarray, mir-31-5p expression was measured with miRNAscope, and mir-31-5p cell positivity was determined with QuPath. Logistic regression was used to test the association between mir-31-5p positive cells and KD recurrence at 1 year. In an independent dataset, associations between mir-31-5p and messenger RNA (mRNA) expression were assessed. Ingenuity Pathway Analysis identified target genes and pathways impacted by mir-31-5p. RESULTS: Of the 58 KD patients, 42 (72%) received adjuvant triamcinolone injections, and 8 recurred (14%). mir-31-5p was expressed in 48 (83%) specimens. Increasing mir-31-5p expression was associated with decreased risk of recurrence (p = .031), with an odds ratio of 0.86 (95% CI 0.75-0.98) for each 20% increase in mir-31-5p cellular positivity. This effect persisted with triamcinolone treatment (odds ratio 0.82; 95% CI 0.71-0.95; p = .015). mir-31-5p correlated with gene expression enriched in KD pathways, including mRNA splicing and autophagy. CONCLUSION: Taken together, our data supports the association between mir-31-5p expression and KD recurrence. Its potential as a prognostic biomarker should be further investigated. LEVEL OF EVIDENCE: Level 2.

Hematology-Oncology
Loveless IM, Kemp SB, **Hartway KM**, Mitchell JT, Wu Y, **Zwernik SD**, **Salas-Escabillas DJ**, **Brender S**, **George M**, **Makinwa Y**, **Stockdale T**, **Gartrelle K**, **Reddy RG**, Long DW, **Wombwell A**, **Clark JM**, **Levin AM**, **Kwon D**, **Huang L**, **Francescone R**, **Vendramini-Costa DB**, Stanger B, Alessio A, Waters AM, Cui Y, Fertig EJ, Kagohara LT, **Theisen B**, **Crawford HC**, and **Steele NG**. Human pancreatic cancer single cell atlas reveals association of CXCL10+ fibroblasts and basal subtype tumor cells. *Clin Cancer Res* 2024; Epub ahead of print. PMID: 39636224. Full Text

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Henry Ford Hospital, Detroit, MI, United States.

PURPOSE: Pancreatic ductal adenocarcinoma (PDAC) patients with tumors enriched for the basal-like molecular subtype exhibit enhanced resistance to standard of care treatments and have significantly worse overall survival (OS) compared to patients with classical subtype enriched tumors. It is important to develop genomic resources, enabling identification of novel putative targets in a statistically rigorous manner. EXPERIMENTAL DESIGN: We compiled a single cell RNA sequencing (scRNAseq) atlas of the human pancreas with 229 patient samples, aggregated from publicly available raw data. We mapped cell-type specific scRNAseq gene signatures in bulk RNAseq (n=744) and spatial transcriptomics (ST) (n=22) and performed validation using multiplex immunostaining. RESULTS: Analysis of tumor cells from our scRNAseq atlas revealed nine distinct populations, two of which aligned with the basal subtype, correlating with worse OS in bulk RNAseq. Deconvolution identified one of the basal populations to be the predominant tumor subtype in non-dissociated ST tissues and in vitro tumor cell and patient-derived organoid lines. We discovered a novel enrichment and spatial association of CXCL10+ cancer associated fibroblasts (CAFs) with basal tumor cells. We identified that besides immune cells, ductal cells also express CXCR3, the receptor for CXCL10, suggesting a relationship between these cell types in PDAC tumor microenvironment. CONCLUSIONS: We show that our scRNAseq atlas (700,000 cells), integrated with ST data, has increased statistical power and is a powerful resource, allowing for expansion of current subtyping paradigms in PDAC. We uncovered a novel signaling niche marked by CXCL10+ CAFs and basal tumor cells that could be explored for future targeted therapies.

Hematology-Oncology

Mandal S, Teslow EA, Huang M, Yu Y, **Sridhar S**, **Crawford HC**, Hockenberry AJ, Stoppler MC, **Levin AM**, and **Huang L**. Molecular Differences in Pancreatic Ductal Adenocarcinomas from Black Versus White Patients. *Cancer Res Commun* 2024; Epub ahead of print. PMID: 39699266. Full Text

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Tempus Labs, Detroit, MI, United States.
Tempus Labs, New York, NY, United States.
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Henry Ford Health System, Detroit, United States.
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Tempus AI, Inc., Chicago, IL, United States.
Tempus Labs, United States.

Pancreatic cancer is the third leading cause of cancer-related death in the US. Black or African American patients have a higher incidence of pancreatic cancer compared to other racial groups. It is unclear whether distinct molecular mechanisms are involved in the development of pancreatic cancer in different racial groups. To identify tumor molecular features that are distinctly associated with race in Black or African American and White patients with pancreatic ductal adenocarcinoma (the main subtype of pancreatic cancer), we analyzed de-identified patient records, including tumor sequencing data and expression of PD-L1, from the Tempus multimodal database. Patients with a primary diagnosis of pancreatic ductal adenocarcinoma and who received molecular testing between 2017-11 and 2023-03 were included in analyses. Among 4,249 patients analyzed in this study, 452 (10.6%) were Black or African American and 3797 (89.4%) were White. Black patients had a higher prevalence of TP53 mutations compared to White patients ($p<0.001$). KRASG12R mutations occurred more frequently in female patients in the Black vs White group ($p=0.007$). Compared to White patients, Black patients had a higher tumor mutational burden ($p<0.001$) and PD-L1 overexpression ($p=0.047$). In a separate analysis of recent clinical trials testing immunotherapies for pancreatic cancer, we found that Black patients and other minorities were underrepresented in most trials. These findings suggest race-associated molecular differences in tumors that may impact patient responses to immunotherapies. Our study also supports the importance of improving patient diversity in clinical trials on pancreatic cancer treatments.

Hematology-Oncology

Raymond D, Fukui M, **Zwernik S**, Kassam A, Rovin R, and Akhtar P. Evaluating soluble Axl as a biomarker for glioblastoma: A pilot study. *PLoS One* 2024; 19(7):e0301739. PMID: 38968207. Full Text

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With current imaging, discriminating tumor progression from treatment effect following immunotherapy or oncolytic virotherapy of glioblastoma (GBM) is challenging. A blood based diagnostic biomarker would therefore be helpful. Axl is a receptor tyrosine kinase that is highly expressed by many cancers including GBM. Axl expression is regulated through enzymatic cleavage of its extracellular domain. The resulting fragment can be detected in serum as soluble Axl (sAxl). sAxl levels can distinguish patients with melanoma, hepatocellular carcinoma, and pancreatic ductal adenocarcinoma from healthy controls. This is a pilot study to determine if sAxl is a candidate biomarker for GBM. The sAxl levels in the serum of 40 healthy volunteers and 20 GBM patients were determined using an enzyme-linked immunosorbent assay (ELISA). Pre- and post- operative sAxl levels were obtained. Volumetric MRI evaluation provided GBM tumor volume metrics. There was no significant difference in the sAxl levels of the volunteers (30.16±1.88 ng/ml) and GBM patients (30.74±1.96 ng/ml) p = 0.27. The postoperative sAxl levels were significantly higher than preoperative levels (32.32±2.26 ng/ml vs 30.74±1.96 ng/ml, p = 0.03). We found no correlation between tumor volume and sAxl levels. Axl expression was low or absent in 6 of 11 (55%) patient derived GBM cell lines. Given the wide range of Axl expression by GBM tumors, sAxl may not be a reliable indicator of GBM. However, given the small sample size in this study, a larger study may be considered.

Hematology-Oncology

Salas-Escabillas DJ, **Hoffman MT**, **Brender SM**, **Moore JS**, **Wen HJ**, **Benitz S**, **Davis ET**, **Long D**, **Wombwell AM**, Chianis ERD, Allen-Petersen BL, **Steele NG**, Sears RC, Matsumoto I, DelGiorno KE, and **Crawford HC**. Tuft cells transdifferentiate to neural-like progenitor cells in the progression of pancreatic cancer. *Dev Cell* 2024; Epub ahead of print. PMID: 39721583. Full Text

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Pancreatic ductal adenocarcinoma (PDA) is partly initiated through the transdifferentiation of acinar cells to metaplasia, which progresses to neoplasia and cancer. Tuft cells (TCs) are chemosensory cells not found in the normal pancreas but arise in cancer precursor lesions and diminish during progression to carcinoma. These metaplastic TCs (mTCs) suppress tumor progression through communication with the tumor microenvironment, but their fate during progression is unknown. To determine the fate of mTCs during PDA progression, we created a dual recombinase lineage trace model, wherein a pancreas-specific FlpO was used to induce tumorigenesis, while a tuft-cell specific Pou2f3(CreERT/+) driver was used to induce expression of a tdTomato reporter. We found that mTCs in carcinoma transdifferentiate into neural-like progenitor cells (NRPs), a cell type associated with poor survival in patients. Using conditional knockout and overexpression systems, we found that Myc activity in mTCs is necessary and sufficient to induce this tuft-to-neuroendocrine transition (TNT).

Hematology-Oncology

Shroff RT, King G, Colby S, Scott AJ, Borad MJ, Goff L, Matin K, Mahipal A, Kalyan A, Javle MM, El Dika I, Tan B, Cheema P, Patel A, Iyer R, Kelley RK, Thumar J, El-Khoueiry A, Guthrie KA, Chiorean EG, Hochster H, and **Philip PA**. SWOG S1815: A Phase III Randomized Trial of Gemcitabine, Cisplatin, and Nab-Paclitaxel Versus Gemcitabine and Cisplatin in Newly Diagnosed, Advanced Biliary Tract Cancers. *J Clin Oncol* 2024; 2401383. Epub ahead of print. PMID: 39671534. Full Text

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University of Texas MD Anderson Cancer Center, Houston, TX.
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Dana-Farber Harvard Cancer Center, Boston, MA.
Roswell Park Comprehensive Cancer Center, Buffalo, NY.
Hellen Diller Family Comprehensive Cancer Center, University of California San Francisco Medical Center, San Francisco, CA.
Yale Cancer Center, New Haven, CT.
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PURPOSE: SWOG S1815 was a randomized, open label phase III trial, evaluating gemcitabine, nab-paclitaxel, and cisplatin (GAP) versus gemcitabine and cisplatin (GC) in patients with newly diagnosed advanced biliary tract cancers (BTCs). METHODS: Patients with newly diagnosed locally advanced unresectable or metastatic BTC, including intrahepatic cholangiocarcinoma (ICC) and extrahepatic cholangiocarcinoma (ECC) and gallbladder carcinoma (GBC), were randomly assigned 2:1 to either GAP (gemcitabine 800 mg/m(2), cisplatin 25 mg/m(2), and nab-paclitaxel 100 mg/m(2) intravenously once per day on days 1 and 8 of a 21-day cycle) or GC (gemcitabine 1,000 mg/m(2) and cisplatin 25 mg/m(2) intravenously once per day on days 1 and 8 of a 21-day cycle). RESULTS: Among 452 randomly assigned participants, 441 were eligible and analyzable, 67% with ICC, 16% with GBC, and 17% with ECC. There was no significant difference in overall survival (OS) between GAP versus GC. Median OS with GAP was 14.0 months (95% CI, 12.4 to 16.1) and 13.6 months with GC (95% CI, 9.7 to 16.6); hazard ratio (HR), 0.91 (95% CI, 0.72 to 1.14); P = .41. Median progression-free survival (PFS) was similar between groups with median PFS for GAP being 7.5 months (95% CI, 6.4 to 8.5) versus 6.3 months for GC (95% CI, 4.4 to 8.2); HR, 0.89 (95% CI, 0.71 to 1.12); P = .32. In exploratory subset analyses, the OS and PFS benefits of GAP versus GC treatment were greater in locally advanced disease compared with metastatic disease, although not statistically significant (interaction P = .14 for OS and P = .17 for PFS). Moreover, GAP versus GC showed greater improvement in PFS among participants with GBC than those with ICC or ECC (interaction P = .01), but not OS (interaction P = .28). CONCLUSION: The addition of a taxane in the GAP regimen to the standard gemcitabine-cisplatin regimen did not improve OS in newly diagnosed BTC. More toxicity was encountered with GAP versus GC.

Hematology-Oncology

Yamamoto N, Dobersch S, **Loveless I**, Samraj AN, Jang GH, Haraguchi M, Kang LI, Ruzinova MB, Vij KR, Mudd JL, Walsh T, Safyan RA, Chiorean EG, Hingorani SR, Bolton NM, Li L, Fields RC, DeNardo DG, Notta F, **Crawford HC**, **Steele NG**, and Kugel S. HMGA2 Expression Predicts Subtype, Survival, and Treatment Outcome in Pancreatic Ductal Adenocarcinoma. *Clin Cancer Res* 2024; Epub ahead of print. PMID: 39680021. Full Text

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PURPOSE: To establish HMGA2 as a marker of basal-like disease in pancreatic ductal adenocarcinoma (PDAC) and explore its use as a biomarker for prognosis and treatment resistance. EXPERIMENTAL DESIGN: We identified high expression of HMGA2 in basal PDAC cells in a scRNAseq Atlas of 172 patient samples. We then analyzed HMGA2 expression, along with expression of the classical marker GATA6, in a cohort of 580 PDAC samples with multiplex immunohistochemistry. We further supplemented these data with an additional 30 diverse patient samples and multiple independent single-cell RNAseq databases. RESULTS: We found that expression of HMGA2, but not previously described basal markers CK5 or CK17, predicted overall survival in our cohort. Combining HMGA2 and GATA6 status allowed for identification of two key study groups: an HMGA2+/GATA6- cohort with worse survival, low tumor-infiltrating CD8+ T cells, increased FAP+ fibroblasts, and poorer response to gemcitabine-based chemotherapies (n=94, median survival=11.2 months post-surgery); and an HMGA2-/GATA6+ cohort with improved survival, increased CD8+ T-cell infiltrate, decreased FAP+ fibroblasts, and improved survival with gemcitabine-based chemotherapy (n=198, median survival=21.7 months post-surgery). HMGA2 was also prognostic for overall survival in RNA sequencing from an independent cohort. CONCLUSIONS: IHC stratification of primary tumors by HMGA2 and GATA6 status in pancreatic cancer is associated with differential outcomes, survival following chemotherapy, and tumor microenvironments. As a nuclear marker for basal disease, HMGA2 complements GATA6 to identify disease subtypes in PDAC.

Hospital Medicine
Burke KS, Kong X, Haymart B, DeCamillo D, Ali M, Barnes G, and **Kaatz S**. Comparing rates of clinically relevant epistaxis in patients taking warfarin versus direct oral anticoagulants. *Res Pract Thromb Haemost* 2024; 8(8). PMID: Not assigned. Full Text

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Hospital Medicine
May JE, Allen AL, Samuelson Bannow BT, O'Connor C, Sylvester KW, and **Kaatz S**. Safe and effective anticoagulation use: Case studies in anticoagulation stewardship. *J Thromb Haemost* 2024; Epub ahead of print. PMID: 39667688. Full Text

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Anticoagulant use is prevalent and associated with significant potential for harm. Anticoagulation stewardship practice has emerged to address care gaps and promote safe, effective, and cost-conscious anticoagulation use across health care systems. Here we present 4 patient cases describing common challenges in anticoagulation management: inappropriate dosing of direct oral anticoagulants (DOACs), the diagnosis and management of heparin-induced thrombocytopenia (HIT), periprocedural anticoagulation management, and heavy menstrual bleeding on anticoagulation. We discuss available examples of successful stewardship programs that can address the challenges of each case, demonstrating how an investment in anticoagulation stewardship can improve patient outcomes.

Hypertension and Vascular Research

Maskey D, **Granados Pineda J**, and **Ortiz PA**. Update on NKCC2 regulation in the thick ascending limb (TAL) by membrane trafficking, phosphorylation, and protein-protein interactions. *Front Physiol* 2024; 15:1508806. PMID: 39717823. Full Text

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PURPOSE OF REVIEW: The thick ascending limb (TAL) of loop of Henle is essential for NaCl, calcium and magnesium homeostasis, pH balance and for urine concentration. NKCC2 is the main transporter for NaCl reabsorption in the TAL and its regulation is very complex. There have been recent advancements toward understanding how NKCC2 is regulated by protein trafficking, protein-protein interaction, and phosphorylation/dephosphorylation. Here, we update the latest molecular mechanisms and players that control NKCC2 function, which gives an increasingly complex picture of NKKC2 regulation in the apical membrane of the TAL. RECENT FINDINGS: Protein-protein interactions are required as a regulatory mechanism in many cellular processes. A handful of proteins have been recently identified as an interacting partner of NKCC2, which play major roles in regulating NKCC2 trafficking and activity. New players in NKCC2 internalization and trafficking have been identified. NKCC2 activity is also regulated by kinases and phosphatases, and there have been developments in that area as well. SUMMARY: Here we review the current understanding of apical trafficking of NKCC2 in the thick ascending limb (TAL) which is tightly controlled by protein-protein interactions, protein turnover and by phosphorylation and dephosphorylation. We discuss new proteins and processes that regulate NKCC2 that have physiological and pathological significance.

Infectious Diseases

Arena CJ, **Kenney RM**, **Ramesh M**, **Davis SL**, and **Veve MP**. Outcomes of adjunctive eravacycline for severe and fulminant Clostridioides difficile infection. *Int J Infect Dis* 2024; 151:107314. PMID: 39603409. Full Text

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OBJECTIVE: To characterize eravacycline (ERV) treatment for severe or fulminant Clostridioides difficile infection (CDI) and to describe patient outcomes. METHODS: This was an IRB-approved, cross-section of adult hospitalized patients with CDI who received adjunctive ERV with standard of care antibiotics (SOC) for CDI from 01/2019-12/2023 at a 5-hospital health-system. Patients were included if they received ERV with SOC for ≥24 hours for severe or fulminant CDI. Patients with a prior history colectomy or with non-CDI ERV indications were excluded. The primary outcome was the proportion of patients that required colectomy due to C. difficile. Secondary outcomes included time to adjunctive ERV, ERV treatment durations, and in-hospital mortality. RESULTS: Seventy-five patients were included; 25 (33%) had severe and 50 (67%) fulminant CDI; 23 (31%) had refractory severe/fulminant CDI. Eleven (14.7%) required colectomy within 30-days of adjunctive ERV. Patients receiving ERV were mostly immunocompromised with fulminant disease and critical illness. CONCLUSION: ERV may be useful as a potential adjunctive therapy for severe or fulminant CDI. Patients receiving ERV often were immunocompromised and had fulminant disease with critical illness. Future comparative studies are needed to evaluate the impact of adjunctive ERV for CDI.

Infectious Diseases

Boettcher SR, **Kenney RM**, **Arena CJ**, **Beaulac AE**, **Tibbetts RJ**, **Shallal AB**, **Suleyman G**, and **Veve MP**. Say it ain't Steno: a microbiology nudge comment leads to less treatment of Stenotrophomonas maltophilia respiratory colonization. *Infect Control Hosp Epidemiol* 2024; 1-5. Epub ahead of print. PMID: 39623552. Full Text

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OBJECTIVE: To describe the effect of a Stenotrophomonas maltophilia (SM) respiratory culture nudge on antibiotic use in colonized patients. DESIGN: IRB-approved quasi-experiment. SETTING: Five acute-care hospitals in Michigan. PATIENTS: Adult patients with SM respiratory culture between 01/01/2022 and 01/27/2023 (pre-nudge) and 03/27/2023-12/31/2023 (post-nudge). Patients with active community/hospital/ventilator-acquired pneumonia or who received SM-targeted antibiotics at the time of culture were excluded. METHODS: A nudge comment was implemented 02/2023 stating: "S. maltophilia is a frequent colonizer of the respiratory tract. Clinical correlation for infection is required. Colonizers do not require antibiotic treatment." The primary outcome was no treatment with SM-therapy; secondary outcomes were treatment with SM-therapy ≥72 hrs, length of stay, and in-hospital, all-cause mortality. Safety outcomes included antibiotic-associated adverse drug events (ADEs). RESULTS: 94 patients were included: 53 (56.4%) pre- and 41 (43.6%) post-nudge. Most patients were men (53, 56.4%), had underlying lung disease (61, 64.8%), and required invasive ventilatory support (70, 74.5%). Eleven (11.7%) patients resided in a long-term care facility. No treatment with SM therapy was observed in 13 (23.1%) pre- versus 32 (78.0%) post-nudge patients (P <0.001). There were no differences in secondary outcomes. Antibiotic-associated ADEs were common (33/41, 76%) in patients who received ≥72hrs of SM-therapy: fluid overload (18, 44%), hyponatremia (17, 42%), elevated SCr (12, 29%), hyperkalemia (5, 12%). After adjustment for confounders, post-nudge was associated with 11-fold increased odds of no treatment with SM-therapy (adjOR, 11.72; 95%CI, 4.18-32.83). CONCLUSIONS: A targeted SM nudge was associated with a significant reduction in treatment of colonization, with similar patient outcomes. SM-treated patients frequently developed antibiotic-associated ADEs.

Infectious Diseases

Branche A, **Ramesh M**, and Francis B. A Narrative Review of Key Risk Factors for Severe Illness Following SARS-CoV-2, Influenza Virus, and Respiratory Syncytial Virus Infection. *Infect Dis Ther* 2024; Epub ahead of print. PMID: 39739198. Full Text

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza, and respiratory syncytial virus (RSV) are highly infectious respiratory viruses that affect people of all ages and are typically associated with mild symptoms and few complications in immunocompetent individuals. However, the risk of severe outcomes (e.g., hospitalization and death) following infection with these respiratory viruses is higher in certain populations, including older adults and individuals of certain race/ethnic and sociodemographic groups. Additionally, immunocompromising conditions and pre-existing comorbidities, including underlying cardiovascular (e.g., congestive heart failure) and respiratory diseases (e.g., chronic obstructive pulmonary disease), diabetes, chronic kidney disease, and obesity, are key factors that predispose individuals to SARS-CoV-2-, influenza-, and RSV-related severe outcomes. Increased risk for severe outcomes associated with advancing age and comorbidities is compounded by residence in long-term care facilities due to the enhanced spread of respiratory infections in congregate living environments. In this narrative review, risk factors associated with severe outcomes following infection with SARS-CoV-2, influenza, and RSV in adult populations are explored. Additionally, distinct clinical outcomes based on underlying comorbidities following infection are discussed in the context of high-risk populations. Factors unique to each virus that underpin distinct risk profiles are described and suggest the potential for tailored surveillance and healthcare approaches to target and ultimately mitigate SARS-CoV-2-, influenza-, and RSV-associated disease burden in vulnerable populations. Mutual risk factors for severe outcomes are also highlighted; these similarities indicate that cohesive risk reduction strategies may also be feasible, particularly since vaccines are available for each of these respiratory viruses. Ultimately, a more thorough understanding of the risk factors that predispose individuals to develop SARS-CoV-2-, influenza-, and RSV-related severe outcomes may improve risk reduction strategies, inform healthcare policy, and contribute to the expansion and refinement of existing surveillance approaches to ultimately mitigate disease burden in vulnerable populations.

Infectious Diseases

Cabrera-Sanchez J, Tejada H, and **Ordaya EE**. Nocardia otitidiscaviarum Pneumonia and Empyema in a Woman With Colon Adenocarcinoma. *Cureus* 2024; 16(10):e72663. PMID: 39618618. Request Article

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We report a case of necrotizing pneumonia and empyema in a woman with colon adenocarcinoma, which developed shortly after receiving chemotherapy. A chest tube was placed, and analysis of the pleural fluid identified Nocardia otitidiscaviarum. The patient underwent pleural decortication via video-assisted thoracoscopy and was treated with a combination of trimethoprim-sulfamethoxazole and imipenem/cilastatin. After four weeks of treatment, the patient was discharged with oral trimethoprim-sulfamethoxazole, with no recurrence noted during follow-up. Nocardia otitidiscaviarum is an uncommon pathogen that can cause both localized and disseminated disease, similar to other Nocardia species. Its susceptibility to various antibiotics is variable, making susceptibility testing essential when available, along with close monitoring for potential medication side effects.

Infectious Diseases

Lewis NM, Harker EJ, Grant LB, Zhu Y, Grijalva CG, Chappell JD, Rhoads JP, Baughman A, Casey JD, Blair PW, Jones ID, Johnson CA, Lauring AS, Gaglani M, Ghamande S, Columbus C, Steingrub JS, Shapiro NI, Duggal A, Busse LW, Felzer J, Prekker ME, Peltan ID, Brown SM, Hager DN, Gong MN, Mohamed A, Exline MC, Khan A, Hough CL, Wilson JG, Mosier J, Qadir N, Chang SY, Ginde AA, Martinez A, Mohr NM, Mallow C, Harris ES, Johnson NJ, Srinivasan V, Gibbs KW, Kwon JH, **Vaughn IA**, **Ramesh M**, Safdar B, Goyal A, DeLamielleure LE, DeCuir J, Surie D, Dawood FS, Tenforde MW, Uyeki TM, Garg S, Ellington S, and Self WH. Benefit of early oseltamivir therapy for adults hospitalized with influenza A: an observational study. *Clin Infect Dis* 2024; Epub ahead of print. PMID: 39607747. Full Text

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Ronald Reagan UCLA Medical Center, Los Angeles, California.
University of Colorado School of Medicine, Aurora, Colorado.
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BACKGROUND: clinical guidelines recommend initiation of antiviral therapy as soon as possible for patients hospitalized with confirmed or suspected influenza. METHODS: A multicenter US observational sentinel surveillance network prospectively enrolled adults (aged ≥18 years) hospitalized with laboratory-confirmed influenza at 24 hospitals during October 1, 2022-July 21, 2023. A multivariable proportional odds model was used to compare peak pulmonary disease severity (no oxygen support, standard supplemental oxygen, high-flow oxygen/non-invasive ventilation, invasive mechanical ventilation, or death) after the day of hospital admission among patients starting oseltamivir treatment on the day of admission (early) versus those who did not (late or not treated), adjusting for baseline (admission day) severity, age, sex, site, and vaccination status. Multivariable logistic regression models were used to evaluate the odds of intensive care unit (ICU) admission, acute kidney replacement therapy or vasopressor use, and in-hospital death. RESULTS: A total of 840 influenza-positive patients were analyzed, including 415 (49%) who started oseltamivir treatment on the day of admission, and 425 (51%) who did not. Compared with late or not treated patients, those treated early had lower peak pulmonary disease severity (proportional aOR: 0.60, 95% CI: 0.49-0.72), and lower odds of intensive care unit admission (aOR: 0.24, 95% CI: 0.13-0.47), acute kidney replacement therapy or vasopressor use (aOR: 0.40, 95% CI: 0.22-0.67), and in-hospital death (aOR: 0.36, 95% CI: 0.18-0.72). CONCLUSION: Among adults hospitalized with influenza, treatment with oseltamivir on day of hospital admission was associated reduced risk of disease progression, including pulmonary and extrapulmonary organ failure and death.

Infectious Diseases

Shallal A, **Veve MP**, **Kenney RM**, **Alangaden G**, and **Suleyman G**. Characterisation, management, and outcomes of New Delhi metallo-β-lactamase-producing Escherichia coli: A case series. *J Glob Antimicrob Resist* 2024; 40:42-46. PMID: 39631625. Full Text

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OBJECTIVE: New Delhi metallo-β-lactamase (NDM)-producing carbapenem-resistant Enterobacterales (CRE) is a globally growing threat. We sought to describe the microbiology, management and outcomes of patients with this infection at our facility. METHODS: This is a descriptive case series of patients with NDM-producing Escherichia coli isolated from culture in Detroit between July 2021 and February 2023. Demographics, risk factors, clinical characteristics, management and outcomes were described. RESULTS: Nine patients were included in the study. Most patients were female with a median age of 67 years. Hepatobiliary disease accounted for 90% of underlying conditions. Nearly all patients had prior antibiotic exposure and the most common specimen source was intra-abdominal fluid. Three patients were not treated due to colonisation; among those treated, the majority received trimethoprim-sulfamethoxazole. The median treatment duration and length of stay were 7 and 15.5 days, respectively. Six (67%) patients survived. CONCLUSIONS: This report describes a large case series of NDM-producing E. coli infection. Patients with significant comorbidities remain at high risk for CRE infection. Antibiotic options for the treatment of NDM organisms are very limited; new and effective therapies are urgently needed.

Internal Medicine
Abusuliman M, Aboeldahb M, Olimy A, **Abbas O**, Abusuliman A, **Jamali T**, **Gavidia Rosario A**, **Yuan L**, and **Pompa R**. Rare Thymoma With Solitary Liver Metastasis. *ACG Case Rep J* 2024; 11(12):e01562. PMID: 39624200. Full Text

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Thymomas are rare, malignant, epithelial tumors of the thymus gland. Extrathoracic metastasis of thymoma is exceedingly rare, particularly when isolated to the liver. We report an 89-year-old man who presented with urinary retention. Exploratory computed tomography imaging revealed a heterogeneous mass in the aortopulmonary window and a 1.9 cm lesion in the left hepatic lobe. Results from magnetic resonance imaging, positron emission tomography-computed tomography, and histopathological analysis of biopsy samples collectively supported a diagnosis of metastatic type B2 thymoma. To the best of our knowledge, this is the oldest patient to be diagnosed with metastatic type B2 thymoma. Metastatic thymoma is difficult to identify, and patients with mediastinal mass identified after any presentation should be evaluated for malignant spread.

Internal Medicine
Abusuliman M, **Jamali T**, and **El-Nachef N**. Rare Presentation of Cytomegalovirus Colitis Mimicking Colonic Neoplasm. *ACG Case Rep J* 2024; 11(12):e01572. PMID: 39717065. Full Text

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Internal Medicine
Dawod S, and **Brown K**. Non-invasive testing in metabolic dysfunction-associated steatotic liver disease. *Front Med (Lausanne)* 2024; 11:1499013. PMID: 39606621. Full Text

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Metabolic dysfunction-associated steatotic liver disease (MASLD), previously referred to as non-alcoholic fatty liver disease (NAFLD), is a leading cause of chronic liver disease, affecting up to 30% of the global population. MASLD is strongly associated with metabolic risk factors such as obesity and type 2 diabetes, and can progress to advanced stages including cirrhosis and hepatocellular carcinoma. Early diagnosis and accurate staging of fibrosis are critical in managing the disease and preventing complications. While liver biopsy has long been considered the gold standard for assessing fibrosis, it is invasive and carries associated risks. In response, non-invasive tests (NITs) have emerged as essential alternatives for the diagnosis and monitoring of MASLD. Key methods include blood-based biomarkers such as the Fibrosis-4 (FIB-4) score, NAFLD Fibrosis Score (NFS), and Enhanced Liver Fibrosis (ELF) test, as well as imaging modalities like vibration-controlled transient elastography (VCTE) and magnetic resonance elastography (MRE). These tests provide safer, more accessible methods for identifying liver fibrosis and guiding clinical management. They are integral in assessing disease severity, guiding treatment decisions, and monitoring disease progression, particularly in light of emerging therapies. NITs have become increasingly recommended by clinical guidelines as they reduce the need for invasive procedures like liver biopsy, improving patient care and outcomes. In conclusion, non-invasive testing plays a crucial role in the effective management of MASLD, offering reliable alternatives for diagnosis and monitoring while minimizing risks associated with traditional invasive methods.

Internal Medicine

Francis A, **Chaudhary AJ**, Sohail A, Tarar ZI, Jaan A, **Cavataio JP**, **Farooqui S**, **Varma A**, and **Jafri SM**. Impact of Immunosuppressive Therapy, Vaccination, and Monoclonal Antibody Use With Outcomes in Liver and Kidney Transplant Recipients With COVID-19: A Retrospective Study. *JGH Open* 2024; 8(12):e70072. PMID: 39639985. Full Text

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BACKGROUND AND AIM: Patients who have undergone solid organ transplantation are at an elevated risk of severe coronavirus disease (COVID-19) because of post-transplantation immunosuppressive therapy. However, optimization of vaccination, modification of immunosuppression, and implementation of monoclonal antibody (mAb) therapy in transplant recipients with COVID-19 is uncertain. METHODS: A retrospective cross-sectional study was conducted on patients who underwent liver or kidney transplants and were diagnosed with COVID-19. The association of several vaccine doses, mycophenolate therapy, and mAB therapy with mortality outcomes after COVID-19 diagnosis (3 and 6 months), hospitalization, and length of hospital stay were assessed. RESULTS: This study included 255 patients with a median age of 59 (23-89) were included. Many COVID-19 vaccine doses were not associated with any outcome; however, patients with a liver transplanted with mycophenolate had higher 3-month (19% vs. 0%; $p = 0.02$) and 6-month (21% vs. 0%; $p = 0.01$) mortality rates than those who did not. In addition, transplant recipients who received mAb therapy for COVID-19 were less likely to be hospitalized (37% vs. 68%; $p < 0.001$). CONCLUSIONS: For organ transplant recipients with COVID-19, vaccination alone may not be an optimal strategy for preventing serious outcomes. Rather, the types of organ transplant, immunosuppressive therapy (particularly mycophenolate), and COVID-19 treatment strategy should be synergistically considered to promote an optimal therapeutic dynamic for a vulnerable population.

Internal Medicine

Jamil D, **Fadel R**, **Kollman P**, and **Swanson B**. A Case of an Interventricular Septum Pseudoaneurysm With Perforation Mimicking a Ventricular Septal Defect. *Cureus* 2024; 16(11):e73080. PMID: 39640109. Request Article

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Ventricular pseudoaneurysm (PSA) is a ventricular outpouching contained by adherent pericardium or myocardial scar tissue and represents a rare but potentially fatal complication of acute myocardial infarction (AMI). The vast majority of cases involve the left ventricular apex, in the area of infarct. It is extremely rare to see PSA formation within the interventricular septum (IVS). We present a case of ventricular PSA of the IVS, with contained perforation into the right ventricle, mimicking a ventricular septal defect (VSD) in a patient presenting with ST-elevation myocardial infarction (STEMI). This case underscores the importance of maintaining a high index of clinical suspicion and reviews the pathophysiological mechanisms and treatment options for these life-threatening mechanical complications.

Internal Medicine
Jamil M, **Nasser Z**, **Jamil D**, and **Sheqwara JZ**. Unmasking Vitamin B12 Deficiency Misdiagnosed as Myelodysplastic Syndrome. *Case Rep Hematol* 2024; 2024:3258227. PMID: 39655186. Full Text

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Background: Pancytopenia is characterized by a decrease in all three types of blood cells. Instead of being a standalone disease, it acts as a common outcome resulting from various factors, including infections, autoimmune disorders, genetic issues, nutritional deficiencies, and malignancies. Pinpointing the root cause of pancytopenia poses a challenge but is essential for devising an effective treatment plan and predicting the likely prognosis. Vitamin B12 deficiency is a common cause of megaloblastic anemia, pancytopenia, and various neuropsychiatric symptoms. However, diagnosing vitamin B12 deficiency lacks a definitive gold standard. Case Presentation: We present two cases where patients initially exhibited pancytopenia with seemingly normal vitamin B12 levels. Based on a bone marrow biopsy, they were initially diagnosed with myelodysplastic syndrome (MDS). Subsequent investigations revealed elevated serum methylmalonic acid (MMA) levels, leading to a revised diagnosis of vitamin B12 deficiency. Both patients showed positive responses to adequate vitamin B12 supplementation. Conclusion: Our case series highlights the importance of ruling out alternative causes of dysplasia in MDS when solely morphological abnormalities are observed on a bone marrow biopsy. It also underscores the crucial aspect of assessing MMA and homocysteine levels in individuals with normal vitamin B12 levels when there is a high clinical suspicion of B12 deficiency.

Internal Medicine
Mahmood A, Ray R, Bin Salam SST, Haque F, Akkaldevi J, Masmoum MD, Hassan MS, Essani B, Anjum T, and Mirza MSS. The Effectiveness of Cardiac Rehabilitation Programs in Improving Cardiovascular Outcomes: Systematic Review and Meta-Analysis. *Cureus* 2024; 16(10):e72450. PMID: 39600765. Request Article

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Cardiovascular diseases (CVDs) are some of the most common conditions and the major contributors to death and disability globally, hence the need for proper secondary prevention interventions. Cardiac

rehabilitation (CR) programs have been recognized as an essential component in the treatment of CVDs with the goal of decreasing the risk of new cardiovascular events and improving the quality of life. This systematic review and meta-analysis sought to determine the impact of CR as a form of CVD treatment on mortality, morbidity, functional capacity, and quality of life amongst the patient population. The search resulted in 12 studies that fulfilled the inclusion criteria, which included both randomized controlled trials as well as cohort studies. The meta-analysis, therefore, showed that the CR program is effective in reducing all-cause mortality (RR=0 74, 95% CI: 0.62-0. Favorable effects of intervention regarding participation measures were found in the International Classification of Functioning, Disability and Health (ICF) domains of body functions (pool standardized mean differences (SMD)= 0.55, 95% CI: 0.43-0.68). The results confirm the significance of CR programs as an essential element of secondary prevention of CVDs, stressing the ability of CR to lower mortality rates and improve patients' functional status. Despite this, the implementation of CR programs continues to be suboptimal globally for various healthcare facilities; hence the requirement for interventions to ensure that more patients incorporate the protocols and adapt uniform CR protocols.

Internal Medicine

Manivannan A, Pillai A, Liapakis A, Parikh ND, Kumar V, Verna EC, **Salgia R**, **Wu T**, **Lu M**, and **Jesse MT**. Influence of Acuity Circles on Hepatocellular Carcinoma and the Interaction of Gender and Race in Liver Transplantation. *Clin Transplant* 2024; 38(12):e70045. PMID: 39620868. Full Text

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The impact of liver transplant allocation policy using acuity circles (ACs) on interactions between race and gender on waitlist mortality or receipt of deceased donor liver transplant (DDLT) is unknown. Using data from the United Network for Organ Sharing (UNOS), we examined adults listed for DDLT from April 3, 2017, to October 4, 2022 (30 months pre- and post-AC). Fine-Gray sub-distribution hazard model explored AC indicators by race and gender interactions and their effect on receipt of DDLT or waitlist mortality. Also explored was AC's impact on hepatocellular carcinoma (HCC) diagnosis and receipt of DDLT or waitlist mortality. 59 592 patients (30 202 pre-AC, 29 390 post-AC) included. For both receipt of DDLT and waitlist mortality, there were no 3-way (AC by race by gender) interactions, indicating that the effects of race and gender on DDLT or waitlist mortality were consistent pre- and post-AC. Irrespective of AC implementation, Black and Hispanic women were less likely to receive DDLT and had an increased risk of waitlist mortality compared to White women. White, Black, and Hispanic men had lower waitlist mortality risk and greater likelihood of receiving DDLT compared to their female race/ethnic counterparts. Patients with HCC had a significantly greater chance for DDLT than non-HCC, although post-AC this effect was attenuated. Patients with HCC were also at greater risk of waitlist mortality pre- and post-AC compared to those without HCC however, the waitlist mortality post-AC was attenuated only for those patients without HCC. To our knowledge, this is the first study to show the interaction of gender and race on waitlist mortality and access to transplantation since the implementation of AC, showing continued disparate outcomes for women both within and across racial groups.

Internal Medicine

Schwartz B, **Klamer K**, **Zimmerman J**, **Kale-Pradhan PB**, and **Bhargava A**. Multidrug Resistant Pseudomonas aeruginosa in Clinical Settings: A Review of Resistance Mechanisms and Treatment Strategies. *Pathogens* 2024; 13(11). PMID: 39599528. Full Text

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Pseudomonas aeruginosa is causing increasing concern among clinicians due to its high mortality and resistance rates. This bacterium is responsible for various infections, especially in hospital settings, affecting some of the most vulnerable patients. Pseudomonas aeruginosa has developed resistance through multiple mechanisms, making treatment challenging. Diagnostic techniques are evolving, with rapid testing systems providing results within 4-6 h. New antimicrobial agents are continuously being developed, offering potential solutions to these complex clinical decisions. This article provides a review of the epidemiology, at-risk populations, resistance mechanisms, and diagnostic and treatment options for Pseudomonas aeruginosa.

Internal Medicine
Shahzil M, **Chaudhary AJ**, Kashif T, Qureshi AA, Muhammad A, Khan F, **Faisal MS**, Khaqan MA, Ali H, **Dababneh Y**, and **Moonka D**. Switching to Tenofovir Therapy Versus Continuation of Entecavir for Patients With Hepatitis B Virus Infection: A Systematic Review and Meta-Analysis. *JGH Open* 2024; 8(11):e70055. PMID: 39588267. Full Text

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BACKGROUND: Hepatitis B virus (HBV) infection causes liver disease, including hepatocellular carcinoma. Controlling viral activity is crucial to reducing complications. Tenofovir may offer benefits over entecavir, but it is unclear if switching from entecavir to tenofovir improves outcomes. This study assesses the clinical impact of switching to tenofovir therapy for chronic HBV infection. METHODS: Following the PRISMA guidelines, we conducted a literature search within the Cochrane Library, PubMed, MEDLINE, Embase, and Scopus for studies of patients with HBV infection who were switched to tenofovir from entecavir or were maintained on entecavir. Both formulations of tenofovir, that is, tenofovir disoproxil fumarate and tenofovir alafenamide were included and analyzed in subgroup analysis. Meta-analyses were performed with RevMan 5.4 using a random-effects model, with statistical significance set at $p < 0.05$. RESULTS: A total of eight studies, comprising 833 patients, were included in the meta-analysis. Tenofovir showed a significantly higher likelihood of achieving complete virological response (RR 5.60; 95% CI 3.51-8.94; $p < 0.00001$) and a greater reduction in HBV DNA levels (MD -1.03 log IU/mL; 95% CI -1.69 to -0.36; $p = 0.002$) compared to entecavir. However, there was no significant difference in HBsAg reduction or HBeAg seroconversion between the two groups. ALT reductions were not statistically significant overall, although entecavir showed better outcomes in subgroup analysis. CONCLUSION: Switching from entecavir to tenofovir improves virological response and reduces HBV DNA levels, but shows no significant advantage in HBsAg reduction, HBeAg seroconversion, or overall, ALT reduction.

Internal Medicine
Shahzil M, **Chaudhary AJ**, Qureshi AA, Hasan F, **Faisal MS**, Sohail A, Khaqan MA, **Jamali T**, **Khan MZ**, **Alsheik E**, and **Zuchelli T**. Endoscopic Full-Thickness Plication for the Treatment of Gastroesophageal Reflux Disease: A Systematic Review and Meta-Analysis of Randomized Sham Controlled Trials. *JGH Open* 2024; 8(11):e70056. PMID: 39605898. Full Text

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INTRODUCTION: Gastroesophageal reflux disease (GERD) affects approximately 20% of adults in the United States. Proton pump inhibitors are the first-line treatment but are associated with long-term side effects. Endoscopic full-thickness plication (EFTP) is a minimally invasive alternative that improves the valvular mechanism of the gastroesophageal junction. This meta-analysis compared EFTP to a sham procedure for the treatment of refractory GERD. MATERIALS AND METHODS: This meta-analysis followed the Cochrane guidelines and PRISMA standards and was registered with PROSPERO (CRD42023485506). We searched MEDLINE, Embase, SCOPUS, and Cochrane Library through December 2023. Inclusion criteria targeted Randomized controlled trials comparing EFTP with sham procedures for GERD were included. Statistical analyses utilized RevMan with a random-effects model, and the results were considered significant at $p < 0.05$. RESULTS: Of the 2144 screened studies, three RCTs with 272 patients with GERD were included: 136 patients underwent EFTP and 136 underwent sham procedures. Primary outcomes showed a significant reduction in PPI usage (RR 0.51; 95% CI 0.35-0.73; $p < 0.01$) and more than 50% improvement in GERD-HRQL scores at 3 months (RR 15.81; 95% CI 1.40-178.71; $p = 0.03$). No significant difference was found in the DeMeester scores (MD: 12.57; 95% CI -35.12 to 9.98; $p = 0.27$). Secondary outcomes showed no significant difference in time with esophageal $pH < 4$, but a significant reduction in total reflux episodes. CONCLUSIONS: EFTP significantly reduced PPI usage, improved GERD-HRQL scores, and decreased total reflux episodes compared with sham procedures, highlighting its potential as a minimally invasive treatment. Further research is needed to compare EFTP with other minimally invasive techniques to determine the most effective treatment option.

Internal Medicine

Sohail A, **Chaudhary AJ**, Bhinder MM, Zahid K, and Brown K. Readmission Rate, Predictors, Outcomes, and Burden of Readmission of Hepatorenal Syndrome in the United States: A Nationwide Analysis. *JGH Open* 2024; 8(11):e70062. PMID: 39600414. Full Text

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BACKGROUND: Nationwide US data on readmission rates for patients with cirrhosis admitted with hepatorenal syndrome (HRS) is lacking. We reviewed 30-day readmission rates after HRS-related hospitalizations, the associated predictors of readmissions, and their impact on resource utilization and mortality in the United States. METHODS: We identified all adults admitted with HRS between 2016 and 2019 using the Nationwide Readmission database of the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project. The primary outcome was all-cause 30-day readmission rate. Secondary outcomes were inpatient mortality rate, predictors of readmission, and resource utilization. RESULTS: We identified 245 850 hospitalizations of patients admitted for HRS in the United States from 2016 to 2019. Of these, 214 890 met the inclusion criteria. Mean age was 59.16 years, and 61.31% were males. Medicare was the most common primary payer (44.82%) followed by Medicaid (25.58%). The readmission rate was 24.6% within 30 days of discharge from index hospitalization. The most common cause of readmission was alcoholic cirrhosis with ascites (14.87%), followed by sepsis (9.32%) and unspecified hepatic failure (9%). The in-hospital mortality rate for index hospitalization was 29.52% and 14.35% among those readmitted within 30 days. The mean length of stay (12.33 days vs. 7.15 days, $p < 0.01$) and hospitalization costs ($44 903 vs. $22 353, $p < 0.01$) were higher for index hospitalizations than readmissions. CONCLUSIONS: Our study demonstrated that all-cause 30-day readmission and in-hospital mortality rates after the development of HRS were strikingly high. This warrants health policies and interventions at the institutional level, including close post-hospital discharge follow-up, to decrease readmission rates, improve patient outcomes, and reduce cost burden.

Internal Medicine

Tarar ZI, Farooq U, Inayat F, Basida SD, Ibrahim F, Gandhi M, Nawaz G, Afzal A, **Chaudhary AJ**, Kamal F, Ali AH, and Ghouri YA. Statins decrease the risk of hepatocellular carcinoma in metabolic dysfunction-associated steatotic liver disease: A systematic review and meta-analysis. *World J Exp Med* 2024; 14(4):98543. PMID: 39713070. Full Text

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BACKGROUND: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a leading cause of chronic liver disease with a significant risk of developing hepatocellular carcinoma (HCC). Recent clinical evidence indicates the potential benefits of statins in cancer chemoprevention and therapeutics. However, it is still unclear if these drugs can lower the specific risk of HCC among patients with MASLD. AIM: To investigate the impact of statin use on the risk of HCC development in patients with MASLD. METHODS: A systematic review and meta-analysis of all the studies was performed that measured the effect of statin use on HCC occurrence in patients with MASLD. The difference in HCC risk between statin users and non-users was calculated among MASLD patients. We also evaluated the risk difference between lipophilic versus hydrophilic statins and the effect of cumulative dose on HCC risk reduction. RESULTS: A total of four studies consisting of 291684 patients were included. MASLD patients on statin therapy had a 60% lower pooled risk of developing HCC compared to the non-statin group [relative risk (RR) = 0.40, 95%CI: 0.31-0.53, I (2) = 16.5%]. Patients taking lipophilic statins had a reduced risk of HCC (RR = 0.42, 95%CI: 0.28-0.64), whereas those on hydrophilic statins had not shown the risk reduction (RR = 0.57, 95%CI: 0.27-1.20). The higher (> 600) cumulative defined daily doses (cDDD) had a 70% reduced risk of HCC (RR = 0.30, 95%CI: 0.21-0.43). There was a 29% (RR = 0.71, 95%CI: 0.55-0.91) and 43% (RR = 0.57, 95%CI: 0.40-0.82) decreased risk in patients receiving 300-599 cDDD and 30-299 cDDD, respectively. CONCLUSION: Statin use lowers the risk of HCC in patients with MASLD. The higher cDDD and lipophilicity of statins correlate with the HCC risk reduction.

Nephrology

Baik I, **Jantz A**, **Poparad-Stezar A**, **Venkat D**, **Khoury N**, **Samaniego-Picota M**, **Gonzalez HC**, and **Fitzmaurice MG**. Evaluating the use of glucagon-like peptide-1 receptor agonists in a matched cohort of kidney and liver transplant recipients. *J Pharm Pract Res* 2024. PMID: Not assigned. Full Text

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Background: Diabetes mellitus (DM) and obesity are common among solid organ transplant recipients, but are associated with an increased risk of graft failure. Aim: Although glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are effective for managing both conditions in the general population, there is limited evidence regarding their use among transplant recipients. Method: The effect of GLP-1 RAs on post-transplant glucose control (defined as haemoglobin A1c [HbA1c]) among 37 liver and kidney transplant patients was compared to a control cohort. Secondary outcomes included change in total daily insulin requirements and oral DM agents, estimated glomerular filtration rate (eGFR), weight, and body mass index (BMI). Adverse events attributed to GLP-1 RAs, hypoglycaemia, incidence of pancreatitis,

biopsy-proven acute rejection, graft loss, and death were assessed. Ethical approval was granted by the Henry Ford Health Institutional Review Board (Reference no: 15959) and the study conforms with the US Federal Policy for the Protection of Human Subjects. Results: We observed that patients receiving GLP-1 RAs had a median reduction in HbA1c of 0.5% and reduction in insulin and oral anti-DM agents compared to the control group without GLP-1 RAs. There were statistically significant reductions in both weight and BMI in the GLP-1 RA group. Our observed incidence of adverse events was similar to previous literature. Unlike other smaller studies, a decline in eGFR was observed in the GLP-1 RA group. There were no differences in incidence of biopsy-proven acute rejection, graft loss, or death. Conclusion: When compared to patients without GLP-1 RA therapy, GLP-1 RAs modestly reduced HbA1c and insulin requirements and statistically reduced weight/BMI review at 6 months. GLP-1 RAs, even if initiated early post-transplant, were seemingly safe and effective. Larger, prospective studies are warranted to evaluate the safety and efficacy of GLP-1 RAs in this population.

Nephrology

Garcia Valencia OA, Thongprayoon C, Jadlowiec CC, Mao SA, Miao J, Leeaphorn N, Suppadungsuk S, Csongradi E, Budhiraja P, **Khoury N**, Vaitla P, and Cheungpasitporn W. Navigating pancreas transplant perceptions: assessing public sentiment and strategies using AI-driven analysis. *Front Digit Health* 2024; 6:1453341. PMID: 39679143. Full Text

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BACKGROUND: Pancreas transplantation, a crucial treatment for diabetes, is underutilized due to its invasiveness, strict criteria, organ scarcity, and limited centers. This highlights the need for enhanced public education and awareness through digital health platforms. METHODS: We utilized Google's AI-driven, consensus-based model and Claude AI 3.0 Opus by Anthropic to analyze public perceptions of pancreas transplantation. The top 10 websites identified by Google as of April-May 2024 were reviewed, focusing on sentiment, consensus, content readability, and complexity to develop strategies for better public engagement and understanding using digital health technologies. RESULTS: The top 10 websites, originating from the US and UK, showed a neutral and professional tone, targeting medical professionals and patients. Complex content was updated between 2021 and 2024, with a readability level suitable for high school to early college students. AI-driven analysis revealed strategies to increase public interest and understanding, including incorporating patient stories, simplifying medical jargon, utilizing visual aids, emphasizing quality of life improvements, showcasing research progress, facilitating patient outreach, promoting community engagement, partnering with influencers, and regularly updating content through digital health platforms. CONCLUSION: To increase interest in pancreas transplantation in the era of connected health, we recommend integrating real patient experiences, simplifying medical content, using visual explanations, emphasizing post-transplant quality-of-life improvements, highlighting recent research, providing outreach opportunities, encouraging community connections, partnering with influencers, and keeping information current through digital health technologies. These methods aim to make pancreas transplantation more accessible and motivating for a diverse audience, supporting informed decision-making.

Neurology

Elrefaey A, **Mohamedelkhair A**, Fahmy L, Affan M, **Schultz LR**, **Cerghet M**, and **Memon AB**. The clinical, diagnostic and treatment spectrum of seropositive and seronegative autoimmune encephalitis: Single-center cohort study of 51 cases and review of the literature. *Clin Exp Neuroimmunol* 2024; 15(4):186-200. PMID: Not assigned. Full Text

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Objective: Autoimmune encephalitis (AE) comprises a spectrum of inflammatory neurological syndromes characterized by immune responses to neuronal autoantigens, leading to diverse clinical manifestations, particularly behavioral and cognitive decline. Methods: This single-center retrospective study included 51 patients diagnosed with AE from 2013 to 2019 in a southeast Michigan tertiary care hospital. Patients were then divided into two groups, seropositive AE (AE+) and seronegative AE (AE−), based on antibody detection in the serum, cerebrospinal fluid or both when available. The study compares AE+ and AE− subtypes across clinical, diagnostic, and therapeutic parameters. Results: A total of 34 patients were classified as AE+, and 17 as AE−. Demographic analysis showed no significant differences in age, sex or race between the two groups. Clinical presentations varied widely, encompassing psychiatric symptoms, movement disorders, seizures and confusion; 24% patients had a prior malignancy. Laboratory assessments found diverse autoantibodies in AE+ patients' serum. Radiological and electrophysiological assessments showed no significant differences between the groups. AE− patients had higher rates of confusion compared with AE+ patients (59% vs. 18%, P = 0.004). Conclusions: This study focuses on the complexities associated with diagnosing AE, emphasizing the challenges posed by the heterogeneity of symptoms and often negative antibody test results. Rapid identification of AE, regardless of seropositivity or seronegativity, emerges as a critical factor for clinicians, facilitating the prompt initiation of immunotherapy and/or tumor removal if needed. These insights contribute to a better understanding of the landscape of this condition, offering clinicians the tools to refine their diagnostic and treatment strategies. Ultimately, the study aimed to enhance the management of AE, empowering healthcare professionals to make accurate and timely interventions for patients.

Neurology
Kelly BP, **Patel SC**, **Marin HL**, **Corrigan JJ**, **Mitsias PD**, and **Griffith B**. Autoimmune Encephalitis: Pathophysiology and Imaging Review of an Overlooked Diagnosis. *AJNR Am J Neuroradiol* 2024; 45(12):S55-s63. PMID: 39653432. Full Text

Neurology
Lee SY, Klingeborn M, Bulte JWM, Chiu DT, **Chopp M**, Cutler CW, Das S, Egwuagu CE, Fowler CD, Hamm-Alvarez SF, Lee H, Liu Y, Mead B, Moore TL, Ravindran S, Shetty AK, Skog J, Witwer KW, Djalilian AR, and Weaver AM. A perspective from the National Eye Institute Extracellular Vesicle Workshop: Gaps, needs, and opportunities for studies of extracellular vesicles in vision research. *J Extracell Vesicles* 2024; 13(12):e70023. PMID: 39665315. Full Text

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With an evolving understanding and new discoveries in extracellular vesicle (EV) biology and their implications in health and disease, the significant diagnostic and therapeutic potential of EVs for vision research has gained recognition. In 2021, the National Eye Institute (NEI) unveiled its Strategic Plan titled 'Vision for the Future (2021-2025),' which listed EV research as a priority within the domain of Regenerative Medicine, a pivotal area outlined in the Plan. In alignment with this prioritization, NEI organized a workshop inviting twenty experts from within and beyond the visual system. The workshop aimed to review current knowledge in EV research and explore gaps, needs and opportunities for EV research in the eye, including EV biology and applications of EVs in diagnosis, therapy and prognosis within the visual system. This perspective encapsulates the workshop's deliberations, highlighting the current landscape and potential implications of EV research in advancing eye health and addressing visual diseases.

Neurology

Li Y, **Zhang ZG**, **Chopp M**, **Liu Z**, **Golembieski W**, **Landschoot-Ward J**, **Zhang Y**, **Liu XS**, and **Xin H**.
Labeling and isolating cell specific neuronal mitochondria and their functional analysis in mice post stroke. *Exp Neurol* 2024; 385:115126. PMID: 39719208. Full Text

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Dendritic and axonal plasticity, which mediates neurobiological recovery after a stroke, critically depends on the mitochondrial function of neurons. To investigate, in vivo, neuronal mitochondrial function at the stroke recovery stage, we employed Mito-tag mice combined with cerebral cortical infection of AAV9 produced from plasmids carrying Cre-recombinase controlled by two neuronal promoters, synapsin-I (SYN1) and calmodulin-kinase IIa to induce expression of a hemagglutinin (HA)-tagged enhanced green fluorescence protein (EGFP) that localizes to mitochondrial outer membranes of SYN1 positive (SYN(+)) and CaMKIIa positive (CaMKIIa(+)) neurons. These mice were then subjected to permanent middle cerebral artery occlusion (MCAO) and sacrificed 14 days post stroke. Neuronal mitochondria were then selectively isolated from the fresh brain tissues excised from the ischemic core (IC), ischemic boundary zone (IBZ), as well as from the homologous contralateral hemisphere (CON) by anti-HA magnetic beads for functional analyses. We found that the bead pulled neuronal specific mitochondria were co-precipitated with GFP and enriched with mitochondrial markers, e.g. voltage-dependent anion channel, cytochrome C, and COX IV, but lacked the Golgi protein RCAS1 as well as endoplasmic reticulum markers: Heme-oxygenase 1 and Calnexin, indicating that specific neuronal mitochondria have been selectively isolated. Western-blot data showed that oxidative phosphorylation (OXPHOS) components in SYN(+) and CAMKII(+) neuronal mitochondria were significantly decreased in the IBZ and further decreased in the IC compared to the contralateral tissue, which was associated with the significant reductions of mitochondrial function indicated by oxygen consumption rate (OCR) ($p < 0.05$, respectively, for both neuron types). These data suggest dysfunction of neuronal mitochondria post stroke is present during the stroke recovery stage. Collectively, for the first time, we demonstrated that using a Mito-tag mouse line combined with AAV9 carrying Cre recombinase approach, neuronal specific mitochondria can be efficiently isolated from the mouse brain to investigate their functional changes post stroke.

Neurology
Osuala KO, Heyza J, Zhao Z, Xu Y, Moin K, **Ji K**, and Mattingly RR. Carcinoma-Associated Fibroblasts Accelerate Growth and Invasiveness of Breast Cancer Cells in 3D Long-Term Breast Cancer Models. *Cancers (Basel)* 2024; 16(22). PMID: 39594795. Full Text

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Background/Objectives: Carcinoma-associated fibroblasts (CAFs), a prominent cell type in the tumor microenvironment (TME), significantly contributes to cancer progression through interactions with cancer cells and other TME components. Consequently, targeting signaling pathways driven by CAFs has potential to yield new therapeutic approaches to inhibit cancer progression. However, the mechanisms underlying their long-term interactions with cancer cells in vivo remains poorly understood. Methods: To address this, we developed a three-dimensional (3D) parallel coculture model of human triple-negative breast cancer (TNBC) cells and CAFs using our innovative TAME devices. This model allowed for the analysis of TNBC paracrine interactions via their secretome over extended culture periods (at least 70 days). Results: Using TNBC cell lines (MDA-MB-231, MCF10.DCIS, and HCC70), we found that TNBC spheroids in 3D parallel cocultures with CAFs exhibited more pronounced invasive finger-like outgrowths than those in cocultures of TNBC cells and normal fibroblasts (NFs) over a period of 50-70 days. We also established that the CAF-derived secretome affects TNBC migration towards the CAF secretome region. Additionally, we observed a preferential migration of CAFs, but not NFs, toward TNBC spheroids. Conclusions: Overall, our results suggest that paracrine interactions between TNBC cells and CAFs enhance TNBC invasive phenotypes and promote reciprocal migration.

Neurology
Thangavel R, **Kaur H**, Dubova I, Selvakumar GP, **Ahmed ME**, Raikwar SP, Govindarajan R, and Kempuraj D. Parkinson's Disease Dementia Patients: Expression of Glia Maturation Factor in the Brain. *Int J Mol Sci* 2024; 25(2). PMID: 38256254. Full Text

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Parkinson's disease (PD) is the second most common progressive neurodegenerative disease characterized by the presence of dopaminergic neuronal loss and motor disorders. PD dementia (PDD) is a cognitive disorder that affects many PD patients. We have previously demonstrated the proinflammatory role of the glia maturation factor (GMF) in neuroinflammation and neurodegeneration in AD, PD, traumatic brain injury (TBI), and experimental autoimmune encephalomyelitis (EAE) in human brains and animal models. The purpose of this study was to investigate the expression of the GMF in the human PDD brain. We analyzed the expression pattern of the GMF protein in conjunction with amyloid plaques (APs) and neurofibrillary tangles (NFTs) in the substantia nigra (SN) and striatum of PDD brains using immunostaining. We detected a large number of GMF-positive glial fibrillary acidic protein (GFAP) reactive astrocytes, especially abundant in areas with degenerating dopaminergic neurons within the SN and striatum in PDD. Additionally, we observed excess levels of GMF in glial cells in the vicinity of APs, and NFTs in the SN and striatum of PDD and non-PDD patients. We found that the majority of GMF-positive immunoreactive glial cells were co-localized with GFAP-reactive astrocytes. Our findings suggest that the GMF may be involved in the pathogenesis of PDD.

Neurology
Zeidman LA. Robert Wartenberg and the Hallervorden Affair, 1953: A Clash Between Medical Ethics and Cold War Politics. *Neurology* 2025; 104(2):e210122. PMID: 39705629. Full Text

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Robert Wartenberg was an emigrant from Nazi Germany and an iconic pioneer in neurology, describing eponyms and helping to found and nurture the American Academy of Neurology. However, in 1953, ironically, he became embroiled in a controversial event regarding the German neuroscientist and Nazi collaborator Julius Hallervorden. Wartenberg attempted to convince the Dutch delegation to attend the International Neurological Congress in Lisbon from which they had withdrawn in response to Hallervorden's inclusion as a speaker. In addition, he rallied neuroscientists worldwide to help convince the Dutch, largely ignoring and burying their concerns about Hallervorden's ethical transgressions. In numerous letters, Wartenberg wanted to both ignore and exonerate Hallervorden of ethical violations in collecting 700 brains from patients murdered in the Nazi euthanasia program. Wartenberg's unexpected defense of Hallervorden, despite not knowing him professionally, purportedly was to reintegrate German neuroscience to the international community and to create Western "unity" against communism. However, Wartenberg's efforts and the lack of international censure against Hallervorden prevented proper attention to the victims' brains that remained in Hallervorden's collection for decades and the use of these brains in scientific publications. Those who stood against Hallervorden have been vindicated by history, but work remains to uncover all brain specimens in German collections. Wartenberg's misguided and shortsighted involvement in this affair serves as a lesson for future generations of neurologists in the consequences of ignoring ethical concerns for expediency and politics.

Neurology

Zeidman LA, Levine T, and Cangelosi J. Small-Vessel Vasculitis or Perifolliculitis in Small-Fiber Neuropathy With TS-HDS, FGFR-3, or Plexin D1 Antibodies. *J Clin Neuromuscul Dis* 2024; 26(2):63-69. PMID: 39590924. Full Text

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INTRODUCTION: Small-fiber neuropathy (SFN) is highly prevalent but often idiopathic. TS-HDS, FGFR-3, and Plexin D1 autoantibodies (seropositive) may be present in more than 40% of idiopathic cases. Another autoimmune biomarker is a non-length-dependent (NLD) skin biopsy pattern. Our goal was to demonstrate that small-vessel vasculitis and perifolliculitis (inflammation) on skin biopsies are additional biomarkers. METHODS: All pure SFN skin biopsy reports were reviewed for inflammation, and their charts were examined for other relevant history. RESULTS: Seven of 80 patients with pure SFN had inflammation (8.8%); 5 patients were female (71%) and 2 were male (29%); average age was 45 (16-67). All 7 patients with inflammation were seropositive (100%, P = 0.0495), and 6 patients (86%) had either NLD inflammation or NLD pathology (P = 0.0003). DISCUSSION: Inflammation is present only in a small portion of punch biopsies, but may be another autoimmune SFN biomarker. It is strongly associated with seropositivity and NLD-pathology. Further studies are likely indicated to assess inflammation pathophysiology and immunotherapy responsiveness.

Neurosurgery

Akbari H, Bakas S, Sako C, Fathi Kazerooni A, Villanueva-Meyer J, Garcia JA, Mamourian E, Liu F, Cao Q, Shinohara RT, Baid U, Getka A, Pati S, Singh A, Calabrese E, Chang S, Rudie J, Sotiras A, LaMontagne P, Marcus DS, Milchenko M, Nazeri A, Balana C, Capellades J, Puig J, Badve C, Barnholtz-Sloan JS, Sloan AE, Vadmal V, Waite K, Ak M, Colen RR, Park YW, Ahn SS, Chang JH, Choi YS, Lee SK, Alexander GS, Ali AS, Dicker AP, Flanders AE, Liem S, Lombardo J, Shi W, Shukla G, **Griffith B**, **Poisson LM**, **Rogers LR**, Kotrotsou A, Booth TC, Jain R, Lee M, Mahajan A, Chakravarti A, Palmer JD, DiCostanzo D, Fathallah-Shaykh H, Cepeda S, Santonocito OS, Di Stefano AL, Wiestler B, Melhem ER, Woodworth GF, Tiwari P, Valdes P, Matsumoto Y, Otani Y, Imoto R, Aboian M, Koizumi S, Kurozumi K, Kawakatsu T, Alexander K, Satgunaseelan L, Rulseh AM, Bagley SJ, Bilello M, Binder ZA, Brem S, Desai AS, Lustig RA, Maloney E, Prior T, Amankulor N, Nasrallah MLP, O'Rourke DM, Mohan S, and Davatzikos C. Machine Learning-based Prognostic Subgrouping of Glioblastoma: A Multi-center Study. *Neuro Oncol* 2024; Epub ahead of print. PMID: 39665363. Full Text

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BACKGROUND: Glioblastoma is the most aggressive adult primary brain cancer, characterized by significant heterogeneity, posing challenges for patient management, treatment planning, and clinical trial stratification. METHODS: We developed a highly reproducible, personalized prognostication and clinical subgrouping system using machine learning (ML) on routine clinical data, MRI, and molecular measures from 2,838 demographically diverse patients across 22 institutions and 3 continents. Patients were stratified into favorable, intermediate, and poor prognostic subgroups (I, II, III) using Kaplan-Meier analysis (Cox proportional model and hazard ratios [HR]). RESULTS: The ML model stratified patients into distinct prognostic subgroups with HRs between subgroups I-II and I-III of 1.62 (95%CI: 1.43-1.84, p<0.001) and 3.48 (95%CI: 2.94-4.11, p<0.001), respectively. Analysis of imaging features revealed several tumor properties contributing unique prognostic value, supporting the feasibility of a generalizable prognostic classification system in a diverse cohort. CONCLUSIONS: Our ML model demonstrates extensive reproducibility and online accessibility, utilizing routine imaging data rather than complex

imaging protocols. This platform offers a unique approach for personalized patient management and clinical trial stratification in glioblastoma.

Neurosurgery
Chaker AN, **Melhem M**, **Kagithala D**, **Telemi E**, **Mansour TR**, Simo L, **Springer K**, **Schultz L**, **Jarabek K**, **Rademacher AF**, **Brennan M**, **Kim E**, **Nerenz DR**, Khalil JG, Easton R, Perez-Cruet M, Aleem I, Park P, Soo T, Tong D, **Abdulhak M**, **Schwalb JM**, and **Chang V**. A propensity score-matched comparison between single-stage and multistage anterior/posterior lumbar fusion surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2024; 1-8. Epub ahead of print. PMID: 39705706. Full Text

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OBJECTIVE: Patients undergoing anterior/posterior lumbar fusion surgery can undergo either a single-stage or multistage operation, depending on surgeon preference. The goal of this study was to assess different patient outcomes between single-stage and multistage lumbar fusion procedures in a multicenter setting. METHODS: The Michigan Spine Surgery Improvement Collaborative database was queried for anterior/posterior lumbar fusion surgeries between July 2018 and January 2022. Patients who underwent either single-stage or multistage procedures were included. For multistage procedures, the first surgery included both anterior lumbar interbody fusions and lateral lumbar interbody fusions. Primary outcomes included postoperative complications and improvement in patient-reported outcomes: Patient-Reported Outcomes Measurement Information System Physical Function, EQ-5D, and satisfaction. The two cohorts were propensity score matched, while Poisson generalized estimating equation models were used for multivariate analyses. RESULTS: After one-to-one propensity score matching, 355 patients were identified in the single-stage and multistage cohorts. Single-stage procedures were associated with a lower risk of complications ($p = 0.024$), fewer emergency department visits ($p = 0.029$), and higher patient satisfaction after 1 year ($p = 0.026$) and 2 years ($p = 0.007$), compared with multistage procedures. After adjusting for baseline patient and operative characteristics, patients undergoing multistage procedures had a higher risk of complications (relative risk [RR] 1.17, 95% CI 1.02-1.34; $p = 0.026$), were less likely to be satisfied after 1 year (RR 0.83, 95% CI 0.74-0.93; $p < 0.001$), and were less likely to experience improvement in back pain after 90 days (RR 0.86, 95% CI 0.75-0.99; $p = 0.039$) and 2 years (RR 0.76, 95% CI 0.60-0.96; $p = 0.023$). CONCLUSIONS: The authors observed that patients who undergo lumbar fusion surgery using a multistage approach have higher postoperative complication rates and are less likely to report satisfaction compared with a matched, single-stage procedure cohort.

Neurosurgery
Griepp DW, **Caskey J**, Bunjaj A, **Turnbull J**, **Alsalahi A**, **Alexander H**, **Dragonette J**, **Sarcar B**, **Desai S**, **Tong D**, **Soo TM**, **Bono P**, **Kelkar P**, **Houseman C**, **Claus CF**, **Richards BF**, and **Carr DA**. Irradiation safety, anesthesia time, surgical complications, and patient-reported outcomes in the robotic Mazor X versus fluoroscopy guided minimally invasive transforaminal lumbar interbody fusion surgery: a comparative cohort study. *Neurosurg Focus* 2024; 57(6):E11. PMID: 39616637. Full Text

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OBJECTIVE: Robot-assisted (RA) technology is becoming more widely integrated and accepted in spine surgery. The authors sought to evaluate operative and patient-reported outcomes (PROs) in RA versus fluoroscopy-assisted (FA) pedicle screw placement during minimally invasive surgery (MIS) transforaminal lumbar interbody fusion (TLIF). METHODS: The authors retrospectively studied elective patients who underwent single- or multilevel MIS TLIF for degenerative indication using FA versus RA pedicle screw placement. Patients were selected from September 2021 to May 2023 at a single institution with multiple surgeons whose practice consists of primarily MIS. Outcomes included fluoroscopy dosage per screw, operative time per screw, anesthesia time per screw, estimated blood loss (EBL), screw revision rate, inpatient surgical complications, and minimal clinically important difference (MCID) of Oswestry Disability Index (ODI) and numeric rating scale (NRS) scores at the 6- and 12-month follow-ups. Comparability of groups was analyzed by univariate analysis. Multivariable analysis modeling fluoroscopy time per screw was performed, adjusting for confounders. RESULTS: One hundred eighty-three patients (n = 133 in the FA group vs 50 in the RA group) were included. Patients in the RA cohort were significantly younger than those in the FA group (mean age 63.8 ± 11.9 vs 59.8 ± 11.0 years, p = 0.037). A total of 932 pedicle screws were placed (mean 5.1, range 4-8 per patient). The RA cohort demonstrated significantly lower intraoperative fluoroscopy dosage per screw (4.9 ± 7.6 mGy per screw vs 20.3 ± 14.0 mGy per screw, p < 0.001), significantly longer anesthesia time per screw (49.1 ± 12.6 vs 43.6 ± 9.2, p = 0.009), and similar operative time per screw (33.3 vs 30.7 minutes, p = 0.125). The screw revision rate for symptomatic radiculopathy was zero in both groups. Revision surgery requiring screw removal or reposition was performed in 4 total cases (RA group: 1/50 for infection; FA group: 2/133 for infection, 1/133 for foraminotomy). Both groups demonstrated significant improvement in PROs at 6 and 12 months compared with preoperatively. Moreover, both groups achieved MCID at similar rates. CONCLUSIONS: When implementing RA technology, one can expect similar perioperative outcomes as FA techniques in addition to significantly lower radiation exposure. Moreover, there is no statistically significant difference in postoperative PROs between RA and FA. Longer anesthesia times may also be encountered, as in this study, which is likely a result of more complex robotic setup and workflow.

Neurosurgery

Mendez JS, Cohen AL, Eckenstein M, Jensen RL, Burt LM, Salzman KL, Chamberlain M, Hsu HH, Hutchinson M, Iwamoto F, Ligon KL, Mrugala MM, Pelayo M, Plotkin SR, Puduvalli VK, Raizer J, Reardon DA, Sterba M, **Walbert T**, West BL, Wong ET, Zhang C, and Colman H. Phase 1b/2 study of orally administered pexidartinib in combination with radiation therapy and temozolomide in patients with newly diagnosed glioblastoma. *Neurooncol Adv* 2024; 6(1):vdae202. PMID: 39734810. Full Text

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BACKGROUND: Glioblastoma (GBM) has a median survival of <2 years. Pexidartinib (PLX3397) is a small-molecule inhibitor of CSF1R, KIT, and oncogenic FTL3, which are implicated in GBM treatment resistance. Results from glioma models indicate that combining radiation therapy (RT) and pexidartinib reduces radiation resistance. We added pexidartinib to standard-of-care RT/temozolomide (TMZ) in patients with newly diagnosed GBM to assess the therapeutic benefit of altering the tumor microenvironment with pexidartinib. METHODS: In this open-label, dose-escalation, multicenter, Phase 1b/2 trial, pexidartinib was administered in combination with RT/TMZ followed by adjuvant pexidartinib + TMZ. During Phase 1b, pexidartinib was given 5 or 7 days/week at multiple dosing levels. The primary Phase 1b endpoint was the recommended Phase 2 dose (RP2D). Phase 2 patients received the RP2D with the primary endpoint of median progression-free survival (mPFS). Secondary objectives were median overall survival (mOS), pharmacokinetics, and safety. RESULTS: The RP2D of pexidartinib was 800 mg/day for 5 days/week during RT/TMZ, followed by 800 mg/day for 7 days/week with adjuvant TMZ. mPFS was 6.7 months (90% CI: 4.5, 11.5) for the modified intention-to-treat population. The actual mOS was 13.1 months (90% CI: 11.5, 24.5), and the mOS corrected for comparison with matched historical controls was 18.8 months (95% CI: 12.6, 28.0). CONCLUSIONS: This trial established the RP2D of pexidartinib in combination with RT/TMZ and adjuvant TMZ. Pexidartinib was generally safe and well tolerated. Although the study regimen with pexidartinib was not efficacious, pharmacodynamic studies showed modulation of systemic markers that could lead to alteration of the tumor microenvironment.

Neurosurgery

Sajan A, **Griepp DW**, and Isaacson AJ. Variation in Cone Beam Computed Tomography Utilization and Radiation Exposure Associated with Prostatic Artery Embolization on Two Separate Angiography Systems. *J Clin Med* 2024; 13(23). PMID: 39685861. Full Text

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Background: We aimed to compare cone beam computed tomography (CBCT) utilization and radiation exposure during prostatic artery embolization (PAE) procedures on two different angiography systems. Methods: PAEs performed by a single interventionalist between January 2018 and October 2020 on two multivendor angiography systems (AS1 and AS2) at a single center were retrospectively evaluated. Imaging techniques included CBCT acquisition when possible, predominantly from the distal aorta in AS1 and from the bilateral internal iliac arteries in AS2 (Discovery IGS 740, GE HealthCare, Chicago, IL). Baseline demographics, CBCT utilization and radiation doses, and total procedure radiation metrics for each group were collected and compared. Results: One hundred and twenty patients were analyzed in this study, with fifty-three patients (n = 25 in AS1, 28 in AS2) included as embolized bilaterally using CBCT. CBCT was acquired in 31% of the cases in AS1 and in 85% of the cases in AS2. Mean prostate volume was similar in both groups (103.0 mL vs. 130.1 mL, p = 0.23). There was no difference in fluoroscopy time, while the number of DSA series and CBCTs per case did differ in AS1 and AS2 (37.3 min vs. 32.1 min, p = 0.13, 19.8 vs. 8.0, p ≤ 0.001, 1.3 vs. 2.1 p ≤ 0.001). The mean total air kerma, total kerma area product and air kerma per CBCT were higher in AS1 compared to AS2 (2020.4 mGy vs. 490.3 mGy, p ≤ 0.001, 259.3 Gy*cm(2) vs. 72.7 Gy*cm(2), p ≤ 0.001 and 217.8 mGy vs. 45.8 mGy, p ≤ 0.001 respectively). To prevent confounding from a mean difference in body mass index, the data were adjusted using log outcome means, which corroborated the raw data findings. Conclusions: The mean procedural total kerma area product from AS1 was similar to that reported in other PAE studies, but it was substantially lower in AS2. The angiography system used has a significant impact on the ability to leverage CBCT and on overall patient and thus staff radiation exposure.

Neurosurgery

Tracz JA, **Farmer ML**, Hughes M, Mukherjee D, and Brennan PM. Return to play following craniotomy for non-traumatic brain lesions. *World Neurosurg X* 2025; 25:100409. PMID: 39403179. Full Text

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OBJECTIVE: Return to play (RTP) decisions after cranial surgery are important to patients. Most published data relate to RTP following sports-related brain injury. This study investigated factors that influence neurosurgical RTP decision-making following craniotomy for non-traumatic brain lesions. METHODS: A patient scenario-based survey was distributed to U.S. and Europe-based neurosurgeons via the American Association of Neurological Surgeons/Congress of Neurological Surgeons Tumor Section and the European Association of Neuro-Oncology. From one core patient scenario, 5 further scenarios were developed involving patients of varying age, sport preference, tumor pathology, and craniotomy approach. Respondents provided RTP recommendations and factors important in forming these recommendations. RESULTS: Forty-one responses were received; Europe (48%), U.S. (37%). The most commonly cited factors influencing RTP decision-making across scenarios were symptomatic recovery (85.4%), resolution of blood and/or air on imaging (43.4%), and patient demand (31.7%). The sports with the longest average RTP timeline were boxing (10.3 months), rugby (8.7 months), and American football (8.5 months) in the core patient scenario. Twenty-nine percent of neurosurgeons requested neuroimaging before determining RTP recommendations in this scenario, more commonly in America than Europe (46.7% and 5.0% respectively, p = .006). CONCLUSIONS: Although limited by sample size, the data provides a foundation to support development of a systematic approach to RTP decision-making following craniotomy for brain lesions of non-traumatic etiology. Future work to develop consensus guidelines will benefit from objective data about outcomes, particularly in relation to repeat imaging prior to RTP.

Obstetrics, Gynecology and Women's Health Services

Ahsan BU, **Paridon AA**, **Gaba AR**, **Zhang Z**, and **Azordegan N**. Prolapsed Epiploica of Colon Presenting as a Vaginal Polyp After Robotic Hysterectomy: A Case Report and Review of the Literature. *Am J Case Rep* 2024; 25:e944892. PMID: 39604203. Full Text

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BACKGROUND Hysterectomy is a gynecological procedure that can lead to complications arising from structural changes incurred during the surgical process. Vaginal nodules may appear at the vaginal cuff after hysterectomy, which could be indicative of recurring cancer, endometriosis, or formation of fistulae or granulation tissue. In rare instances, abdominal organ prolapse occurs after vaginal cuff dehiscence. Prolapse of the terminal ileum is the most common type of prolapse from vaginal cuff dehiscence, but prolapsed epiploica of colon after hysterectomy occurs in rare instances. Epiploic appendages are a type of fatty tissue attached to the colonic surface that can become inflamed or necrotic and detach from the colon. The purpose of this report is to describe a rare case of prolapsed epiploica of colon at the vaginal cuff. CASE REPORT A 55-year-old woman who had robot-assisted laparoscopic hysterectomy for endometrioid carcinoma presented with a vaginal polyp 2 months after surgery. Histological analysis of the excised polyp revealed adipose tissue with fat necrosis and calcification, indicative of prolapsed epiploica of colon. This is the first report of post-hysterectomy epiploica of colon at the vaginal cuff not associated with obvious dehiscence. CONCLUSIONS This case highlights the importance of thorough histological analysis of excised vaginal nodules and consideration of prolapsed epiploica of colon in the differential diagnoses in addition to benign and malignant vaginal neoplasms.

Obstetrics, Gynecology and Women's Health Services

Iannarino NT, Francis-Levin N, Corrao J, Stelmak D, Tan CY, Ellman E, Zhang A, Herrel LA, **Moravek MB**, Chugh R, Walling EB, and Zebrack BJ. Experts of their own experience: adolescent and young adult cancer patients' advice-giving as a coping mechanism. *J Commun Healthc* 2024; 1-10. Epub ahead of print. PMID: 39663816. Request Article

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BACKGROUND: To better understand informal coping strategies among adolescents and young adults (AYAs) with cancer, the current investigation asked AYA study participants to describe the 'advice' they would offer to hypothetical peers about coping following diagnosis. This study explores the utility of the single item 'advice' prompt for supportive oncology research and practice. METHODS: AYA cancer patients (n = 27) aged 12-25 years were recruited through electronic health record query at a single-institution health system. Participants completed semi-structured interviews. Inductive themes were described regarding advice about informal coping strategies following cancer diagnosis. The Institutional Review Board approved this study (HUM#00157267). RESULTS: Emergent advice themes included (1) attitude re/framing, (2) engage support network, and (3) self-advocacy. Participants advised cultivating a positive yet realistic attitude about the present and future. Reaching out to support network members and accepting help were advised, as was rebuffing unhelpful support. Participants also advocated for addressing medical information needs and building trusting relationships with clinicians. CONCLUSIONS: Soliciting AYA advice serves to identify informal coping mechanisms in response to life-stage-specific concerns. Future research is called to substantiate the utility of 'advice' as a single item tool for research and clinical questionnaires. Practice implications call for creating opportunities for AYAs to impart their advice to others (e.g. anonymous community message board) as a means of personal catharsis, altruistic service, and legitimizing AYAs as 'embodied' experts of their own experiences.

Ophthalmology and Eye Care Services

Trivedi V, Lee S, Lee PSY, Me R, You Q, Im J, Ross B, Tran DV, **Le KH**, Malbin B, and Lin X. Comparative Analysis of Effective Lens Position and Refractive Outcomes in Scleral-Fixated versus Intracapsular Intraocular Lenses. *Clin Ophthalmol* 2024; 18:3949-3955. PMID: 39737363. Full Text

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PURPOSE: To evaluate the outcomes of scleral-fixated intraocular lenses (IOLs) implanted using either Yamane technique or Gore-Tex suture fixation, in comparison to intracapsular lens fixation, and to assess the efficacy of various lens formulas in achieving predicted refractive targets. PATIENTS AND METHODS: This study included 45 eyes from 44 patients with scleral-fixated IOLs, comprising 37 Yamane eyes and 8 Gore-Tex eyes. Preoperative refractive predictions from various formulae were compared with final postoperative refraction. Outcomes assessed included effective lens position (ELP), postoperative predictive error, and changes in visual acuity. The ELP of scleral-fixated IOLs was compared with that of intracapsular IOLs in fellow eyes. RESULTS: Average ELP for Yamane IOLs was 0.62 mm more posterior relative to intracapsular IOLs but was not significantly different for Gore-Tex

IOLs. Average postoperative logMAR acuity change was significant at -1.30 (p=4.5x10(-11)) and -1.65 (p=5x10(-4)) for Yamane and Gore-Tex eyes, respectively. Mean prediction error for Yamane eyes was +0.29±1.3 D, -0.53±0.40 D, +0.80±1.4 D, and +0.43±1.4 D using Barrett Universal II, Holladay, Hill-RBF, and Hoffer QST formulas, respectively. Mean prediction error for Gore-Tex eyes was -0.37±1.24 D and +0.53±1.19 D using Barrett Universal II and Holladay formulas, respectively. CONCLUSION: Different scleral fixation techniques result in variations in ELP compared to intracapsular IOL placement. In our hands, when using the Yamane technique, surgeons should aim for a myopic refractive target to offset hyperopic errors when employing the Barrett Universal II, Hill-RBF, or Hoffer QST formulas, and a hyperopic target when using the Holladay formula. For Gore-Tex IOLs, a slightly hyperopic target is recommended to counter myopic error when using the Barrett Universal II formula, whereas a slightly myopic target is advised with the Holladay formula to offset hyperopic error. A limitation of our study is the small sample size for patients who underwent Gore-Tex suture fixation.

Orthopedics/Bone and Joint Center

Chougule A, **Zhang C**, **Denbow J**, **Vinokurov N**, **Mendez D**, **Vojtisek E**, and **Gardinier J**. P2Y(2) Inhibition Modifies the Anabolic Response to Exercise in Adult Mice. *Aging Cell* 2024; e14464. Epub ahead of print. PMID: 39741419. Full Text

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As the aging population continues to grow, the incidence of osteoporotic fractures increases and is compounded by our lack of therapeutic strategies that increase bone formation. Although exercise and physical activity play a key role in maintaining bone mass throughout our lives, the loads and exertion required to elicit an anabolic response becomes exceedingly difficult to achieve with age. Based on previous work, the P2Y(2) receptor offers a unique therapeutic target to increasing bone mass by modifying the mechanotransduction. Others have also shown P2Y(2) to have a negative effect on osteoblast function. However, the extent to which inhibiting P2Y(2) pharmaceutically improves bone mass or the mechanotransduction of bone remains unknown. Our central hypothesis for this study states that inhibiting P2Y(2) activity can enhance the anabolic response to loading in an aging population. To test this hypothesis, the anabolic response to exercise was examined by treating adult mice, which typically display a minimal response, with the P2Y(2) inhibitor AR-C118925XX (ARC). Our findings from this study demonstrate that ARC treatment of adult mice increases periosteal bone formation in response to exercise. The enhanced response to exercise was characterized by a reduction in osteocytes' induction of osteoclast activity. Endocortical bone formation also increased with treatment independently of exercise, providing gains in mechanical strength and tissue level properties. Overall, inhibiting P2Y(2) activation has a beneficial effect on bone formation and the anabolic response to loading, namely by limiting osteoclast activation.

Orthopedics/Bone and Joint Center

Jamshidi A, Espin-Garcia O, **Wilson TG**, **Loveless I**, Pelletier JP, Martel-Pelletier J, and **Ali SA**. MicroRNA signature for early prediction of knee osteoarthritis structural progression using integrated machine and deep learning approaches. *Osteoarthritis Cartilage* 2024; Epub ahead of print. PMID: 39617204. Full Text

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OBJECTIVE: Conventional methodologies are ineffective in predicting the rapid progression of knee osteoarthritis (OA). MiRNAs show promise as biomarkers for patient stratification. We aimed to develop a miRNA prognosis model for identifying knee OA structural progressors/non-progressors using integrated machine/deep learning tools. METHODS: Baseline serum miRNAs from OAI participants were isolated and sequenced. Participants were categorized based on their likelihood of knee structural progression/non-progression using MRI and X-ray data. For prediction model development, 152 OAI participants (91 progressors, 61 non-progressors) were used. MiRNA features were reduced through VarClusHi clustering. Key miRNAs and OA determinants (age, sex, BMI, race) were identified using seven machine learning tools. The final prediction model was developed using advanced machine/deep learning techniques. Model performance was assessed with AUC (95% confidence intervals) and accuracy. Monte Carlo cross-validation ensured robustness. Model validation used 30 OAI baseline plasma samples from an independent set of participants (14 progressors, 16 non-progressors). RESULTS: Feature clustering selected 107 miRNAs. Elastic Net was chosen for feature selection. An optimized prediction model based on an Artificial Neural Network (ANN) comprising age and four miRNAs (hsa-miR-556-3p, hsa-miR-3157-5p, hsa-miR-200a-5p, hsa-miR-141-3p) exhibited excellent performance (AUC, 0.94 [0.89, 0.97]; accuracy, 0.84 [0.77, 0.89]). Model validation performance (AUC, 0.81 [0.63, 0.92]; accuracy, 0.83 [0.66, 0.93]) demonstrated the potential for generalization. CONCLUSION: This study introduces a novel miRNA prognosis model for knee OA patients at risk of structural progression. It requires five baseline features, demonstrates excellent performance, is validated with an independent set, and holds promise for future personalized therapeutic monitoring.

Orthopedics/Bone and Joint Center

Jenkins SM, Elwell J, **Muh SJ**, Roche CP, Rogalski BL, Eichinger JK, and Friedman RJ. Comparing the Exactech Equinoxe reverse total shoulder arthroplasty for fracture versus degenerative conditions: 5-year minimum follow-up. *J Shoulder Elbow Surg* 2024; Epub ahead of print. PMID: 39510340. Full Text

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BACKGROUND/HYPOTHESIS: Reverse total shoulder arthroplasty (rTSA) has become the operative treatment of choice for acute proximal humerus fractures in the elderly population, but little data exist on the long-term outcomes or how they compare to rTSA done for degenerative conditions. The purpose of this study is to compare the clinical and radiographic outcomes of patients undergoing rTSA for acute fracture versus degenerative conditions with a minimum 5-year follow-up. METHODS: Data was extracted from an international registry of patients with the Exactech Equinoxe rTSA implant from 2007 to 2018. Patients with a minimum follow-up of 5 years were then split into fracture and degenerative cohorts and matched 1:3 based on age, sex, and follow-up duration. Clinical and radiographic outcomes were compared between the cohorts including range of motion, patient-reported outcome measures, visual analouge scale pain score, complication and revision rates, implant characteristics, and scapular notching. This data was analyzed using Welch's t-test, Fisher's exact test, or Wilcoxon rank sum test. RESULTS: There were 384 total patients included in the study, with 96 fractures and 288 degenerative. At a mean follow-up of 6.4 years, the degenerative cohort had significant improvements in all patient-reported outcome measures and range of motion, compared to their preoperative status. At the latest

follow-up, the mean American Shoulder and Elbow Surgeons score was 83 and the mean visual analouge scale pain score was 1.1 for both cohorts. Patients with degenerative indications had greater forward elevation which did not meet the minimally clinically important difference and greater internal rotation which did not meet the substantial clinical benefit threshold. Patient satisfaction was very high for both cohorts, with 97% in the degenerative cohort and 91% in the fracture cohort satisfied with the procedure (P = .276). Complication and revision rates were similar between the 2 cohorts. Patients in the fracture cohort had a larger glenosphere diameter (P = .045) and greater combined liner/tray offset (P = .05). Patients in the elective cohort more frequently required an augmented baseplate (P < .001). Scapular notching was 11% in the degenerative cohort and 9% in the fracture cohort (P = .82). CONCLUSION: This study demonstrates no significant differences in the clinical or radiographic outcomes at a minimum of 5 years follow-up for patients undergoing rTSA for acute fracture versus degenerative conditions. Patients undergoing rTSA for either indication have similar rates of complications, revisions, and scapular notching, with high patient satisfaction. Patients undergoing rTSA for an acute fracture can expect similar results to those undergoing rTSA for degenerative conditions at minimum 5-year follow-up.

Orthopedics/Bone and Joint Center
Jiang EX, and **Day CS**. Complications of Volar Versus Low-Profile Dorsal Plating of Distal Radius Fractures. *J Am Acad Orthop Surg* 2024; Epub ahead of print. PMID: 39602628. Full Text

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Distal radius fractures are one of the most common injuries of the upper extremity. Although nonsurgical management is common, surgical intervention, particularly using volar and dorsal plate fixation, is essential in a subset of injuries. Historically, dorsal plates were avoided due to a high rate of extensor tendon irritation and rupture. Volar locking plates were developed in the early 1990s and first published in 2000 to avoid the complications associated with dorsal plating and have since become widely considered the workhorse for most distal radius fractures. Despite advancements, both fixation methods are still associated with complications, warranting careful selection based on fracture patterns. The purpose of this review is to summarize the most recent literature on the complications associated with the use of volar and low-profile dorsal distal radius plates.

Orthopedics/Bone and Joint Center
Kazi O, Alvero AB, **Castle JP**, Vogel MJ, Boden SA, Wright-Chisem J, and Nho SJ. Demographic Disparities and Outcomes Following Hip Arthroscopy: Exploring the Impact of Social Determinants of Health in Femoroacetabular Impingement Syndrome. *J Bone Joint Surg Am* 2024; 106(23):2232-2240. PMID: 39630138. Full Text

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BACKGROUND: The purpose of this study was to explore the impact of social deprivation on preoperative characteristics and postoperative outcomes following hip arthroscopy (HA) for femoroacetabular impingement syndrome (FAIS). METHODS: Patients undergoing primary HA for FAIS were identified, and their social deprivation index (SDI) score was assigned on the basis of the provided ZIP code. Quartiles (Q1 to Q4) were established using national percentiles, with Q4 representing patients from the areas of greatest deprivation. Patient-reported outcomes (PROs) were collected preoperatively and at a minimum follow-up of 2 years. Achievement rates for clinically meaningful outcomes, including the minimal clinically important difference (MCID), patient acceptable symptom state (PASS), and substantial clinical benefit (SCB), were determined. The incidences of revision HA and conversion to total hip arthroplasty (THA) were recorded. SDI groups were compared with respect to preoperative characteristics and postoperative outcome measures. Predictors of MCID, PASS, and SCB achievement; revision HA; and conversion to THA were identified with use of multivariable logistic regression. RESULTS: In total, 2,060 hips were included, which had the following SDI distribution: Q1 = 955, Q2 = 580, Q3 = 281, and Q4 = 244. The composition of the included patients with respect to race and/or

ethnicity was 85.3% Caucasian, 3.8% African American, 3.7% Hispanic, 1.7% Asian, and 5.4% "other." Patients with more social deprivation presented at a later age and with a higher body mass index (BMI), a longer duration of preoperative hip pain, and greater joint degeneration ($p \leq 0.035$ for all). The most socially deprived groups had higher proportions of African American and Hispanic individuals, less participation in physical activity, and greater prevalences of smoking, lower back pain, and Workers' Compensation ($p \leq 0.018$ for all). PRO scores and achievement of the PASS and SCB were worse among patients from areas of greater social deprivation ($p \leq 0.017$ for all). Age, BMI, activity status, race and/or ethnicity classified as "other," SDI quartile, Workers' Compensation, preoperative back pain, duration of preoperative hip pain, and Tönnis grade were independent predictors of clinically meaningful outcome achievement, revision arthroscopy, and/or THA conversion ($p \leq 0.049$ for all). CONCLUSIONS: Individuals with more social deprivation demonstrated inferior postoperative outcome measures. This was driven primarily by preoperative characteristics such as SDI, hip pain duration, joint degeneration, and overall health at presentation. Despite differential outcomes, patients still showed clinical improvement regardless of SDI quartile. LEVEL OF EVIDENCE: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

Orthopedics/Bone and Joint Center
Livingston N, **Jiang E**, **Hansen L**, **Williams A**, **Wu M**, **Carrier J**, and **Day CS**. Self-Reported Improvement After Carpal Tunnel Release in Patients with Motor Axonal Loss. *J Hand Surg Am* 2024; Epub ahead of print. PMID: 39641678. Full Text

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PURPOSE: Electrodiagnostic studies can identify evidence of sensory and motor axonal loss (AL) in carpal tunnel syndrome (CTS) patients. However, the impact of sensory and motor AL on outcomes following carpal tunnel release (CTR) remains unclear. We hypothesize that patients with no evidence of sensory and motor AL will experience greater improvement following CTR compared to those with evidence of AL. METHODS: Patients undergoing open and endoscopic CTR by four fellowship-trained orthopedic hand surgeons were identified. Sensory and motor AL were identified using preoperative electromyography and nerve conduction studies. Patients completed the following before surgery and 3-month postoperative patient-reported outcomes: Patient-Reported Outcomes Measurement Information System Upper Extremity (UE) and Pain Interference (PI) as well as Disabilities of the Arm, Shoulder, and Hand (QuickDASH [QD]). Preoperative and postoperative scores, changes in scores, and rates of achieving the minimally clinically important difference (MCID) were compared between patients with and without sensory and motor AL. RESULTS: One hundred and seventy-five patients were included. Of these, 91 exhibited sensory AL and 98 exhibited motor AL. Demographic matched analysis of patients with and without sensory AL showed no differences in before surgery, after surgery, difference, or proportion meeting MCID for UE, PI, or QD. Matched analysis revealed no difference in preoperative PROMs between patients with and without motor AL. Patients with motor AL had increased postoperative UE (better function), decreased postoperative PI (less PI) and QD (less disability), increased changes in PI and QD, as well as a greater proportion meeting MCID for QD compared to those without motor AL. CONCLUSIONS: There was no difference in post-CTR improvement between patients with and without sensory AL. However, contrary to our hypothesis, motor AL patients experienced greater postoperative improvement according to QD. These findings suggest surgery should be recommended for severe CTS patients with evidence of AL. These results can better inform physicians and patients as they discuss expectations of CTR outcomes. TYPE OF STUDY/LEVEL OF EVIDENCE: Prognosis II.

Orthopedics/Bone and Joint Center
Timoteo T, **Nerys-Figueroa J**, **Keinath C**, **Movassaghi A**, **Daher N**, **Jurayj A**, **Mahylis JM**, and **Muh SJ**. Lower socioeconomic status is correlated with worse outcomes after arthroscopic rotator cuff repair. *J Orthop Surg Res* 2024; 19(1):865. PMID: 39710714. Full Text

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BACKGROUND: Socioeconomic status has been recognized as a crucial social determinant of health influencing patient outcomes. Area Deprivation Index (ADI) is a validated measure of an area's socioeconomic status. Limited data exists on the impact of ADI and clinical outcomes and complications following rotator cuff repair (RCR). The purpose of this study was to investigate the impact socioeconomic factors have on outcomes following primary arthroscopic RCR. METHODS: This is a retrospective cohort study with 1-year follow-up. Patients who underwent primary rotator cuff repair at a single institution from March 2014 to September 2022 were identified. Patient demographics, pre-and post-operative visual analog scale (VAS) scores, Patient-Reported Outcomes Measurement Information System (PROMIS) scores, range of motion, complications, and subsequent ipsilateral shoulder surgeries were collected. ADI was collected from an online mapping database using each patient's home address. Patients were split into ADI terciles, with ADI1 representing the least disadvantaged group and ADI3 representing the most disadvantaged group. Analysis of variance and T-test were used for continuous variables, and chi-square analyses were conducted for categorical variables. RESULTS: In total, 467 patients underwent RCR and had complete demographic data and postoperative follow-ups over a year. There was a significant difference in race, with 78.2% of patients identifying as black in ADI3 and 18.1% in ADI1 ($P < .001$). Pre-operative PROMIS-Pain Interference, VAS, forward flexion, and abduction were significantly worse in ADI3 compared to ADI1 ($P = .001$, $P < .001$, $P = .012$, and $P = .023$). At one-year postoperative, patients in ADI3 scored significantly worse than patients in ADI1 in PROMIS- Upper Extremity score ($P = .016$), PROMIS- Pain Interference ($P < .001$), VAS ($P < .001$), forward flexion ($P < .001$) and abduction ($P = .034$). Higher ADI scores were associated with a positive correlation for pain ($r = .258$, $P = < 0.001$) a negative correlation with upper extremity function ($r = - .233$, $P = .026$), a positive correlation with pain interference ($r = .355$, $P < .001$), and negative correlation with forward flexion ($r = - .227$, $P < .001$). There were no significant differences in postoperative complications ($P = .54$), retears ($P = .47$), or reoperations rates ($P = .22$). CONCLUSION: Lower socioeconomic status measured by ADI is associated with worse preoperative and 1-year postoperative pain, shoulder function, and range of motion following RCR. However, no differences were appreciated between cohorts regarding reoperation or complications. LEVEL OF EVIDENCE III: Retrospective Cohort Study.

Orthopedics/Bone and Joint Center

Yadav RN, **Oravec DJ**, **Cushman T**, **Rao SD**, and **Yeni YN**. Strength and strain distributions obtained from digital wrist tomosynthesis discriminate patients with and without a history of fragility fracture. *Bone* 2024; 192:117368. PMID: 39672218. Full Text

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Bone fractures due to osteoporosis are a significant problem. Limited accuracy of standard bone mineral density (BMD) for fracture risk assessment, combined with low adherence to bone health screening precludes identification of those at risk of fracture. Because of the wide availability of digital breast tomosynthesis (DBT) imaging, bone screening using a DBT scanner at the time of breast screening has been proposed. Earlier studies have shown that BMD, microstructure, and stiffness of the distal radius can be calculated using digital tomosynthesis imaging of the wrist (DWT). However, strength and stress/strain parameters, which are more relevant to structural failure, and have the potential to enhance the utility of DWT, were not examined previously. Therefore, this study aimed to examine the ability of

DWT to discriminate patients with and without fragility fracture using DWT based finite element (DWT-FE) derived strength and stress/strain distribution properties, and to determine in vivo repeatability of these biomechanical properties. Twenty-two postmenopausal women with any fragility fracture (included spine, hip, distal radius, humerus and tibia fractures) and 68 without were recruited. Each participant's nondominant arm (dominant arm if history of fracture in the nondominant arm) was scanned with DWT and compressive loading was simulated using FE modeling. Six additional patients were DWT-scanned thrice, with repositioning, to determine the repeatability of the study variables. Age and T-score were not different between fracture and nonfracture groups ($p > 0.1$), but strength and stress/strain parameters were significant predictors of fracture status (AUC = 0.64-0.74). Standard deviation of tensile strain was the most discriminatory variable for fracture status (AUC = 0.74) and was independent from stiffness. Repeatability error of DWT biomechanical properties was 0.7 % to 5.8 %. This study demonstrated that DWT-FE based strength and standard deviation of tensile strain were reproducible and predict fracture status independent from BMD and stiffness. The results suggest that the accuracy of fracture risk screening can be improved in the highly accessible environment of mammographic imaging.

Orthopedics/Bone and Joint Center

Zang K, Brossard M, **Wilson T**, **Ali SA**, and Espin-Garcia O. A scoping review of statistical methods to investigate colocalization between genetic associations and microRNA expression in osteoarthritis. *Osteoarthr Cartil Open* 2024; 6(4):100540. PMID: 39640910. Full Text

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BACKGROUND: Genetic colocalization analysis is a statistical method that evaluates whether two traits (e.g., osteoarthritis [OA] risk and microRNA [miRNA] expression levels) share the same or distinct genetic association signals in a locus typically identified in genome-wide association studies (GWAS). This method is useful for providing insights into the biological relevance of genetic association signals, particularly in intergenic regions, which can help to elucidate disease mechanisms in OA and other complex traits. OBJECTIVES: To review the existing literature on genetic colocalization methods, assess their suitability for studying OA, and investigate their capacity to integrate miRNA data, while bearing in view their statistical assumptions. DESIGN: We followed scoping review methodology and used Covidence software for data management. Search terms for colocalization, GWAS, and genetic or statistical models were used in the databases MEDLINE and EMBASE, searched till March 4, 2024. RESULTS: Our search returned 546 peer-reviewed papers, of which 96 were included following title/abstract and full-text screening. Based on both cumulative and annual publication counts, the most cited method for colocalization analysis was coloc. Four papers examined OA-related phenotypes, and none examined miRNA. An approach to colocalization analysis using miRNA was postulated based on further hand-searching. CONCLUSIONS: Colocalization analysis is a largely unexplored method in OA. Many of the approaches to colocalization analysis identified in this review, including the integration of GWAS and miRNA data, may help to elucidate genetic and epigenetic factors implicated in OA and other complex traits.

Otolaryngology – Head and Neck Surgery

Almansour YM, **Alani A**, **Wilson CP**, **Eide JG**, and **Craig JR**. Medial Flap Turbinoplasty is Unlikely to Cause Empty Nose Syndrome. *Laryngoscope* 2024; Epub ahead of print. PMID: 39673254. Full Text

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BACKGROUND: Empty nose syndrome (ENS) is a poorly understood condition that affects a minority of patients who undergo inferior turbinate (IT) surgery. The Empty Nose Syndrome 6-item Questionnaire (ENS6Q) was validated to diagnose ENS following IT reduction, with an ENS6Q ≥ 11 being suggestive of ENS. Medial flap turbinoplasty (MFT) involves IT bone removal ± submucosal reduction (SMR) and is highly effective at surgically treating IT hypertrophy. This study's purpose was to determine the incidence of ENS following MFT by comparing ENS6Q scores preoperatively and postoperatively. METHODS: A retrospective cohort study was conducted on consecutive patients who underwent bilateral MFT with or without septoplasty to address nasal obstruction. Preoperative and postoperative nasal obstruction and septoplasty effectiveness (NOSE, 0-20) and ENS6Q (0-30) scores were compared at a minimum 12 months postoperatively. RESULTS: Of 100 patients, mean age was 48.9 years and 53% were male. Mean follow-up was 25.0 months (range: 12-66 months). Patients underwent MFT with SMR in 70% of cases, whereas 30% had bone removal only, and 79% had septoplasty. NOSE scores decreased significantly postoperatively (mean 9-point reduction, $p < 0.0001$). Mean preoperative and postoperative ENS6Qs were 8.5 and 3.0, respectively, with a mean 5.6-point decrease postoperatively ($p < 0.0001$). While some patients developed elevated ENS6Q scores mainly in the first 3 months postoperatively, no patients had ENS6Q scores ≥11 at final follow-up. CONCLUSIONS: MFT ± septoplasty led to significant long-term reduction in nasal obstruction, with no patients ultimately developing ENS6Q ≥ 11 postoperatively. Therefore, MFT was unlikely to cause ENS. LEVEL OF EVIDENCE: Level 4 Laryngoscope, 2024.

Otolaryngology – Head and Neck Surgery

Imbrogno G, Lorenzi A, Borloni R, Scaini R, Testori T, Felisati G, Saibene AM, and **Craig JR**. Maxillary Sinusitis Following Orthognathic Surgery: Should It Be Considered Odontogenic Sinusitis? *Clin Case Rep* 2024; 12(12):e9654. PMID: 39619300. Full Text

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Maxillary sinusitis is a recognized complication following dental procedures, but its occurrence after orthognathic surgery, such as Le Fort osteotomies, remains less documented. This case report presents a 58-year-old female who developed unilateral maxillary sinusitis 23 years post-orthognathic surgery. The patient was asymptomatic, aside from occasional cacosmia, and was incidentally found to have sinus opacification on a computed tomography (CT) scan performed for implant-prosthetic rehabilitation. Nasal endoscopy revealed purulence and mucosal edema, prompting endoscopic sinus surgery (ESS). Intraoperatively, purulent material and fungal debris were removed from the maxillary sinus, confirming bacterial sinusitis with a concurrent fungal ball. S. salivarius and Klebsiella species were identified from the cultures. The patient's condition improved following the removal of both the sinus contents and the retained titanium plates and screws. This case underscores the potential for maxillary sinusitis to develop long after orthognathic surgery, particularly in the presence of retained dental hardware. It highlights the importance of thorough imaging and endoscopic evaluation in patients with a history of dental or facial surgeries presenting with sinonasal symptoms. Additionally, it raises questions about the role of retained hardware in the persistence or recurrence of infection and the possible association with fungal ball formation. The need for further research to establish guidelines for the management of sinusitis in such contexts, particularly regarding the removal of facial hardware, is emphasized.

Otolaryngology – Head and Neck Surgery

Levin AM, **Okifo O**, **Buhl K**, **Ouchi T**, **Parker B**, **Tan J**, **Datta I**, **Dai X**, **Chen Y**, **Palanisamy N**, **Veenstra J**, **Carskadon S**, **Li J**, **Ozog D**, **Keller CE**, **Chitale D**, **Bobbitt KR**, **Crawford HC**, **Steele N**, **Mi QS**, and **Jones LR**. Higher expression of mir-31-5p is associated with reduced risk of head and neck keloid recurrence following surgical resection. *Laryngoscope Investig Otolaryngol* 2024; 9(6):e70040. PMID: 39664781. Full Text

Department of Public Health Science Henry Ford Health Detroit Michigan USA.
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OBJECTIVE: In this study, we aimed to evaluate mir-31-5p as a prognostic biomarker of keloid disease (KD) recurrence using a retrospective, treatment naïve, surgical cohort of head and neck KD cases from Henry Ford Health. METHODS: Using a tissue microarray, mir-31-5p expression was measured with miRNAscope, and mir-31-5p cell positivity was determined with QuPath. Logistic regression was used to test the association between mir-31-5p positive cells and KD recurrence at 1 year. In an independent dataset, associations between mir-31-5p and messenger RNA (mRNA) expression were assessed. Ingenuity Pathway Analysis identified target genes and pathways impacted by mir-31-5p. RESULTS: Of the 58 KD patients, 42 (72%) received adjuvant triamcinolone injections, and 8 recurred (14%). mir-31-5p was expressed in 48 (83%) specimens. Increasing mir-31-5p expression was associated with decreased risk of recurrence (p = .031), with an odds ratio of 0.86 (95% CI 0.75-0.98) for each 20% increase in mir-31-5p cellular positivity. This effect persisted with triamcinolone treatment (odds ratio 0.82; 95% CI 0.71-0.95; p = .015). mir-31-5p correlated with gene expression enriched in KD pathways, including mRNA splicing and autophagy. CONCLUSION: Taken together, our data supports the association between mir-31-5p expression and KD recurrence. Its potential as a prognostic biomarker should be further investigated. LEVEL OF EVIDENCE: Level 2.

Otolaryngology – Head and Neck Surgery

Mansour Y, Haddad L, Breeden Z, and Kulesza RJ, Jr. Impact of repeated intranasal gentamicin irrigation on auditory brainstem evoked potentials in rats. *Exp Brain Res* 2024; 243(1):20. PMID: 39656249. Full Text

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Gentamicin is a bactericidal aminoglycoside antibiotic that broadly targets Gram-negative microbes. Both human and animal studies have shown that administration of gentamicin is ototoxic by several routes of administration and results in sensorineural hearing loss due to damaged hair cell at the base of the cochlea. However, gentamicin is also administered intranasally to treat sinusitis in humans, but no animal studies have examined ototoxicity of gentamicin administered via this route. We hypothesized that intranasal irrigation of gentamicin will result in ototoxicity and impaired auditory function similar to systemic delivery. We investigated this hypothesis in Sprague-Dawley rats that received intranasal irrigations of gentamicin or saline from postnatal day (P) 21-31. We examined auditory function by assessing brainstem auditory evoked potentials in response to both broadband clicks and pure tone-pips (4, 8, 16, 24 and 32 kHz) on P41. We found significant changes in auditory function in gentamicin-exposed animals. Specifically, gentamicin-exposed animals had significantly higher thresholds in response to both clicks and tone-pips. In response to broadband clicks, there were no changes in latency for waves I through IV. However, we found significantly longer wave and interwave latencies for all waves in response to the 24 kHz tone-pip. Together, these findings suggest that intranasal administration of gentamicin results in impaired auditory function consistent with other routes of delivery.

Otolaryngology – Head and Neck Surgery

Nguyen TV, Abiri A, Idowu V, Patel S, Truong T, Lerner DK, Workman AD, Batra PS, Campbell RG, **Craig JR**, Crosby DL, Douglas JE, Eide JG, Kohanski MA, Kshirsagar RS, Locke TB, Papagiannopoulos P, Tajudeen BA, Tong CCL, Adappa ND, Palmer JN, and Kuan EC. Outcomes of Autologous versus Synthetic Inlay Grafts After Skull Base Reconstruction for High-Flow Defects: A Multicenter Case-Control Analysis. *Int Forum Allergy Rhinol* 2024; Epub ahead of print. PMID: 39740087. Full Text

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Otolaryngology – Head and Neck Surgery

Pearl ES, **Murray MF**, **Haley EN**, **Snodgrass M**, **Braciszewski JM**, **Carlin AM**, and **Miller-Matero LR**. Weight and shape overvaluation and its relation to anxiety, depression, and maladaptive eating symptoms for patients up to 4 years after bariatric surgery. *Surg Obes Relat Dis* 2024; Epub ahead of print. PMID: 39710526. Full Text

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BACKGROUND: Weight and shape overvaluation (WSO; undue influence of weight and shape on self-evaluation) is common among individuals undergoing bariatric surgery. Little is known about how WSO relates to poorer outcomes for patients remote from surgery. OBJECTIVES: To examine associations between WSO with anxiety and depression symptoms and various maladaptive eating behaviors in patients up to 4 years post-bariatric surgery. SETTING: Henry Ford Health, United States. METHODS: Patients who underwent surgery between 2018 and 2021 were invited to complete the study between 2021 and 2022. Participants (N = 765) completed anxiety and depression symptom and eating behavior measures. RESULTS: Participants endorsed moderate WSO (M = 3.62, standard deviation = 1.87), which was positively related to anxiety (r = .37) and depression (r = .20) symptoms; eating in response to anger/frustration (r = .26), anxiety (r = .28), and depression (r = .31); and addictive eating behaviors (r = .26); and was significantly associated with the presence of loss-of-control (odds ratio [OR] = 1.39), binge (OR = 1.39), and graze (OR = 1.24) eating. WSO also was related to more frequent grazing (r = .23) but not loss-of-control or binge eating frequency for participants who endorsed behavior presence. CONCLUSIONS: Findings underscore that links between WSO, psychiatric distress, and maladaptive eating behaviors persist up to 4 years after bariatric surgery. These domains should be assessed at bariatric follow-ups, and assessment of WSO may help providers identify patients at risk for poorer outcomes. Findings should be used to inform temporal modeling of how WSO may predispose patients to poorer bariatric outcomes.

Otolaryngology – Head and Neck Surgery

Prince ADP, **Oslin K**, Smith JD, Hershey E, Chionis L, Allevato M, Chinn SB, and Prince MEP. Parotidectomy Trends Toward Outpatient for Benign Disease. *Otolaryngol Head Neck Surg* 2024; Epub ahead of print. PMID: 39550622. Full Text

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OBJECTIVE: We evaluate the safety of outpatient parotidectomy. We evaluate factors that lead to planned admission and compare costs. We evaluate trends toward outpatient, and the outcomes of switching admission status, total versus superficial approach, and ambulatory versus hospital site. STUDY DESIGN: Retrospective cohort study. SETTING: Single tertiary academic center. METHODS: Retrospective review of patients who underwent parotidectomy for benign tumors from 2018 to 2023. RESULTS: Of 370 parotidectomies performed, there were a planned 162 admissions and 208 outpatient procedures. A travel time > 60 minutes (odds ratio [OR] = 0.487, confidence interval [CI]: 0.296-0.803, P = .005) and total parotidectomy (OR = 0.448, CI: 0.226-0.89, P = .022) decreased the odds of a planned outpatient procedure. In a multivariable model, longer operative time increased the odds of switching to inpatient (n = 29, OR = 1.02, CI: 1.007-1.033, P = .002) and drain placement decreased the odds of switching to outpatient (n = 15, OR = 0.035, CI: 0.004-0.298, P = .002). There was no significant difference in surgical complications, phone calls, clinic visits, readmission rates, or recurrence between outpatient and inpatient. This remained true when comparing surgical facility and superficial versus total parotidectomy. After COVID was declared an emergency, there was a trend toward outpatient parotidectomy (72.7% vs 48.9%, P < .001), but no change in complication rates. At our institution, outpatient parotidectomy saved $3838 compared to overnight admission. CONCLUSION: This study supports that outpatient parotidectomy is safe. This remained true for patients switching admission status, undergoing superficial or total parotidectomy, and having their operation at an ambulatory site. We demonstrate that institutions can safely increase outpatient parotidectomy rates and outpatient parotidectomy is cost effective.

Pathology and Laboratory Medicine

Abusuliman M, Aboeldahb M, Olimy A, **Abbas O**, Abusuliman A, **Jamali T**, **Gavidia Rosario A**, **Yuan L**, and **Pompa R**. Rare Thymoma With Solitary Liver Metastasis. *ACG Case Rep J* 2024; 11(12):e01562. PMID: 39624200. Full Text

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Thymomas are rare, malignant, epithelial tumors of the thymus gland. Extrathoracic metastasis of thymoma is exceedingly rare, particularly when isolated to the liver. We report an 89-year-old man who presented with urinary retention. Exploratory computed tomography imaging revealed a heterogeneous mass in the aortopulmonary window and a 1.9 cm lesion in the left hepatic lobe. Results from magnetic resonance imaging, positron emission tomography-computed tomography, and histopathological analysis of biopsy samples collectively supported a diagnosis of metastatic type B2 thymoma. To the best of our knowledge, this is the oldest patient to be diagnosed with metastatic type B2 thymoma. Metastatic thymoma is difficult to identify, and patients with mediastinal mass identified after any presentation should be evaluated for malignant spread.

Pathology and Laboratory Medicine

Ahsan BU, **Paridon AA**, **Gaba AR**, **Zhang Z**, and **Azordegan N**. Prolapsed Epiploica of Colon Presenting as a Vaginal Polyp After Robotic Hysterectomy: A Case Report and Review of the Literature. *Am J Case Rep* 2024; 25:e944892. PMID: 39604203. Full Text

Department of Pathology and Laboratory Medicine, Henry Ford Health, Detroit, MI, USA.
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BACKGROUND Hysterectomy is a gynecological procedure that can lead to complications arising from structural changes incurred during the surgical process. Vaginal nodules may appear at the vaginal cuff after hysterectomy, which could be indicative of recurring cancer, endometriosis, or formation of fistulae or granulation tissue. In rare instances, abdominal organ prolapse occurs after vaginal cuff dehiscence. Prolapse of the terminal ileum is the most common type of prolapse from vaginal cuff dehiscence, but prolapsed epiploica of colon after hysterectomy occurs in rare instances. Epiploic appendages are a type of fatty tissue attached to the colonic surface that can become inflamed or necrotic and detach from the colon. The purpose of this report is to describe a rare case of prolapsed epiploica of colon at the vaginal cuff. CASE REPORT A 55-year-old woman who had robot-assisted laparoscopic hysterectomy for endometrioid carcinoma presented with a vaginal polyp 2 months after surgery. Histological analysis of the excised polyp revealed adipose tissue with fat necrosis and calcification, indicative of prolapsed epiploica of colon. This is the first report of post-hysterectomy epiploica of colon at the vaginal cuff not associated with obvious dehiscence. CONCLUSIONS This case highlights the importance of thorough histological analysis of excised vaginal nodules and consideration of prolapsed epiploica of colon in the differential diagnoses in addition to benign and malignant vaginal neoplasms.

Pathology and Laboratory Medicine

Boettcher SR, **Kenney RM**, **Arena CJ**, **Beaulac AE**, **Tibbetts RJ**, **Shallal AB**, **Suleyman G**, and **Veve MP**. Say it ain't Steno: a microbiology nudge comment leads to less treatment of Stenotrophomonas maltophilia respiratory colonization. *Infect Control Hosp Epidemiol* 2024; 1-5. Epub ahead of print. PMID: 39623552. Full Text

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OBJECTIVE: To describe the effect of a Stenotrophomonas maltophilia (SM) respiratory culture nudge on antibiotic use in colonized patients. DESIGN: IRB-approved quasi-experiment. SETTING: Five acute-care hospitals in Michigan. PATIENTS: Adult patients with SM respiratory culture between 01/01/2022 and 01/27/2023 (pre-nudge) and 03/27/2023-12/31/2023 (post-nudge). Patients with active community/hospital/ventilator-acquired pneumonia or who received SM-targeted antibiotics at the time of culture were excluded. METHODS: A nudge comment was implemented 02/2023 stating: "S. maltophilia is a frequent colonizer of the respiratory tract. Clinical correlation for infection is required. Colonizers do not require antibiotic treatment." The primary outcome was no treatment with SM-therapy; secondary outcomes were treatment with SM-therapy ≥72 hrs, length of stay, and in-hospital, all-cause mortality. Safety outcomes included antibiotic-associated adverse drug events (ADEs). RESULTS: 94 patients were included: 53 (56.4%) pre- and 41 (43.6%) post-nudge. Most patients were men (53, 56.4%), had underlying lung disease (61, 64.8%), and required invasive ventilatory support (70, 74.5%). Eleven (11.7%) patients resided in a long-term care facility. No treatment with SM therapy was observed in 13 (23.1%) pre- versus 32 (78.0%) post-nudge patients (P <0.001). There were no differences in secondary outcomes. Antibiotic-associated ADEs were common (33/41, 76%) in patients who received ≥72hrs of SM-therapy: fluid overload (18, 44%), hyponatremia (17, 42%), elevated SCr (12, 29%), hyperkalemia (5, 12%). After adjustment for confounders, post-nudge was associated with 11-fold increased odds of no treatment with SM-therapy (adjOR, 11.72; 95%CI, 4.18-32.83). CONCLUSIONS: A targeted SM nudge was associated with a significant reduction in treatment of colonization, with similar patient outcomes. SM-treated patients frequently developed antibiotic-associated ADEs.

Pathology and Laboratory Medicine

Kady N, Abdelrahman S, Rauf A, Burgess A, Weiss J, Gunasekara H, Ramseier NT, Maine IP, Zevallos-Morales A, Perez-Silos V, Wolfe A, Hristov A, Brown NA, **Inamdar KV**, Sverdlov M, Hu YS, Murga-Zamalloa C, Wang C, and Wilcox RA. The GATA-3-dependent transcriptome and tumor microenvironment are regulated by eIF4E and XPO1 in T-cell lymphomas. *Blood* 2024; Epub ahead of print. PMID: 39652777. Full Text

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The transcription factor GATA-3 and the transcriptional program it regulates have emerged as oncogenic drivers across diverse T-cell lymphomas (TCL), many of which are resistant to conventional chemotherapeutic agents and characterized by recurrent losses of key tumor suppressor genes, including TP53 and PTEN, both of which are clients of the nuclear export protein XPO1. Here we demonstrated that XPO1 is highly expressed by malignant T cells expressing GATA-3 and by lymphoma-associated macrophages (LAM) within their tumor microenvironment (TME). Using complementary genetically engineered mouse (GEM) models, we demonstrated that TP53 and/or PTEN deficient TCL, and LAM within their TME, are sensitive to the selective XPO1 antagonist selinexor. In an effort to identify TP53 and PTEN independent mechanisms, we used complementary and orthogonal approaches to investigate the role of eIF4E and XPO1-dependent mRNA nuclear export in these TCL. We identified a novel role for eIF4E/XPO1 in exporting GATA-3 and GATA-3-dependent transcripts from the nucleus in TCL, and in the export of therapeutically relevant transcripts, including CSF-1R, from LAM. Therefore, XPO1 antagonism, by impairing oncogenic transcriptional programs in TCL and depleting LAM from their TME, is a novel approach to target two independent dependencies in a group of therapeutically challenging TCL.

Pathology and Laboratory Medicine

Levin AM, **Okifo O**, **Buhl K**, **Ouchi T**, **Parker B**, **Tan J**, **Datta I**, **Dai X**, **Chen Y**, **Palanisamy N**, **Veenstra J**, **Carskadon S**, **Li J**, **Ozog D**, **Keller CE**, **Chitale D**, **Bobbitt KR**, **Crawford HC**, **Steele N**, **Mi QS**, and **Jones LR**. Higher expression of mir-31-5p is associated with reduced risk of head and neck keloid recurrence following surgical resection. *Laryngoscope Investig Otolaryngol* 2024; 9(6):e70040. PMID: 39664781. Full Text

Department of Public Health Science Henry Ford Health Detroit Michigan USA.
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OBJECTIVE: In this study, we aimed to evaluate mir-31-5p as a prognostic biomarker of keloid disease (KD) recurrence using a retrospective, treatment naïve, surgical cohort of head and neck KD cases from Henry Ford Health. METHODS: Using a tissue microarray, mir-31-5p expression was measured with miRNAscope, and mir-31-5p cell positivity was determined with QuPath. Logistic regression was used to test the association between mir-31-5p positive cells and KD recurrence at 1 year. In an independent dataset, associations between mir-31-5p and messenger RNA (mRNA) expression were assessed. Ingenuity Pathway Analysis identified target genes and pathways impacted by mir-31-5p. RESULTS: Of the 58 KD patients, 42 (72%) received adjuvant triamcinolone injections, and 8 recurred (14%). mir-31-5p was expressed in 48 (83%) specimens. Increasing mir-31-5p expression was associated with decreased risk of recurrence ($p = .031$), with an odds ratio of 0.86 (95% CI 0.75-0.98) for each 20% increase in mir-31-5p cellular positivity. This effect persisted with triamcinolone treatment (odds ratio 0.82; 95% CI 0.71-0.95; $p = .015$). mir-31-5p correlated with gene expression enriched in KD pathways, including mRNA splicing and autophagy. CONCLUSION: Taken together, our data supports the association between mir-

31-5p expression and KD recurrence. Its potential as a prognostic biomarker should be further investigated. LEVEL OF EVIDENCE: Level 2.

Pathology and Laboratory Medicine
Loveless IM, Kemp SB, **Hartway KM**, Mitchell JT, Wu Y, **Zwernik SD**, **Salas-Escabillas DJ**, **Brender S**, **George M**, **Makinwa Y**, **Stockdale T**, **Gartrelle K**, **Reddy RG**, Long DW, **Wombwell A**, **Clark JM**, **Levin AM**, **Kwon D**, **Huang L**, **Francescone R**, **Vendramini-Costa DB**, Stanger B, Alessio A, Waters AM, Cui Y, Fertig EJ, Kagohara LT, **Theisen B**, **Crawford HC**, and **Steele NG**. Human pancreatic cancer single cell atlas reveals association of CXCL10+ fibroblasts and basal subtype tumor cells. *Clin Cancer Res* 2024; Epub ahead of print. PMID: 39636224. Full Text

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PURPOSE: Pancreatic ductal adenocarcinoma (PDAC) patients with tumors enriched for the basal-like molecular subtype exhibit enhanced resistance to standard of care treatments and have significantly worse overall survival (OS) compared to patients with classical subtype enriched tumors. It is important to develop genomic resources, enabling identification of novel putative targets in a statistically rigorous manner. EXPERIMENTAL DESIGN: We compiled a single cell RNA sequencing (scRNAseq) atlas of the human pancreas with 229 patient samples, aggregated from publicly available raw data. We mapped cell-type specific scRNAseq gene signatures in bulk RNAseq (n=744) and spatial transcriptomics (ST) (n=22) and performed validation using multiplex immunostaining. RESULTS: Analysis of tumor cells from our scRNAseq atlas revealed nine distinct populations, two of which aligned with the basal subtype, correlating with worse OS in bulk RNAseq. Deconvolution identified one of the basal populations to be the predominant tumor subtype in non-dissociated ST tissues and in vitro tumor cell and patient-derived organoid lines. We discovered a novel enrichment and spatial association of CXCL10+ cancer associated fibroblasts (CAFs) with basal tumor cells. We identified that besides immune cells, ductal cells also express CXCR3, the receptor for CXCL10, suggesting a relationship between these cell types in PDAC tumor microenvironment. CONCLUSIONS: We show that our scRNAseq atlas (700,000 cells), integrated with ST data, has increased statistical power and is a powerful resource, allowing for expansion of current subtyping paradigms in PDAC. We uncovered a novel signaling niche marked by CXCL10+ CAFs and basal tumor cells that could be explored for future targeted therapies.

Pathology and Laboratory Medicine
Wen T, Shayota BJ, Wallace L, Mani C, Davis N, and Zhao J. A Case Report on 13q12.3 Microdeletion Syndrome Caused by HMGB1 Haploinsufficiency. *Case Rep Genet* 2024; 2024:1912620. PMID: 39635340. Full Text

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Heterozygous microdeletions at 13q12.3 are associated with a rare genetic disorder, 13q12.3 microdeletion syndrome, characterized by intellectual disability, microcephaly, development delay, facial dysmorphisms, atopy, and obesity. Reported 13q12.3 microdeletions vary in size and typically encompass multiple genes. Previous studies have defined a minimal overlap region of 13q12.3 microdeletions and suggested that most of the phenotype associated with the 13q12.3 microdeletion syndrome could be attributed to the loss of the high mobility group box 1 (HMGB1) gene within the overlap region. Here, we report a pediatric patient who had typical phenotypic features of 13q12.3 microdeletion syndrome, including motor and moderate speech developmental delays, microcephaly, and severe atopy, along with anxiety and aggressive behaviors. Trio-based microarray analysis identified a 62-kb apparently de novo heterozygous deletion at 13q12.3 in the proband, fully encompassing all coding exons of the HMGB1 gene yet not affecting any other neighboring genes. This case report presents a rare HMGB1 single-gene deletion in a patient with classic features of 13q12.3 microdeletion syndrome, allowing a better delineation of clinical phenotypes associated with the loss of HMGB1. Our findings, together with previous reports, strongly support the pathogenic role of HMGB1 haploinsufficiency in the 13q12.3 microdeletion syndrome.

Pathology and Laboratory Medicine

Xu Z, **Theisen BK**, **Chang Q**, **Schultz D**, and **Ahsan BU**. Survival outcomes of poorly differentiated colorectal carcinoma variants: Insights from a single teaching institute. *Hum Pathol* 2024; 154:105710. PMID: 39716575. Full Text

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The morphologic diagnosis of colorectal carcinoma (CRC) is typically straight forward. However, there are certain subtypes of CRC that pose diagnostic challenges for daily practice due to sometimes overlapping morphologic and immunohistochemical features. These subtypes include poorly differentiated adenocarcinoma NOS, in the absence of conventional morphology (PDA-NOS), large cell neuroendocrine carcinoma (LCNEC), medullary carcinoma (MC), undifferentiated carcinoma (UC) and lymphoepithelioma-like carcinoma (LELC). This study aims to see if there is a survival difference between poorly differentiated variants of CRC, as well as other clinicopathological features that may affect prognosis. Additionally, we analyzed interobserver agreement among gastrointestinal pathologists (GP) at our institution in subclassifying poorly differentiated CRC. All consecutive patients with the diagnoses of PDA-NOS, MC, LCNEC, UC and LELC between July 2018 and July 2023 were included. Cox proportional regression test was used for multivariate analysis, while log-rank and Kaplan-Meier tests were used for univariate and survival analyses. Out of the same cohort of patients, 58 samples identified and reviewed by 3 GI-subspecialty-trained pathologists who were asked to assign the cases as PDA-NOS, LCNEC, MC, UC and LELC. Interobserver agreement was analyzed using Fleiss Kappa. Of the total 77 patients, 63 were PDA-NOS, 3 were LCNEC, 6 were MC, 4 were UC and 1 was LELC patients. Multivariate analysis using Cox proportional regression showed that tumor size (p = 0.001, HR = 1.22, 95% CI 1.08-1.38), patient age (p = 0.001, HR 1.73, 95% CI 1.24-2.40), and M stage (p = 0.02, HR 2.22, 95% CI 1.14-4.32) were significantly associated with worse OS. For the 58 cases analyzed, 3 GP agreed on 42 (72%) cases. The most common diagnosis was PDA-NOS and for 33 (57%) agreement was unanimous. There was moderate agreement (k 0.41-0.60) between all 3 GP. Our study evaluated the challenges associated with histological evaluation of colon cancers with poorly differentiated morphologies. Among the diagnoses considered in the study, MC and LCNEC had different prognostic implications compared to PDA-NOS and UC. Additionally, our GP showed moderate interobserver agreement, indicating that some level of variability in diagnosing poorly differentiated CRC subtypes may be inevitable.

Patient Engagement

Llamocca EN, **Bossick AS**, **Perkins DW**, **Ahmedani BK**, **Behrendt R**, **Bloemen A**, **Murphy A**, **Kulkarni A**, and **Lockhart E**. Health-related social needs screening, reporting, and assistance in a large health system. *Prev Med* 2024; 190:108182. PMID: 39586330. Full Text

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BACKGROUND: National mandates require screening for and addressing health-related social needs (HRSNs) in healthcare settings. However, differences in HRSN screening process (i.e., completed screenings, screening results, documented offer of assistance, documented assistance request) have been reported by population subgroup. Knowledge of the most effective HRSN screening and intervention methods is limited. We sought to describe differences in completed HRSN screenings, screening results, and assistance request rates across patient and healthcare visit characteristics. METHODS: We examined data from all patients aged ≥18 years and residing in the US receiving services at a large, Midwestern healthcare system with a goal to screen all patients for HRSN at least once annually between July 2021-June 2023 (n = 1,190,488). We examined the proportion of patients with any HRSN screening, with any reported HRSN, asked whether they wanted assistance, or who requested assistance for a reported HRSN stratified by patient demographics and healthcare visit characteristics (i.e., payer, screening location, who completed the screening). RESULTS: Less than half of eligible patients (47.0 %) were screened for HRSNs. About one-sixth (16.9 %) reported any HRSN. Although most patients reporting HRSNs were asked whether they wanted assistance, only about one-quarter (26.8 %) responded affirmatively. Proportions included in each step of the HRSN screening process significantly differed by patient and healthcare visit characteristics. DISCUSSION: This study is one of the first to investigate various steps of a population-wide HRSN screening program. Our findings suggest that examining differences in HRSN screening process by population subgroup is key to addressing HRSNs through a health equity lens.

Pediatrics

Afrah A, Finkel MA, Fonseca C, Asato MT, Jay MS, **Pappas A**, **Gowda SB**, and **Jay A**. Demineralization of Osseous Structures as Presentation of a Rare Genetic Disorder That Is Associated With a High Rate of Mortality. *Case Rep Endocrinol* 2024; 2024:6063059. PMID: 39703927. Full Text

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Objectives: Describe the details of the clinical presentation, diagnostic challenges, and management of a female neonate with neonatal severe hyperparathyroidism (NSHPT). Methods: This case report was developed from a retrospective chart review. The female infant was born to consanguineous parents-first cousins, with multiple prenatal concerns, including gestational diabetes, intrauterine growth restriction, polyhydramnios, and suspicion of a hypoplastic left atrium on prenatal echocardiogram (ECHO). Following a planned C-section at 37 weeks gestation, the neonate exhibited moderate respiratory distress with subcostal retractions. On physical examination, craniotabes, a bell-shaped chest, and a continuous machinery-type murmur were noted. Results: Evaluation at birth revealed a large Patent Ductus Arteriosus and significant demineralization of skeletal structures with atypical rib morphology. Lab work at 24 h of life (HOL) showed elevated serum calcium level (14.3 mg/dL), ionized calcium-iCal (2.32 mmol/L), and normal 25-OH Vitamin D (54.2 ng/mL). A comprehensive skeletal survey uncovered generalized osteopenia, metaphyseal lucencies, and evidence of healing fractures. Repeat lab work at 43 HOL, showed serum calcium of 18.0 mg/dL, iCal 2.67 mmol/L, and elevated parathyroid hormone (PTH) of 2116 pg/mL. Diagnosis of NSHPT was established based on laboratory findings. Molecular testing confirmed a homozygous variant (c.1744T >A; p.Cys582Ser) in the calcium-sensing receptor (CaSR) gene which confirmed the diagnosis of NSHPT. NSHPT, a rare genetic disorder associated with high mortality rates, is often caused by inactivating CaSR gene variants. The patient's family history revealed a strong correlation with familial hypocalciuric hypercalcemia (FHH), a benign condition associated with asymptomatic hypercalcemia, normal to minimally elevated parathyroid level, and hypocalciuria, it is caused by heterozygous inactivating mutations in the CaSR gene. Treatment of NSHPT typically involves total or subtotal parathyroidectomy; however, initial medical intervention is often necessary. In this case, the neonate underwent medical treatment with calcitonin, furosemide to help facilitate renal clearance of calcium, and intravenous fluids before a successful parathyroidectomy. Conclusions: This case accentuates the importance of considering rare genetic disorders in neonates with complex clinical presentations and affirms the need for comprehensive counseling and education, particularly in consanguineous parents, to address familial implications and guide appropriate interventions.

Pediatrics

Benn P, Wang Y, Gray J, Dugan EK, Hajjar M, Prigmore B, Souter V, and **Wolf B**. Evaluating Reproductive Carrier Screening using Biotinidase Deficiency as a Model: Variants Identified, Variant Rates and Management. *Genet Med* 2024; 101345. Epub ahead of print. PMID: 39688110. Full Text

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PURPOSE: To review biotinidase gene (BTD) variants identified in a large, diverse, reproductive carrier screening (RCS) cohort and outline management of heterozygotes with pathogenic or likely pathogenic (P/LP) variants. METHODS: This retrospective observational study included samples tested from January 2020 to September 2022 in a 274-gene panel. The study involved females aged 18 to 55 years. Screening was performed using next generation sequencing covering exons and 10 base-pair flanking introns. The heterozygote frequency was calculated for P/LP variants for the entire population and individual racial/ethnic groups. RESULTS: Of the 91,637 women tested, 5,625 (6.1%) had a P/LP variant in BTD. NM_000060.4:c.1330G>C p.(Asp444His) (referred to as D444H or D424H) alone, or in combination with another variant, accounted for 5,193 (92.3%) of the positive tests. P/LP heterozygote rates differed between racial and ethnic groups. We ascertained seven novel P/LP variants not previously recorded in databases. CONCLUSIONS: The BTD P/LP variants identified through RCS were substantially compatible with those found through positive newborn screening. Therefore, RCS provides a potential for earlier diagnosis. We observed significant differences in P/LP heterozygote rates for

biotinidase deficiency among different racial and ethnic groups. Most reported variants can be interpreted without requiring determination of serum biotinidase activity.

Pediatrics

Lestishock L, Cuomo C, Hickam T, **Johnson-Hooper T**, Maddux M, Muzzall E, McManus M, and White P. Self-perceived importance and confidence of adolescents transitioning to adult care. *Health Care Transit* 2025; 3:100086. PMID: 39712478. Full Text

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PURPOSE: Motivational interviewing (MI) techniques are used by health care teams to engage adolescents and young adults (AYAs) in health care self-management and pediatric to adult health care transition (HCT) planning efforts. The aim of this study was to assess the initial level of motivation of AYAs prior to receipt of HCT anticipatory guidance and to determine associations with demographic and health coverage factors. METHODS: This retrospective study included 5112 AYAs, aged 12-26 years, from four health systems. All AYAs completed the Got Transition readiness assessment that includes MI questions on importance and confidence related to the move to an adult provider.Independent variables included demographic and health coverage factors: age, sex, race, ethnicity, language, and insurance type. The statistical approach included summary statistics, chi-square tests of independence and log-likelihood ratio tests, and generalized linear models and contrasts. RESULTS: The study results demonstrate initial trends in importance and confidence scores for AYAs before they became part of a HCT planning process. Importance scores increased from 12-14 through 18-20 years of age, then decreased in the 21-26-year group. Confidence scores increased from the 12-14 through the 21-26-year group.Confidence scores were generally higher than importance scores and were accompanied by smaller standard deviations. Ethnicity and insurance type also demonstrated an association with MI scoring. DISCUSSION: This study provides baseline scores on two key MI importance and confidence questions that can facilitate clinician understanding of AYA engagement in discussing the changes needed to move to adult care and guides the clinician to start earlier than just before transfer that often occurs around age 21.

Pharmacy

Afrah A, Finkel MA, Fonseca C, Asato MT, Jay MS, **Pappas A**, **Gowda SB**, and **Jay A**. Demineralization of Osseous Structures as Presentation of a Rare Genetic Disorder That Is Associated With a High Rate of Mortality. *Case Rep Endocrinol* 2024; 2024:6063059. PMID: 39703927. Full Text

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Objectives: Describe the details of the clinical presentation, diagnostic challenges, and management of a female neonate with neonatal severe hyperparathyroidism (NSHPT). Methods: This case report was developed from a retrospective chart review. The female infant was born to consanguineous parents-first

cousins, with multiple prenatal concerns, including gestational diabetes, intrauterine growth restriction, polyhydramnios, and suspicion of a hypoplastic left atrium on prenatal echocardiogram (ECHO). Following a planned C-section at 37 weeks gestation, the neonate exhibited moderate respiratory distress with subcostal retractions. On physical examination, craniotabes, a bell-shaped chest, and a continuous machinery-type murmur were noted. Results: Evaluation at birth revealed a large Patent Ductus Arteriosus and significant demineralization of skeletal structures with atypical rib morphology. Lab work at 24 h of life (HOL) showed elevated serum calcium level (14.3 mg/dL), ionized calcium-iCal (2.32 mmol/L), and normal 25-OH Vitamin D (54.2 ng/mL). A comprehensive skeletal survey uncovered generalized osteopenia, metaphyseal lucencies, and evidence of healing fractures. Repeat lab work at 43 HOL, showed serum calcium of 18.0 mg/dL, iCal 2.67 mmol/L, and elevated parathyroid hormone (PTH) of 2116 pg/mL. Diagnosis of NSHPT was established based on laboratory findings. Molecular testing confirmed a homozygous variant (c.1744T >A; p.Cys582Ser) in the calcium-sensing receptor (CaSR) gene which confirmed the diagnosis of NSHPT. NSHPT, a rare genetic disorder associated with high mortality rates, is often caused by inactivating CaSR gene variants. The patient's family history revealed a strong correlation with familial hypocalciuric hypercalcemia (FHH), a benign condition associated with asymptomatic hypercalcemia, normal to minimally elevated parathyroid level, and hypocalciuria, it is caused by heterozygous inactivating mutations in the CaSR gene. Treatment of NSHPT typically involves total or subtotal parathyroidectomy; however, initial medical intervention is often necessary. In this case, the neonate underwent medical treatment with calcitonin, furosemide to help facilitate renal clearance of calcium, and intravenous fluids before a successful parathyroidectomy. Conclusions: This case accentuates the importance of considering rare genetic disorders in neonates with complex clinical presentations and affirms the need for comprehensive counseling and education, particularly in consanguineous parents, to address familial implications and guide appropriate interventions.

Pharmacy

Arena CJ, **Kenney RM**, **Ramesh M**, **Davis SL**, and **Veve MP**. Outcomes of adjunctive eravacycline for severe and fulminant Clostridioides difficile infection. *Int J Infect Dis* 2024; 151:107314. PMID: 39603409. Full Text

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OBJECTIVE: To characterize eravacycline (ERV) treatment for severe or fulminant Clostridioides difficile infection (CDI) and to describe patient outcomes. METHODS: This was an IRB-approved, cross-section of adult hospitalized patients with CDI who received adjunctive ERV with standard of care antibiotics (SOC) for CDI from 01/2019-12/2023 at a 5-hospital health-system. Patients were included if they received ERV with SOC for ≥24 hours for severe or fulminant CDI. Patients with a prior history colectomy or with non-CDI ERV indications were excluded. The primary outcome was the proportion of patients that required colectomy due to C. difficile. Secondary outcomes included time to adjunctive ERV, ERV treatment durations, and in-hospital mortality. RESULTS: Seventy-five patients were included; 25 (33%) had severe and 50 (67%) fulminant CDI; 23 (31%) had refractory severe/fulminant CDI. Eleven (14.7%) required colectomy within 30-days of adjunctive ERV. Patients receiving ERV were mostly immunocompromised with fulminant disease and critical illness. CONCLUSION: ERV may be useful as a potential adjunctive therapy for severe or fulminant CDI. Patients receiving ERV often were immunocompromised and had fulminant disease with critical illness. Future comparative studies are needed to evaluate the impact of adjunctive ERV for CDI.

Pharmacy

Baik I, **Jantz A**, **Poparad-Stezar A**, **Venkat D**, **Khoury N**, **Samaniego-Picota M**, **Gonzalez HC**, and **Fitzmaurice MG**. Evaluating the use of glucagon-like peptide-1 receptor agonists in a matched cohort of kidney and liver transplant recipients. *J Pharm Pract Res* 2024. PMID: Not assigned. Full Text

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Background: Diabetes mellitus (DM) and obesity are common among solid organ transplant recipients, but are associated with an increased risk of graft failure. Aim: Although glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are effective for managing both conditions in the general population, there is limited evidence regarding their use among transplant recipients. Method: The effect of GLP-1 RAs on post-transplant glucose control (defined as haemoglobin A1c [HbA1c]) among 37 liver and kidney transplant patients was compared to a control cohort. Secondary outcomes included change in total daily insulin requirements and oral DM agents, estimated glomerular filtration rate (eGFR), weight, and body mass index (BMI). Adverse events attributed to GLP-1 RAs, hypoglycaemia, incidence of pancreatitis, biopsy-proven acute rejection, graft loss, and death were assessed. Ethical approval was granted by the Henry Ford Health Institutional Review Board (Reference no: 15959) and the study conforms with the US Federal Policy for the Protection of Human Subjects. Results: We observed that patients receiving GLP-1 RAs had a median reduction in HbA1c of 0.5% and reduction in insulin and oral anti-DM agents compared to the control group without GLP-1 RAs. There were statistically significant reductions in both weight and BMI in the GLP-1 RA group. Our observed incidence of adverse events was similar to previous literature. Unlike other smaller studies, a decline in eGFR was observed in the GLP-1 RA group. There were no differences in incidence of biopsy-proven acute rejection, graft loss, or death. Conclusion: When compared to patients without GLP-1 RA therapy, GLP-1 RAs modestly reduced HbA1c and insulin requirements and statistically reduced weight/BMI review at 6 months. GLP-1 RAs, even if initiated early post-transplant, were seemingly safe and effective. Larger, prospective studies are warranted to evaluate the safety and efficacy of GLP-1 RAs in this population.

Pharmacy

Boettcher SR, **Kenney RM**, **Arena CJ**, **Beaulac AE**, **Tibbetts RJ**, **Shallal AB**, **Suleyman G**, and **Veve MP**. Say it ain't Steno: a microbiology nudge comment leads to less treatment of Stenotrophomonas maltophilia respiratory colonization. *Infect Control Hosp Epidemiol* 2024; 1-5. Epub ahead of print. PMID: 39623552. Full Text

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OBJECTIVE: To describe the effect of a Stenotrophomonas maltophilia (SM) respiratory culture nudge on antibiotic use in colonized patients. DESIGN: IRB-approved quasi-experiment. SETTING: Five acute-care hospitals in Michigan. PATIENTS: Adult patients with SM respiratory culture between 01/01/2022 and 01/27/2023 (pre-nudge) and 03/27/2023-12/31/2023 (post-nudge). Patients with active community/hospital/ventilator-acquired pneumonia or who received SM-targeted antibiotics at the time of culture were excluded. METHODS: A nudge comment was implemented 02/2023 stating: "S. maltophilia is a frequent colonizer of the respiratory tract. Clinical correlation for infection is required. Colonizers do not require antibiotic treatment." The primary outcome was no treatment with SM-therapy; secondary outcomes were treatment with SM-therapy ≥72 hrs, length of stay, and in-hospital, all-cause mortality. Safety outcomes included antibiotic-associated adverse drug events (ADEs). RESULTS: 94 patients were included: 53 (56.4%) pre- and 41 (43.6%) post-nudge. Most patients were men (53, 56.4%), had underlying lung disease (61, 64.8%), and required invasive ventilatory support (70, 74.5%). Eleven (11.7%) patients resided in a long-term care facility. No treatment with SM therapy was observed in 13 (23.1%) pre- versus 32 (78.0%) post-nudge patients (P <0.001). There were no differences in secondary

outcomes. Antibiotic-associated ADEs were common (33/41, 76%) in patients who received ≥72hrs of SM-therapy: fluid overload (18, 44%), hyponatremia (17, 42%), elevated SCr (12, 29%), hyperkalemia (5, 12%). After adjustment for confounders, post-nudge was associated with 11-fold increased odds of no treatment with SM-therapy (adjOR, 11.72; 95%CI, 4.18-32.83). CONCLUSIONS: A targeted SM nudge was associated with a significant reduction in treatment of colonization, with similar patient outcomes. SM-treated patients frequently developed antibiotic-associated ADEs.

Pharmacy

Schwartz B, **Klamer K**, **Zimmerman J**, **Kale-Pradhan PB**, and **Bhargava A**. Multidrug Resistant Pseudomonas aeruginosa in Clinical Settings: A Review of Resistance Mechanisms and Treatment Strategies. *Pathogens* 2024; 13(11). PMID: 39599528. Full Text

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Pseudomonas aeruginosa is causing increasing concern among clinicians due to its high mortality and resistance rates. This bacterium is responsible for various infections, especially in hospital settings, affecting some of the most vulnerable patients. Pseudomonas aeruginosa has developed resistance through multiple mechanisms, making treatment challenging. Diagnostic techniques are evolving, with rapid testing systems providing results within 4-6 h. New antimicrobial agents are continuously being developed, offering potential solutions to these complex clinical decisions. This article provides a review of the epidemiology, at-risk populations, resistance mechanisms, and diagnostic and treatment options for Pseudomonas aeruginosa.

Pharmacy

Shallal A, **Veve MP**, **Kenney RM**, **Alangaden G**, and **Suleyman G**. Characterisation, management, and outcomes of New Delhi metallo-β-lactamase-producing Escherichia coli: A case series. *J Glob Antimicrob Resist* 2024; 40:42-46. PMID: 39631625. Full Text

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OBJECTIVE: New Delhi metallo-β-lactamase (NDM)-producing carbapenem-resistant Enterobacterales (CRE) is a globally growing threat. We sought to describe the microbiology, management and outcomes of patients with this infection at our facility. METHODS: This is a descriptive case series of patients with NDM-producing Escherichia coli isolated from culture in Detroit between July 2021 and February 2023. Demographics, risk factors, clinical characteristics, management and outcomes were described. RESULTS: Nine patients were included in the study. Most patients were female with a median age of 67 years. Hepatobiliary disease accounted for 90% of underlying conditions. Nearly all patients had prior antibiotic exposure and the most common specimen source was intra-abdominal fluid. Three patients were not treated due to colonisation; among those treated, the majority received trimethoprim-sulfamethoxazole. The median treatment duration and length of stay were 7 and 15.5 days, respectively. Six (67%) patients survived. CONCLUSIONS: This report describes a large case series of NDM-producing E. coli infection. Patients with significant comorbidities remain at high risk for CRE infection.

Antibiotic options for the treatment of NDM organisms are very limited; new and effective therapies are urgently needed.

Pharmacy

Shields RK, Abbo LM, Ackley R, Aitken SL, Albrecht B, Babiker A, Burgoon R, Cifuentes R, Claeys KC, Curry BN, DeSear KE, Gallagher JC, Golnabi EY, Gross AE, Hand J, Heil EL, Hornback KM, Kaye KS, Khuu TV, Klatt ME, Kline EG, Kubat RC, Kufel WD, Lee JH, Lepak AJ, Lim A, Ludwig JM, Macdougall C, Majumdar A, Mathers AJ, McCreary EK, Miller WR, Monogue ML, Moore WJ, Olson S, Oxer J, Pearson JC, Pham C, Pinargote P, Polk C, Satlin MJ, Satola SW, Shah S, Tamma PD, Tran TT, van Duin D, VanNatta M, Vega A, Venugopalan V, **Veve MP**, Wangchinda W, Witt LS, Wu JY, and Pogue JM. Effectiveness of ceftazidime-avibactam versus ceftolozane-tazobactam for multidrug-resistant Pseudomonas aeruginosa infections in the USA (CACTUS): a multicentre, retrospective, observational study. *Lancet Infect Dis* 2024; Epub ahead of print. PMID: 39701120. Full Text

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BACKGROUND: Ceftolozane-tazobactam and ceftazidime-avibactam are preferred treatment options for multidrug-resistant Pseudomonas aeruginosa infections; however, real-world comparative effectiveness studies are scarce. Pharmacokinetic and pharmacodynamic differences between the agents might affect clinical response rates. We aimed to compare the effectiveness of ceftolozane-tazobactam and ceftazidime-avibactam for treatment of invasive multidrug-resistant P aeruginosa infections. METHODS: This multicentre, retrospective, observational study was conducted at 28 hospitals in the USA between Jan 1, 2016, and Dec 31, 2023. Eligible patients were adults (age ≥18 years old) with microbiologically confirmed multidrug-resistant P aeruginosa pneumonia or bacteraemia treated with ceftolozane-tazobactam or ceftazidime-avibactam for more than 48 h. Patients were matched (1:1) by study site, severity of illness, time to treatment initiation (≤72 h or >72 h), and infection type. The primary outcome was clinical success at day 30, which was defined as survival, resolution of signs and symptoms of infection with the intended treatment course, and the absence of recurrent infection due to P aeruginosa. Secondary outcomes included all-cause mortality and development of resistance to study drug. FINDINGS: 420 eligible patients were included (210 in each treatment group), of whom 350 (83%) had pneumonia and 70 (17%) had bacteraemia. Baseline demographics, comorbidities, and severity of illness indicators were similar between groups. On treatment initiation, 336 (80%) patients were in the intensive care unit, 296 (70%) were receiving mechanical ventilation, and 168 (40%) required vasopressor support. Clinical success was observed in 128 (61%) of 210 patients treated with ceftolozane-tazobactam and 109 (52%) of 210 patients treated with ceftazidime-avibactam. By conditional logistic regression analysis, the adjusted odds ratio (aOR) of success after treatment with ceftolozane-tazobactam compared with ceftazidime-avibactam was 2·07 (95% CI 1·16-3·70). For patients with pneumonia, clinical success was observed in 110 (63%) of 175 patients in the ceftolozane-tazobactam group and 89 (51%) of 175 patients in the ceftazidime-avibactam group (aOR 2·34 [95% CI 1·22-4·47]). Among patients with bacteraemia, rates of clinical success were 51% (18 of 35 patients) for patients treated with ceftolozane-tazobactam and 57% (20 of 35 patients) for those treated with ceftazidime-avibactam (0·76 [0·23-2·57]). There were no significant differences between groups in 30-day or 90-day mortality. Among patients whose baseline isolates were tested for susceptibility, resistance developed in 22% (38 of 173) of patients treated with ceftolozane-tazobactam and 23% (40 of 177) of patients treated with ceftazidime-avibactam. INTERPRETATION: Treatment with ceftolozane-tazobactam resulted in higher rates of clinical success compared with ceftazidime-avibactam for invasive infections due to multidrug-resistant P aeruginosa. Differences were driven by improved response rates for patients with pneumonia who were treated with ceftolozane-tazobactam. There were no significant differences between study groups with respect to all-cause mortality; treatment-emergent resistance was common with both agents. FUNDING: Merck Sharp & Dohme.

Pharmacy

Zimmerman J, **Giuliano C**, and **Kale-Pradhan PB**. Ceftobiprole Medocaril: A New Fifth-Generation Cephalosporin. *Ann Pharmacother* 2024; Epub ahead of print. PMID: 39644134. Full Text

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OBJECTIVE: The objective was to review the pharmacology, efficacy, and safety of intravenous ceftobiprole in the treatment of bloodstream infections, acute bacterial skin and skin structure infections (ABSSSIs), community-acquired pneumonia (CAP), and hospital-acquired pneumonia (HAP), or ventilator-associated pneumonia (VAP). DATA SOURCES: PubMed and ClinicalTrials.gov were searched using the following terms: ceftobiprole, ceftobiprole medocaril, ceftobiprole medocaril sodium, Zevtera, and BAL5788. STUDY SELECTION AND DATA EXTRACTION: Articles published in English between January 1985 and August 15, 2024, related to pharmacology, safety, efficacy, and clinical trials were reviewed. DATA SYNTHESIS: Ceftobiprole has shown similar efficacy to comparator antibiotics in CAP, ABSSSIs, and bloodstream infections. Overall treatment success in patients with bacteremia was 69.8% and 68.7%; 91.3% and 88.1% with ABSSSIs and 86.6% and 87.4% with CAP in ceftobiprole and comparator groups, respectively. Finally, in the management of HAP and VAP, ceftobiprole was inferior in the VAP population. Ceftobiprole had a favorable safety profile with gastrointestinal adverse effects occurring more frequently than comparators. RELEVANCE TO PATIENT CARE AND CLINICAL

PRACTICE IN COMPARISON TO EXISTING DRUGS: Clinicians have limited options to treat multidrug-resistant infections. Ceftobiprole has demonstrated efficacy against causative pathogens in specific infections including methicillin-resistant Staphylococcus aureus bacteremia (SAB), ABSSSI, and CAP and may be considered a viable alternative. However, ceftobiprole's impact on HAP, VAP, and febrile neutropenia needs to be further delineated. CONCLUSION: Ceftobiprole's broad-spectrum activity makes it a viable option for treating patients hospitalized with CAP, ABSSSI, and SAB. Further studies are needed in severely ill HAP or VAP, febrile neutropenia, and pediatric patients.

Public Health Sciences

Akbari H, Bakas S, Sako C, Fathi Kazerooni A, Villanueva-Meyer J, Garcia JA, Mamourian E, Liu F, Cao Q, Shinohara RT, Baid U, Getka A, Pati S, Singh A, Calabrese E, Chang S, Rudie J, Sotiras A, LaMontagne P, Marcus DS, Milchenko M, Nazeri A, Balana C, Capellades J, Puig J, Badve C, Barnholtz-Sloan JS, Sloan AE, Vadmal V, Waite K, Ak M, Colen RR, Park YW, Ahn SS, Chang JH, Choi YS, Lee SK, Alexander GS, Ali AS, Dicker AP, Flanders AE, Liem S, Lombardo J, Shi W, Shukla G, **Griffith B**, **Poisson LM**, **Rogers LR**, Kotrotsou A, Booth TC, Jain R, Lee M, Mahajan A, Chakravarti A, Palmer JD, DiCostanzo D, Fathallah-Shaykh H, Cepeda S, Santonocito OS, Di Stefano AL, Wiestler B, Melhem ER, Woodworth GF, Tiwari P, Valdes P, Matsumoto Y, Otani Y, Imoto R, Aboian M, Koizumi S, Kurozumi K, Kawakatsu T, Alexander K, Satgunaseelan L, Rulseh AM, Bagley SJ, Bilello M, Binder ZA, Brem S, Desai AS, Lustig RA, Maloney E, Prior T, Amankulor N, Nasrallah MLP, O'Rourke DM, Mohan S, and Davatzikos C. Machine Learning-based Prognostic Subgrouping of Glioblastoma: A Multi-center Study. *Neuro Oncol* 2024; Epub ahead of print. PMID: 39665363. Full Text

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BACKGROUND: Glioblastoma is the most aggressive adult primary brain cancer, characterized by significant heterogeneity, posing challenges for patient management, treatment planning, and clinical trial stratification. METHODS: We developed a highly reproducible, personalized prognostication and clinical subgrouping system using machine learning (ML) on routine clinical data, MRI, and molecular measures from 2,838 demographically diverse patients across 22 institutions and 3 continents. Patients were stratified into favorable, intermediate, and poor prognostic subgroups (I, II, III) using Kaplan-Meier analysis (Cox proportional model and hazard ratios [HR]). RESULTS: The ML model stratified patients into distinct prognostic subgroups with HRs between subgroups I-II and I-III of 1.62 (95%CI: 1.43-1.84, p<0.001) and 3.48 (95%CI: 2.94-4.11, p<0.001), respectively. Analysis of imaging features revealed several tumor properties contributing unique prognostic value, supporting the feasibility of a generalizable prognostic classification system in a diverse cohort. CONCLUSIONS: Our ML model demonstrates extensive reproducibility and online accessibility, utilizing routine imaging data rather than complex imaging protocols. This platform offers a unique approach for personalized patient management and clinical trial stratification in glioblastoma.

Public Health Sciences

Almansour YM, **Alani A**, **Wilson CP**, **Eide JG**, and **Craig JR**. Medial Flap Turbinoplasty is Unlikely to Cause Empty Nose Syndrome. *Laryngoscope* 2024; Epub ahead of print. PMID: 39673254. Full Text

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BACKGROUND: Empty nose syndrome (ENS) is a poorly understood condition that affects a minority of patients who undergo inferior turbinate (IT) surgery. The Empty Nose Syndrome 6-item Questionnaire (ENS6Q) was validated to diagnose ENS following IT reduction, with an ENS6Q ≥ 11 being suggestive of ENS. Medial flap turbinoplasty (MFT) involves IT bone removal ± submucosal reduction (SMR) and is highly effective at surgically treating IT hypertrophy. This study's purpose was to determine the incidence of ENS following MFT by comparing ENS6Q scores preoperatively and postoperatively. METHODS: A retrospective cohort study was conducted on consecutive patients who underwent bilateral MFT with or without septoplasty to address nasal obstruction. Preoperative and postoperative nasal obstruction and septoplasty effectiveness (NOSE, 0-20) and ENS6Q (0-30) scores were compared at a minimum 12 months postoperatively. RESULTS: Of 100 patients, mean age was 48.9 years and 53% were male. Mean follow-up was 25.0 months (range: 12-66 months). Patients underwent MFT with SMR in 70% of cases, whereas 30% had bone removal only, and 79% had septoplasty. NOSE scores decreased significantly postoperatively (mean 9-point reduction, p < 0.0001). Mean preoperative and postoperative ENS6Qs were 8.5 and 3.0, respectively, with a mean 5.6-point decrease postoperatively (p < 0.0001). While some patients developed elevated ENS6Q scores mainly in the first 3 months postoperatively, no patients had ENS6Q scores ≥11 at final follow-up. CONCLUSIONS: MFT ± septoplasty led to significant long-term reduction in nasal obstruction, with no patients ultimately developing ENS6Q ≥ 11 postoperatively. Therefore, MFT was unlikely to cause ENS. LEVEL OF EVIDENCE: Level 4 Laryngoscope, 2024.

Public Health Sciences

Aspiras O, **Hutchings H**, Dawadi A, **Wang A**, **Poisson L**, **Okereke IC**, and Lucas T. Medical mistrust and receptivity to lung cancer screening among African American and white American smokers. *Psychol Health Med* 2024; 1-12. Epub ahead of print. PMID: 39608370. Full Text

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Although medical mistrust is associated with lower cancer screening uptake among racial minorities, such as African Americans, potential impacts on cancer screening among White Americans are generally understudied. In this study, we examined links from medical mistrust to lung cancer screening among African American (N = 203) and White American (N = 201) smokers. Participants completed the Group-Based Medical Mistrust Scale and viewed a brief online educational module about lung cancer risks, etiology, and screening. Thereafter, participants reported their receptivity to lung cancer screening using a Theory of Planned Behavior (TPB) measurement framework (attitudes, normative beliefs, perceived control, and intentions). Medical mistrust predicted lower screening receptivity across all TPB measures for both racial groups. Although medical mistrust was higher among African Americans, there were no race differences in screening receptivity. However, there was some evidence that race moderates the relationship between medical mistrust and screening attitudes. While greater mistrust predicted more negative attitudes among both races, this effect was stronger among White Americans than African Americans. Findings suggest that group-based medical mistrust is a barrier to lung cancer screening for both African Americans and White Americans and illustrates the need to address medical mistrust as a barrier to screening for both racial minority and nonminority populations.

Public Health Sciences

Brunwasser SM, Gebretsadik T, Satish A, Cole JC, Dupont WD, **Joseph C**, Bendixsen CG, Calatroni A, Arbes SJ, Jr., Fulkerson PC, Sanders J, Bacharier LB, Camargo CA, Jr., **Johnson CC**, Furuta GT, Gruchalla RS, Gupta RS, Khurana Hershey GK, Jackson DJ, Kattan M, Liu A, O'Connor GT, Rivera-Spoljaric K, Phipatanakul W, Rothenberg ME, Seibold MA, Seroogy CM, Teach SJ, **Zoratti EM**, Togias A, and Hartert TV. Caregiver worry about COVID-19 as a predictor of social mitigation behaviours and SARS-CoV-2 infection in a 12-city U.S. surveillance study of households with children. *Prev Med Rep* 2025; 49:102936. PMID: 39697187. Full Text

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OBJECTIVE: Understanding compliance with COVID-19 mitigation recommendations is critical for informing efforts to contain future infectious disease outbreaks. This study tested the hypothesis that higher levels of worry about COVID-19 illness among household caregivers would predict lower (a) levels of overall and discretionary social exposure activities and (b) rates of household SARS-CoV-2 infections. METHODS: Data were drawn from a surveillance study of households with children (N = 1913) recruited from 12 U.S. cities during the initial year of the pandemic and followed for 28 weeks (data collection: 1-May-2020 through 22-Feb-2021). Caregivers rated how much they worried about family members getting COVID-19 and subsequently reported household levels of outside-the-home social activities that could increase risk for SARS-CoV-2 transmission at 14 follow-ups. Caregivers collected household nasal swabs on a fortnightly basis and peripheral blood samples at study conclusion to monitor for SARS-CoV-2 infections by polymerase chain reaction and serology. Primary analyses used generalized linear and generalized mixed-effects modelling. RESULTS: Caregivers with high enrollment levels of worry about COVID-19 illness were more likely to reduce direct social contact outside the household, particularly during the U.S.'s most deadly pandemic wave. Households of caregivers with lower COVID-19 worry had higher odds of (a) reporting discretionary outside-the-home social interaction and (b) SARS-CoV-2 infection. CONCLUSIONS: This was, to our knowledge, the first study showing that caregiver COVID-19 illness worry was predictive of both COVID-19 mitigation compliance and laboratory-determined household infection. Findings should inform studies weighing the adaptive value of worrying about infectious disease outbreaks against established detrimental health effects.

Public Health Sciences

Chaker AN, **Melhem M**, **Kagithala D**, **Telemi E**, **Mansour TR**, Simo L, **Springer K**, **Schultz L**, **Jarabek K**, **Rademacher AF**, **Brennan M**, **Kim E**, **Nerenz DR**, Khalil JG, Easton R, Perez-Cruet M, Aleem I, Park P, Soo T, Tong D, **Abdulhak M**, **Schwalb JM**, and **Chang V**. A propensity score-matched comparison between single-stage and multistage anterior/posterior lumbar fusion surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2024; 1-8. Epub ahead of print. PMID: 39705706.
Full Text

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OBJECTIVE: Patients undergoing anterior/posterior lumbar fusion surgery can undergo either a single-stage or multistage operation, depending on surgeon preference. The goal of this study was to assess different patient outcomes between single-stage and multistage lumbar fusion procedures in a multicenter setting. METHODS: The Michigan Spine Surgery Improvement Collaborative database was queried for anterior/posterior lumbar fusion surgeries between July 2018 and January 2022. Patients who underwent either single-stage or multistage procedures were included. For multistage procedures, the first surgery included both anterior lumbar interbody fusions and lateral lumbar interbody fusions. Primary outcomes included postoperative complications and improvement in patient-reported outcomes: Patient-Reported Outcomes Measurement Information System Physical Function, EQ-5D, and satisfaction. The two cohorts were propensity score matched, while Poisson generalized estimating equation models were used for multivariate analyses. RESULTS: After one-to-one propensity score matching, 355 patients were identified in the single-stage and multistage cohorts. Single-stage procedures were associated with a

lower risk of complications (p = 0.024), fewer emergency department visits (p = 0.029), and higher patient satisfaction after 1 year (p = 0.026) and 2 years (p = 0.007), compared with multistage procedures. After adjusting for baseline patient and operative characteristics, patients undergoing multistage procedures had a higher risk of complications (relative risk [RR] 1.17, 95% CI 1.02-1.34; p = 0.026), were less likely to be satisfied after 1 year (RR 0.83, 95% CI 0.74-0.93; p < 0.001), and were less likely to experience improvement in back pain after 90 days (RR 0.86, 95% CI 0.75-0.99; p = 0.039) and 2 years (RR 0.76, 95% CI 0.60-0.96; p = 0.023). CONCLUSIONS: The authors observed that patients who undergo lumbar fusion surgery using a multistage approach have higher postoperative complication rates and are less likely to report satisfaction compared with a matched, single-stage procedure cohort.

Public Health Sciences

Chiarelli G, **Davis M**, **Stephens A**, **Finati M**, **Cirulli GO**, **Morrison C**, Sood A, Carrieri G, Briganti A, Montorsi F, Lughezzani G, Buffi N, **Rogers C**, and **Abdollah F**. Racial Disparities in Future Development of Lethal Prostate Cancer Based on Midlife Baseline Prostate-Specific Antigen. *Prostate* 2024; e24834. Epub ahead of print. PMID: 39651707. Full Text

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BACKGROUND: Previous studies found that Midlife Baseline PSA (MB PSA) predicts the risk of developing lethal prostate cancer (PCa), although the cohorts were homogenous in terms of racial compositions. We aimed to investigate racial disparities in the predictive value of MB PSA for lethal PCa in a diverse, contemporary, North American population. METHODS: Our cohort included White and Black men aged 40-59 years, who underwent MB PSA through our health system. Cumulative incidence curves depicted lethal PCa stratified by race and MB PSA above/below the median. We utilized time-dependent Receiver Operating Characteristic (ROC) curves and Area Under the ROC Curve (AUC) to compare the performance of MB PSA in predicting lethal PCa based on race. Multivariable regression (MVA) was used to examine the impact of the MB PSA in predicting lethal PCa by race. RESULTS: We included 112,967 men, of whom 27% were Black. The cumulative incidence estimate with MB PSA values equal to the median at 15 years of follow-up was 0.13 (0.04, 0.32) for White men and 0.55 (0.24, 1.11) for Black men. AUCs comparison showed no statistically significant differences in the predictive role of MB PSA for lethal PCa between White and Black men. At MVA, using White patients with PSA ≤ median as the reference group, the HR of lethal PCa for White men with PSA > median aged 40-44, 45-49, 50-54, and 55-59 was respectively 2.98 (1.59-5.57), 3.01 (1.89-4.81), 5.10 (3.38-7.70), and 3.38 (2.32-4.92). While for Black men was respectively 5.50 (2.94-10.27), 4.19 (2.59-6.78), 9.79 (6.37-15.04), and 7.53 (5.03-11.26) (all p < 0.001). CONCLUSION: Our findings indicate that for the same MB PSA and within the same age category, Black men have a greater risk of developing lethal PCa than White men. A separate cut-off should be created for MB PSA, if this is to be used to guide PSA screening in clinical practice.

Public Health Sciences

Chiarelli G, **Stephens A**, **Finati M**, **Cirulli GO**, **Tinsley S**, **Wang Y**, Kolanukuduru K, Sood A, Carrieri G, Briganti A, Montorsi F, Lughezzani G, Buffi N, **Rogers C**, and **Abdollah F**. Active surveillance follow-up for prostate cancer: from guidelines to real-world clinical practice. *World J Urol* 2024; 42(1):646. PMID: 39589591. Full Text

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PURPOSE: To assess active surveillance (AS) adherence for prostate cancer (PCa) in a "real-world" clinical practice. MATERIALS AND METHODS: We utilized our institutional database which was built by interrogating electronic medical records for all men who got diagnosed with PCa from 1995 to 2022. Our cohort included all patients aged < 76 years, with PCa Gleason Grade (GG) 1 or 2, ≤ cT2c, PSA ≤ 20 ng/ml at diagnosis, enrolled on AS, and with at least one biopsy after diagnosis. Patients were separated into two groups based on the monitoring intensity. Patients with at least 1 PSA/year and at least 1 biopsy every 4 years were categorized as adherent to guidelines. Univariable and Multivariable logistic regression analyses were used to examine the impact of covariates on non-adherence to guidelines. Competing risks cumulative incidence was used to depict prostate cancer-specific mortality (PCSM). RESULTS: A total of 546 men met the inclusion criteria. Overall, 63 (11%) patients were adherent to guidelines (Group 1), while 483 (89%) were not (Group 2). Median PSAs/year and median biopsies/year were 2.3 (2.0-2.7) and 0.4 (0.3-0.6) for Group 1, and 1.2 (0.7-1.8) and 0.2 (0.1-0.2) for Group 2, respectively (both $p < 0.0001$). At multivariable analysis, Black men had a 2.20-fold higher risk of being in Group 2 than White men ($p < 0.05$). Patients with cT2 (OR:0.24, CI:0.11-0.52) and those with CCI ≥2 (OR:0.40, CCI:0.19-0.82) were less likely to be in Group 2, when compared to cT1 stage and CCI = 0, respectively (both $p < 0.05$). At 10 years, the cumulative incidence estimate of PCSM for the entire cohort was 2.1%. CONCLUSION: We found substantial deviations from AS monitoring guidelines, particularly in biopsy frequency, which did not seem to compromise PCSM in patients with stable PSA. Notably, our findings suggest that strict adherence to guidelines, especially in patients with cT2 at diagnosis, remains crucial.

Public Health Sciences

Chrissian AA, Abbas H, Chaddha U, **Debiane LG**, DeBiasi E, Filsoof D, **Hashmi MD**, Morton C, Naselsky WC, Pannu J, Ronaghi R, Salguero BD, Salmon C, Stewart SJ, and Channick CL. American Association of Bronchology and Interventional Pulmonology Essential Knowledge in Interventional Pulmonology Series: Selected Topics in Malignant Pleural Disease. *J Bronchology Interv Pulmonol* 2025; 32(1). PMID: 39704161. Full Text

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The goal of the American Association of Bronchology and Interventional Pulmonology Essential Knowledge in Interventional Pulmonology Series is to provide clinicians with concise, up-to-date reviews of important topics in the field of interventional pulmonology. This 3-year alternating rotation of primary topics will start with a focus on selected topics in malignant pleural disease. In this article, we update the reader on malignant pleural effusion in 3 parts: part 1-diagnosis, focusing on imaging and fluid biomarkers; part 2-management, with review of multimodal approaches, cost considerations, and evolving targeted therapies; and part 3-pleural mesothelioma. These reviews complement the Essential Knowledge in Interventional Pulmonology Lecture Series presented at the 2023 AABIP Annual Conference, available for viewing on the AABIP website (https://aabip.memberclicks.net/essential-knowledge-in-interventional-pulmonology-series).

Public Health Sciences

Elrefaey A, **Mohamedelkhair A**, Fahmy L, Affan M, **Schultz LR**, **Cerghet M**, and **Memon AB**. The clinical, diagnostic and treatment spectrum of seropositive and seronegative autoimmune encephalitis: Single-center cohort study of 51 cases and review of the literature. *Clin Exp Neuroimmunol* 2024; 15(4):186-200. PMID: Not assigned. Full Text

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Objective: Autoimmune encephalitis (AE) comprises a spectrum of inflammatory neurological syndromes characterized by immune responses to neuronal autoantigens, leading to diverse clinical manifestations, particularly behavioral and cognitive decline. Methods: This single-center retrospective study included 51 patients diagnosed with AE from 2013 to 2019 in a southeast Michigan tertiary care hospital. Patients were then divided into two groups, seropositive AE (AE+) and seronegative AE (AE−), based on antibody detection in the serum, cerebrospinal fluid or both when available. The study compares AE+ and AE− subtypes across clinical, diagnostic, and therapeutic parameters. Results: A total of 34 patients were classified as AE+, and 17 as AE−. Demographic analysis showed no significant differences in age, sex or race between the two groups. Clinical presentations varied widely, encompassing psychiatric symptoms, movement disorders, seizures and confusion; 24% patients had a prior malignancy. Laboratory assessments found diverse autoantibodies in AE+ patients' serum. Radiological and electrophysiological assessments showed no significant differences between the groups. AE− patients had higher rates of confusion compared with AE+ patients (59% vs. 18%, P = 0.004). Conclusions: This study focuses on the complexities associated with diagnosing AE, emphasizing the challenges posed by the heterogeneity of symptoms and often negative antibody test results. Rapid identification of AE, regardless of seropositivity or seronegativity, emerges as a critical factor for clinicians, facilitating the prompt initiation of immunotherapy and/or tumor removal if needed. These insights contribute to a better understanding of the landscape of this condition, offering clinicians the tools to refine their diagnostic and treatment strategies. Ultimately, the study aimed to enhance the management of AE, empowering healthcare professionals to make accurate and timely interventions for patients.

Public Health Sciences

Finati M, **Stephens A**, **Cirulli GO**, **Chiarelli G**, **Tinsley S**, **Morrison C**, Sood A, Buffi N, Lughezzani G, Salonia A, Briganti A, Montorsi F, Busetto GM, **Rogers C**, **Carrieri G**, and **Abdollah F**. Association of race and area of deprivation index with prostate cancer incidence and lethality: results from a contemporary North American cohort. *JNCI Cancer Spectr* 2024; 8(6). PMID: 39576690. Full Text

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BACKGROUND: Socioeconomic and demographic factors contribute to disparity in prostate cancer (PCa) outcomes. We examined the impact of Area of Deprivation Index (ADI) and race on PCa incidence and lethality in a North American cohort. METHODS: Our cohort included men who received at least 1 prostate-Specifig Antigen (pSA) test within our Health System (1995-2022). An ADI score was assigned to each patient based on their residential census block, ranked as a percentile of deprivation relative to the national level. Individuals were further categorized into quartiles, where the fourth one (ADI 75-100) represented those living in the most deprived areas. We investigated PCa incidence and lethality, using cumulative incidence estimates and competing-risk regression. An ADI × Race interaction term examined whether the relationship between ADI and outcomes varied based on race. RESULTS: We included 134366 patients, 25% of whom were non-Hispanic Black (NHB). Median (IQR) follow-up was 8.8 (5-17) years. At multivariate analysis, individuals from the third quartile (ADI 50-74, 95% CI = 0.83 to 0.95) and the fourth quartile (ADI ≥75, 95% CI = 0.75 to 0.86) showed significant reduced hazard ratios for PCa incidence, when compared with the first quartile (ADI <25, all P < .001). In contrast to the overall cohort, PCa incidence increased with ADI in NHB men, who were persistently at higher hazard for both PCa incidence and lethality than non-Hispanic White (NHW), across all ADI strata (all P < .001). CONCLUSIONS: Living in more deprived areas was associated with lower PCa incidence and higher lethal disease rate. Conversely, PCa incidence increased with ADI for NHB, who consistently showed worse outcomes than NHW individuals, regardless of ADI.

Public Health Sciences

Greimann E, Freigeh GE, Wettenstein RP, **Nelson B**, Carpenter LM, Mohan A, and **Baptist A**. Mild Asthma- What Matters to Patients and Parents. *Ann Allergy Asthma Immunol* 2024; Epub ahead of print. PMID: 39608675. Full Text

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BACKGROUND: Mild asthma has received less attention despite accounting for the majority of asthma patients. However, asthma complications including hospitalizations and progressive loss of lung function frequently occur in such patients. The priorities of mild asthma patients are unknown, hindering the ability to advance care. OBJECTIVE: To identify patient and parent perspectives on the definition of mild asthma, treatment preferences, concerns and goals of care. METHODS: Participants with self-defined mild/intermittent asthma were recruited using emails distributed through the Allergy & Asthma Network (AAN) and Allergy Foundation of America (AAFA). A demographic survey and measures of asthma control/quality of life were completed. Focus groups consisting of approximately 5 participants and a focus group leader were conducted. RESULTS: A total of 20 patients and 20 parents of children with mild asthma participated. Focus groups revealed significant variability in the definition and treatment preferences. Frequency of symptoms appears to be a key driver in treatment decisions for mild asthma, and those with infrequent symptoms were opposed to the addition of an inhaled corticosteroid to albuterol. Use of recommended asthma monitoring strategies such as asthma action plans or peak flow meters was low among adults. Participants desired more education from their providers regarding asthma remission and long-term complications associated with mild asthma. CONCLUSION: There is significant heterogeneity in the definition and treatment preferences among patients and parents of those with mild asthma. Shared decision making between patients and providers is necessary to personalize medical decisions in those with mild asthma.

Public Health Sciences

Jamshidi A, Espin-Garcia O, **Wilson TG**, **Loveless I**, Pelletier JP, Martel-Pelletier J, and **Ali SA**. MicroRNA signature for early prediction of knee osteoarthritis structural progression using integrated machine and deep learning approaches. *Osteoarthritis Cartilage* 2024; Epub ahead of print. PMID: 39617204. Full Text

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OBJECTIVE: Conventional methodologies are ineffective in predicting the rapid progression of knee osteoarthritis (OA). MiRNAs show promise as biomarkers for patient stratification. We aimed to develop a miRNA prognosis model for identifying knee OA structural progressors/non-progressors using integrated machine/deep learning tools. METHODS: Baseline serum miRNAs from OAI participants were isolated and sequenced. Participants were categorized based on their likelihood of knee structural progression/non-progression using MRI and X-ray data. For prediction model development, 152 OAI participants (91 progressors, 61 non-progressors) were used. MiRNA features were reduced through VarClusHi clustering. Key miRNAs and OA determinants (age, sex, BMI, race) were identified using seven machine learning tools. The final prediction model was developed using advanced machine/deep learning techniques. Model performance was assessed with AUC (95% confidence intervals) and accuracy. Monte Carlo cross-validation ensured robustness. Model validation used 30 OAI baseline plasma samples from an independent set of participants (14 progressors, 16 non-progressors). RESULTS: Feature clustering selected 107 miRNAs. Elastic Net was chosen for feature selection. An optimized prediction model based on an Artificial Neural Network (ANN) comprising age and four miRNAs (hsa-miR-556-3p, hsa-miR-3157-5p, hsa-miR-200a-5p, hsa-miR-141-3p) exhibited excellent performance (AUC, 0.94 [0.89, 0.97]; accuracy, 0.84 [0.77, 0.89]). Model validation performance (AUC, 0.81 [0.63, 0.92]; accuracy, 0.83 [0.66, 0.93]) demonstrated the potential for generalization. CONCLUSION: This study introduces a novel miRNA prognosis model for knee OA patients at risk of structural progression. It requires five baseline features, demonstrates excellent performance, is validated with an independent set, and holds promise for future personalized therapeutic monitoring.

Public Health Sciences

Joseph J, Luo Z, Epstein RA, Gracey K, Kuhn TM, Cull MJ, and Raman R. Analysis of longitudinal patterns of child maltreatment reports in the United States. *Child Abuse Negl* 2024; 160:107223. PMID: 39721223. Full Text

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BACKGROUND: Child maltreatment is a continuous and prevalent issue, and victims of maltreatment often suffer adverse effects well into adulthood. Since child maltreatment rates tend to be clustered geographically and temporally, intervention programs are best implemented at a local level, targeting local risk factors for sustained and effective reduction over time. OBJECTIVE: Quantifying geographic variation in child maltreatment rate trajectories can help states identify local risk factors to guide program development and resource allocation. PARTICIPANTS AND SETTING: National child maltreatment data from 2011 to 2020 from the National Child Abuse and Neglect Data System (NCANDS) was used to quantify child maltreatment rates (overall and substantiated) over time. METHODS: Latent trajectory analysis was conducted to identify groups of states in the United States that share distinct temporal patterns of child maltreatment rates. Child maltreatment data was linked to the American Community Survey data to obtain community-level characteristics. RESULTS: Three groups of states with distinct child maltreatment trajectories were identified: 43 states with stable trajectory, 4 states with increasing number of reports over time, and 5 states with decreasing reports over time. Although states with a stable trajectory had some characteristics associated with higher socioeconomic status, such as lower percentage of families below poverty level, and lower percentage of unemployed laborers, there was not a consistent trend in socioeconomic characteristics between the three groups. CONCLUSIONS: Our results indicate there to be three groups of states with distinct child maltreatment trajectories, with majority of the states following a stable trajectory over time. There was not a consistent trend in socioeconomic characteristics between the three groups. While the results do not allow us to draw firm conclusions about socioeconomic characteristics associated with maltreatment trajectories, it does provide data-driven evidence for the existing assumption of a national average maltreatment trajectory.

Public Health Sciences

Kashyap B, Crouse B, Fields B, Aguirre A, Ali T, Hays R, Li X, Shapiro LN, **Tao MH**, **Vaughn IA**, and Hanson LR. How do researchers identify and recruit dementia caregivers? A scoping review. *Gerontologist* 2024; Epub ahead of print. PMID: 39693374. Full Text

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BACKGROUND AND OBJECTIVES: Studies involving dementia caregivers are essential to transform care and inform new policies. However, identifying and recruiting this population for research is an ongoing challenge. This scoping review aimed to capture the current methodology for identifying and recruiting dementia caregivers in clinical studies. A focus was placed on methods for underrepresented populations and pragmatic trials to guide pragmatic and equitable clinical studies. RESEARCH DESIGN AND METHODS: Researchers conducted a literature search using PubMed, PsycINFO, EMBASE and Web of Science databases. Studies conducted in the United States that enrolled at least 10 caregivers and were published within the last 10 years (2013-2023) were included. RESULTS: Overall, 148 articles were included in the review. The most common method for identification was community outreach, and paper advertisements for recruitment. Caregivers were most often approached in community settings, formal organizations, and/or dementia research centers. Most enrolled caregivers were female, White, and spouses of persons living with dementia. Race and ethnicity were underreported, as were the target recruitment goals. Limited studies were self-reported as pragmatic. Additionally, limited studies reported adaptations for methods of identification and recruitment in underrepresented populations. DISCUSSION AND IMPLICATIONS: We identified gaps in current practices for the identification and recruitment of dementia caregivers. Future identification and recruitment methodologies should be tailored to the intervention's intent, health care setting, and the research questions that need to be answered, while

balancing available resources. Additionally, transparent reporting of identification and recruitment procedures, target recruitment goals, and comprehensive demographic data is warranted.

Public Health Sciences

Levin AM, **Okifo O**, **Buhl K**, **Ouchi T**, **Parker B**, **Tan J**, **Datta I**, **Dai X**, **Chen Y**, **Palanisamy N**, **Veenstra J**, **Carskadon S**, **Li J**, **Ozog D**, **Keller CE**, **Chitale D**, **Bobbitt KR**, **Crawford HC**, **Steele N**, **Mi QS**, and **Jones LR**. Higher expression of mir-31-5p is associated with reduced risk of head and neck keloid recurrence following surgical resection. *Laryngoscope Investig Otolaryngol* 2024; 9(6):e70040. PMID: 39664781. Full Text

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OBJECTIVE: In this study, we aimed to evaluate mir-31-5p as a prognostic biomarker of keloid disease (KD) recurrence using a retrospective, treatment naïve, surgical cohort of head and neck KD cases from Henry Ford Health. METHODS: Using a tissue microarray, mir-31-5p expression was measured with miRNAscope, and mir-31-5p cell positivity was determined with QuPath. Logistic regression was used to test the association between mir-31-5p positive cells and KD recurrence at 1 year. In an independent dataset, associations between mir-31-5p and messenger RNA (mRNA) expression were assessed. Ingenuity Pathway Analysis identified target genes and pathways impacted by mir-31-5p. RESULTS: Of the 58 KD patients, 42 (72%) received adjuvant triamcinolone injections, and 8 recurred (14%). mir-31-5p was expressed in 48 (83%) specimens. Increasing mir-31-5p expression was associated with decreased risk of recurrence ($p = .031$), with an odds ratio of 0.86 (95% CI 0.75-0.98) for each 20% increase in mir-31-5p cellular positivity. This effect persisted with triamcinolone treatment (odds ratio 0.82; 95% CI 0.71-0.95; $p = .015$). mir-31-5p correlated with gene expression enriched in KD pathways, including mRNA splicing and autophagy. CONCLUSION: Taken together, our data supports the association between mir-31-5p expression and KD recurrence. Its potential as a prognostic biomarker should be further investigated. LEVEL OF EVIDENCE: Level 2.

Public Health Sciences

Lewis NM, Harker EJ, Grant LB, Zhu Y, Grijalva CG, Chappell JD, Rhoads JP, Baughman A, Casey JD, Blair PW, Jones ID, Johnson CA, Lauring AS, Gaglani M, Ghamande S, Columbus C, Steingrub JS, Shapiro NI, Duggal A, Busse LW, Felzer J, Prekker ME, Peltan ID, Brown SM, Hager DN, Gong MN, Mohamed A, Exline MC, Khan A, Hough CL, Wilson JG, Mosier J, Qadir N, Chang SY, Ginde AA, Martinez A, Mohr NM, Mallow C, Harris ES, Johnson NJ, Srinivasan V, Gibbs KW, Kwon JH, **Vaughn IA**, **Ramesh M**, Safdar B, Goyal A, DeLamielleure LE, DeCuir J, Surie D, Dawood FS, Tenforde MW, Uyeki TM, Garg S, Ellington S, and Self WH. Benefit of early oseltamivir therapy for adults hospitalized with influenza A: an observational study. *Clin Infect Dis* 2024; Epub ahead of print. PMID: 39607747. Full Text

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Stanford University School of Medicine, Stanford, California.
University of Arizona, Tucson, Arizona.
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University of Colorado School of Medicine, Aurora, Colorado.
University of Iowa School of Medicine, Iowa City, Iowa.
University of Miami School of Medicine, Miami, Florida.
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BACKGROUND: clinical guidelines recommend initiation of antiviral therapy as soon as possible for patients hospitalized with confirmed or suspected influenza. METHODS: A multicenter US observational sentinel surveillance network prospectively enrolled adults (aged ≥18 years) hospitalized with laboratory-confirmed influenza at 24 hospitals during October 1, 2022-July 21, 2023. A multivariable proportional odds model was used to compare peak pulmonary disease severity (no oxygen support, standard supplemental oxygen, high-flow oxygen/non-invasive ventilation, invasive mechanical ventilation, or death) after the day of hospital admission among patients starting oseltamivir treatment on the day of admission (early) versus those who did not (late or not treated), adjusting for baseline (admission day) severity, age, sex, site, and vaccination status. Multivariable logistic regression models were used to evaluate the odds of intensive care unit (ICU) admission, acute kidney replacement therapy or vasopressor use, and in-hospital death. RESULTS: A total of 840 influenza-positive patients were analyzed, including 415 (49%) who started oseltamivir treatment on the day of admission, and 425 (51%) who did not. Compared with late or not treated patients, those treated early had lower peak pulmonary disease severity (proportional aOR: 0.60, 95% CI: 0.49-0.72), and lower odds of intensive care unit admission (aOR: 0.24, 95% CI: 0.13-0.47), acute kidney replacement therapy or vasopressor use (aOR: 0.40, 95% CI: 0.22-0.67), and in-hospital death (aOR: 0.36, 95% CI: 0.18-0.72). CONCLUSION: Among adults hospitalized with influenza, treatment with oseltamivir on day of hospital admission was associated reduced risk of disease progression, including pulmonary and extrapulmonary organ failure and death.

Public Health Sciences

Llamocca EN, **Bossick AS**, **Perkins DW**, **Ahmedani BK**, **Behrendt R**, **Bloemen A**, **Murphy A**, **Kulkarni A**, and **Lockhart E**. Health-related social needs screening, reporting, and assistance in a large health system. *Prev Med* 2024; 190:108182. PMID: 39586330. Full Text

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BACKGROUND: National mandates require screening for and addressing health-related social needs (HRSNs) in healthcare settings. However, differences in HRSN screening process (i.e., completed screenings, screening results, documented offer of assistance, documented assistance request) have been reported by population subgroup. Knowledge of the most effective HRSN screening and intervention methods is limited. We sought to describe differences in completed HRSN screenings, screening results, and assistance request rates across patient and healthcare visit characteristics. METHODS: We examined data from all patients aged ≥18 years and residing in the US receiving services at a large, Midwestern healthcare system with a goal to screen all patients for HRSN at least once annually between July 2021-June 2023 (n = 1,190,488). We examined the proportion of patients with any HRSN screening, with any reported HRSN, asked whether they wanted assistance, or who requested assistance for a reported HRSN stratified by patient demographics and healthcare visit characteristics (i.e., payer, screening location, who completed the screening). RESULTS: Less than half of eligible patients (47.0 %) were screened for HRSNs. About one-sixth (16.9 %) reported any HRSN. Although most patients reporting HRSNs were asked whether they wanted assistance, only about one-quarter (26.8 %) responded affirmatively. Proportions included in each step of the HRSN screening process significantly differed by patient and healthcare visit characteristics. DISCUSSION: This study is one of the first to investigate various steps of a population-wide HRSN screening program. Our findings suggest that examining differences in HRSN screening process by population subgroup is key to addressing HRSNs through a health equity lens.

Public Health Sciences
Lockhart E, **Gootee J**, **Copeland L**, and Turner D. Willingness to Be Contacted via a Patient Portal for Health Screening, Research Recruitment, and at-Home Self-Test Kits for Health Monitoring: Pilot Quantitative Survey. *JMIR Form Res* 2024; 8:e59837. PMID: 39584575. Full Text

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BACKGROUND: Patient portals are being increasingly used by health systems in the United States. Although some patients use portals for clinical use, patient perspectives on using portals for research-related activities, to complete health screenings, and to request at-home self-test kits are unclear. OBJECTIVE: We aimed to understand patient perspectives on using electronic health portals for research; health-related screenings; and patient-initiated, home-based self-testing. METHODS: Patients (N=105) from the Patient Engaged Research Center at a large, urban, midwestern health system completed a 23-item web-based survey on patient portal (MyChart) use and willingness to use the patient portal for research, risk assessments, and self-test kits. Frequencies and percentages were generated. RESULTS: Almost all participants (102/105, 97.1%) had accessed MyChart at least once, with most (44/102, 43.1%) indicating they logged in at least once per month. Participants indicated logging into MyChart to check laboratory results or other health data (89/105, 84.8%), because they received a message to log in (85/105, 81%), and to message their health care professional (83/105, 79%). Fewer participants logged in to see what medications they had been prescribed (16/105, 15.2%) and to learn more about their health conditions (29/105, 27.6%). Most participants indicated logging into MyChart on a computer via a website (70/105, 66.7%) or on a smartphone via an app (54/105, 51.4%). When asked about how likely they would be to participate in different types of research if contacted via MyChart, most (90/105, 85.7%) said they would be likely to answer a survey, fill out a health assessment (87/105, 82.9%), or watch a video (86/105, 81.9%). Finally, participants would be willing to answer risk assessment questions on MyChart regarding sleep (74/101, 73.3%), stress (65/105, 61.9%), diabetes (60/105, 57.1%), anxiety (59/105, 56.2%), and depression (54/105, 51.4%) and would be interested in

receiving an at-home self-test kit for COVID-19 (66/105, 62.9%), cholesterol (63/105, 60%), colon cancer (62/105, 59%), and allergies (56/105, 53.3%). There were no significant demographic differences for any results (all P values were >.05). CONCLUSIONS: Patient portals may be used for research recruitment; sending research-related information; and engaging patients to answer risk assessments, read about health information, and complete other clinical tasks. The lack of significant findings based on race and gender suggests that patient portals may be acceptable tools for recruiting research participants and conducting research. Allowing patients to request self-test kits and complete risk assessments in portals may help patients to take agency over their health care. Future research should examine if patient portal recruitment may help address persistent biases in clinical trial recruitment to increase enrollment of women and racial minority groups.

Public Health Sciences

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PURPOSE: Pancreatic ductal adenocarcinoma (PDAC) patients with tumors enriched for the basal-like molecular subtype exhibit enhanced resistance to standard of care treatments and have significantly worse overall survival (OS) compared to patients with classical subtype enriched tumors. It is important to develop genomic resources, enabling identification of novel putative targets in a statistically rigorous manner. EXPERIMENTAL DESIGN: We compiled a single cell RNA sequencing (scRNAseq) atlas of the human pancreas with 229 patient samples, aggregated from publicly available raw data. We mapped cell-type specific scRNAseq gene signatures in bulk RNAseq (n=744) and spatial transcriptomics (ST) (n=22) and performed validation using multiplex immunostaining. RESULTS: Analysis of tumor cells from our scRNAseq atlas revealed nine distinct populations, two of which aligned with the basal subtype, correlating with worse OS in bulk RNAseq. Deconvolution identified one of the basal populations to be the predominant tumor subtype in non-dissociated ST tissues and in vitro tumor cell and patient-derived organoid lines. We discovered a novel enrichment and spatial association of CXCL10+ cancer associated fibroblasts (CAFs) with basal tumor cells. We identified that besides immune cells, ductal cells also express CXCR3, the receptor for CXCL10, suggesting a relationship between these cell types in PDAC tumor microenvironment. CONCLUSIONS: We show that our scRNAseq atlas (700,000 cells), integrated with ST data, has increased statistical power and is a powerful resource, allowing for expansion of current subtyping paradigms in PDAC. We uncovered a novel signaling niche marked by CXCL10+ CAFs and basal tumor cells that could be explored for future targeted therapies.

Public Health Sciences

Mandal S, Teslow EA, Huang M, Yu Y, **Sridhar S**, **Crawford HC**, Hockenberry AJ, Stoppler MC, **Levin AM**, and **Huang L**. Molecular Differences in Pancreatic Ductal Adenocarcinomas from Black Versus White Patients. *Cancer Res Commun* 2024; Epub ahead of print. PMID: 39699266. Full Text

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Pancreatic cancer is the third leading cause of cancer-related death in the US. Black or African American patients have a higher incidence of pancreatic cancer compared to other racial groups. It is unclear whether distinct molecular mechanisms are involved in the development of pancreatic cancer in different racial groups. To identify tumor molecular features that are distinctly associated with race in Black or African American and White patients with pancreatic ductal adenocarcinoma (the main subtype of pancreatic cancer), we analyzed de-identified patient records, including tumor sequencing data and expression of PD-L1, from the Tempus multimodal database. Patients with a primary diagnosis of pancreatic ductal adenocarcinoma and who received molecular testing between 2017-11 and 2023-03 were included in analyses. Among 4,249 patients analyzed in this study, 452 (10.6%) were Black or African American and 3797 (89.4%) were White. Black patients had a higher prevalence of TP53 mutations compared to White patients ($p<0.001$). KRASG12R mutations occurred more frequently in female patients in the Black vs White group ($p=0.007$). Compared to White patients, Black patients had a higher tumor mutational burden ($p<0.001$) and PD-L1 overexpression ($p=0.047$). In a separate analysis of recent clinical trials testing immunotherapies for pancreatic cancer, we found that Black patients and other minorities were underrepresented in most trials. These findings suggest race-associated molecular differences in tumors that may impact patient responses to immunotherapies. Our study also supports the importance of improving patient diversity in clinical trials on pancreatic cancer treatments.

Public Health Sciences

Manivannan A, Pillai A, Liapakis A, Parikh ND, Kumar V, Verna EC, **Salgia R**, **Wu T**, **Lu M**, and **Jesse MT**. Influence of Acuity Circles on Hepatocellular Carcinoma and the Interaction of Gender and Race in Liver Transplantation. *Clin Transplant* 2024; 38(12):e70045. PMID: 39620868. Full Text

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The impact of liver transplant allocation policy using acuity circles (ACs) on interactions between race and gender on waitlist mortality or receipt of deceased donor liver transplant (DDLT) is unknown. Using data from the United Network for Organ Sharing (UNOS), we examined adults listed for DDLT from April 3, 2017, to October 4, 2022 (30 months pre- and post-AC). Fine-Gray sub-distribution hazard model explored AC indicators by race and gender interactions and their effect on receipt of DDLT or waitlist mortality. Also explored was AC's impact on hepatocellular carcinoma (HCC) diagnosis and receipt of DDLT or waitlist mortality. 59 592 patients (30 202 pre-AC, 29 390 post-AC) included. For both receipt of DDLT and waitlist mortality, there were no 3-way (AC by race by gender) interactions, indicating that the effects of race and gender on DDLT or waitlist mortality were consistent pre- and post-AC. Irrespective of AC implementation, Black and Hispanic women were less likely to receive DDLT and had an increased risk of waitlist mortality compared to White women. White, Black, and Hispanic men had lower waitlist mortality risk and greater likelihood of receiving DDLT compared to their female race/ethnic

counterparts. Patients with HCC had a significantly greater chance for DDLT than non-HCC, although post-AC this effect was attenuated. Patients with HCC were also at greater risk of waitlist mortality pre- and post-AC compared to those without HCC however, the waitlist mortality post-AC was attenuated only for those patients without HCC. To our knowledge, this is the first study to show the interaction of gender and race on waitlist mortality and access to transplantation since the implementation of AC, showing continued disparate outcomes for women both within and across racial groups.

Public Health Sciences

Non AL, Li X, Jones MR, Oken E, Hartert T, Schoettler N, Gold DR, Ramratnam S, Schauberger EM, Tantisira K, Bacharier LB, Conrad DJ, Carroll KN, Nkoy FL, Luttmann-Gibson H, Gilliland FD, Breton CV, Kattan M, Lemanske RF, Jr., Litonjua AA, McEvoy CT, Rivera-Spoljaric K, Rosas-Salazar C, **Joseph CLM**, Palmore M, Ryan PH, **Wegienka G**, **Sitarik AR**, Singh AM, Miller RL, **Zoratti EM**, Ownby D, Camargo CA, Jr., Aschner JL, Stroustrup A, Farzan SF, Karagas MR, Jackson DJ, and Gern JE. Comparison of Race-neutral Versus Race-specific Spirometry Equations for Evaluation of Child Asthma. *Am J Respir Crit Care Med* 2024; Epub ahead of print. PMID: 39642347. Full Text

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RATIONALE: Race-based estimates of pulmonary function in children could influence the evaluation of asthma in children from racial and ethnic minoritized backgrounds. OBJECTIVES: To determine if race-neutral (GLI-Global) versus race-specific (GLI-Race-Specific) reference equations differentially impact spirometry evaluation of childhood asthma. METHODS: The analysis included 8,719 children aged 5 to <12 years from 27 cohorts across the United States grouped by parent-reported race and ethnicity. We analyzed how the equations affected forced expiratory volume in 1 second (FEV(1)), forced vital capacity (FVC), and FEV(1)/FVC z-scores. We used multivariable logistic models to evaluate associations between z-scores calculated with different equations and asthma diagnosis, emergency department (ED) visits, and hospitalization. MEASUREMENTS AND MAIN RESULTS: For Black children, the GLI-Global vs. Race-Specific equations estimated significantly lower z-scores for FEV(1) and FVC but similar values for FEV(1)/FVC, thus increasing the proportion of children classified with low FEV(1) by 14%. While both equations yielded strong inverse relationships between FEV(1) and FEV(1)/FVC z-scores and asthma outcomes, these relationships varied across racial and ethnic groups ($p<0.05$). For any given FEV(1) or FEV(1)/FVC z-score, asthma diagnosis and ED visits were higher among Black and Hispanic versus White children ($p<0.05$). For FEV(1), GLI-Global equations estimated asthma outcomes that were more uniform across racial and ethnic groups. CONCLUSIONS: Parent-reported race and ethnicity influenced relationships between lung function and asthma outcomes. Our data show no advantage to race-specific equations for evaluating childhood asthma, and the potential for race-specific equations to obscure lung impairment in disadvantaged children strongly supports using race-neutral equations.

Public Health Sciences

Schildroth S, Bond JC, Wesselink AK, Abrams J, Calafat AM, Cook Botelho J, White KO, **Wegienka G**, Hatch EE, and Wise LA. Associations between per- and polyfluoroalkyl substances (PFAS) and female sexual function in a preconception cohort. *Environ Res* 2024; 266:120556. PMID: 39644984. Request Article

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BACKGROUND: Female sexual function is important for sexual well-being, general health, fertility, and relationship satisfaction. Distressing impairments in sexual function, clinically recognized as female sexual dysfunction (FSD), can manifest as issues with interest/desire, arousal, orgasm, and pain during vaginal penetration. Some evidence suggests that exposure to endocrine-disrupting chemicals may adversely affect female sexual function, but associations for per- and polyfluoroalkyl substances (PFAS) have not been previously evaluated. OBJECTIVE: We investigated associations between serum PFAS concentrations and female sexual function among U.S. pregnancy planners. METHODS: We used cross-sectional data from participants from Pregnancy Study Online (PRESTO), a prospective preconception cohort study. Participants reported sexual function and distress at baseline on two validated measures: a modified version of the Female Sexual Function Index-6 (FSFI-6) and the Female Sexual Distress Scale (FSDS). We quantified PFAS serum concentrations in samples collected in the preconception period (i.e., at baseline) using solid phase extraction-high performance liquid chromatography-isotope-dilution-mass spectrometry. Participants reported sociodemographic information on structured baseline questionnaires. We included 78 participants with complete PFAS and sexual function data and fit multivariable linear regression models to estimate mean differences in FSFI-6 scores (β) or percent differences (%) in FSDS scores per interquartile range (IQR) increase in PFAS concentrations, adjusting for age, annual household income, years of education, parity, and body mass index. We further investigated effect

measure modification by parity (parous vs. nulliparous) in stratified models. RESULTS: An IQR increase in perfluorohexanesulfonic acid was associated with a 1.0-point decrease (95% CI = -1.8, -0.1) in reported FSFI-6 scores, reflecting poorer sexual function. PFAS were consistently associated with lower FSFI-6 scores among parous participants. PFAS were also associated, though imprecisely, with greater sexual distress. CONCLUSION: Some PFAS were associated with poorer sexual function among U.S. pregnancy planners, but future studies are needed to clarify the extent to which PFAS influences female sexual health.

Public Health Sciences

Tenebe IT, Babatunde EO, Ogarekpe NM, **Emakhu J**, Etu EE, Edo OC, Omeje M, and Benson NU. Detection and Measurement of Bacterial Contaminants in Stored River Water Consumed in Ekpoma. *Water* 2024; 16(18):16. PMID: Not assigned. Full Text

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This study was conducted in Ekpoma, a town dependent on rainwater and river water from nearby areas because of a lack of groundwater sources, and the physicochemical and bacteriological (heterotrophic plate count [HPC], total coliform count [TCC], and fecal coliform count [FCC]) properties of 123 stored river water samples grouped into five collection districts (EK1 to EK5). The results were compared with regulatory standards and previous regional studies to identify water quality trends. While most physicochemical properties met drinking water standards, 74% of samples had pH values > 8.5. Twenty-seven samples were fit for drinking, with EK4 having the highest number of bacterio-logically unsuitable samples. Ten bacterial species were identified, with Gram-negative short-rod species such as Escherichia coli, Klebsiella pneumoniae, and Salmonella typhimurium being predominant. HPC values varied from 367 x 10(4) to 1320 x 10(4) CFU/mL, with EK2 (2505 x 10(4) CFU/mL) and EK5 (1320 x 10(4) CFU/mL) showing particularly high counts. The TCC values ranged from 1049 x 10(4) to 4400 x 10(4) CFU/mL, and the FCC values from 130 x 10(4) to 800 x 10(4) CFU/mL, all exceeding WHO limits (1.0 x 10(2) CFU/mL). Historical data show no improvement in water quality, emphasizing the need for individuals to treat water properly before consumption. The findings provide baseline data for local water authorities and serve as a wake-up call for adequate water treatment, storage interventions, and community education on water security. Additionally, this study offers a practical process for improving the quality of water stored in similar regions.

Public Health Sciences

Veenstra J, **Loveless I**, **Dimitrion P**, **Adrianto I**, **Ozog D**, and **Mi QS**. Unveiling intratumoral heterogeneity in high-risk cutaneous squamous cell carcinoma using single-cell spatial enhanced resolution omics-sequencing (Stereo-seq). *J Dermatol Sci* 2024; Epub ahead of print. PMID: 39643570. Full Text

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Public Health Sciences

Yamamoto N, Dobersch S, **Loveless I**, Samraj AN, Jang GH, Haraguchi M, Kang LI, Ruzinova MB, Vij KR, Mudd JL, Walsh T, Safyan RA, Chiorean EG, Hingorani SR, Bolton NM, Li L, Fields RC, DeNardo DG, Notta F, **Crawford HC**, **Steele NG**, and Kugel S. HMGA2 Expression Predicts Subtype, Survival, and Treatment Outcome in Pancreatic Ductal Adenocarcinoma. *Clin Cancer Res* 2024; Epub ahead of print. PMID: 39680021. Full Text

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PURPOSE: To establish HMGA2 as a marker of basal-like disease in pancreatic ductal adenocarcinoma (PDAC) and explore its use as a biomarker for prognosis and treatment resistance. EXPERIMENTAL DESIGN: We identified high expression of HMGA2 in basal PDAC cells in a scRNAseq Atlas of 172 patient samples. We then analyzed HMGA2 expression, along with expression of the classical marker GATA6, in a cohort of 580 PDAC samples with multiplex immunohistochemistry. We further supplemented these data with an additional 30 diverse patient samples and multiple independent single-cell RNAseq databases. RESULTS: We found that expression of HMGA2, but not previously described basal markers CK5 or CK17, predicted overall survival in our cohort. Combining HMGA2 and GATA6 status allowed for identification of two key study groups: an HMGA2+/GATA6- cohort with worse survival, low tumor-infiltrating CD8+ T cells, increased FAP+ fibroblasts, and poorer response to gemcitabine-based chemotherapies (n=94, median survival=11.2 months post-surgery); and an HMGA2-/GATA6+ cohort with improved survival, increased CD8+ T-cell infiltrate, decreased FAP+ fibroblasts, and improved survival with gemcitabine-based chemotherapy (n=198, median survival=21.7 months post-surgery).

HMGA2 was also prognostic for overall survival in RNA sequencing from an independent cohort. CONCLUSIONS: IHC stratification of primary tumors by HMGA2 and GATA6 status in pancreatic cancer is associated with differential outcomes, survival following chemotherapy, and tumor microenvironments. As a nuclear marker for basal disease, HMGA2 complements GATA6 to identify disease subtypes in PDAC.

Public Health Sciences

Young KZ, **Loveless I**, **Su WK**, **Veenstra J**, **Yin C**, **Dimitrion P**, **Krevh R**, **Zhou L**, **She R**, **Pan M**, **Levin AM**, **Young A**, **Samir E**, **Dai A**, **Ge J**, **Huggins RH**, **de Guzman Strong C**, **Lim HW**, **Ozog DM**, **Hamzavi I**, **Adrianto I**, and **Mi QS**. A diverse hidradenitis suppurativa cohort: A retrospective cross-sectional study of 13,130 patients from a large US health care system database from 1995 to 2022. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 39532232. Full Text

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BACKGROUND: Most epidemiological studies of hidradenitis suppurativa (HS) have described homogeneous patient populations. OBJECTIVE: To characterize demographics, modifiable health behaviors, and comorbidities of HS patients within a diverse cohort. METHODS: A retrospective cross-sectional study of 13,130 HS patients within a health care system was conducted. RESULTS: A female sex bias of ~3:1 in all racial/ethnic subgroups was observed. Black/African American (AA) patients had a lower age at HS diagnosis than White patients (37.1 years vs 39.4 years, P < .001). A higher proportion of Black/AA females than White females with HS had body mass index in the obese range (69.9% vs 56.5%; P = .03). In contrast, fewer Black/AA males with HS had a body mass index in the obese range compared to White males (51.4% vs 61.0%; P < .001). More Black/AA patients than White patients with HS had congestive heart failure (odds ratio (OR) = 2.10, confidence interval (CI) = 1.19-3.78; P < .05), chronic pulmonary disease (OR = 1.34; CI = 1.02-1.78; P < .05), diabetes with chronic complication (OR = 1.73; CI = 1.16-2.60; P < .05), renal disease (OR = 2.66; CI = 1.67-4.34; P < .05), and Charlson comorbidity index score ≥4 (OR = 1.67; CI = 1.09-2.58; P < .05). Furthermore, male patients were more likely than female patients to have renal disease (OR = 2.62; CI = 1.66-4.14; P < .05). LIMITATIONS: A single-center study. CONCLUSION: Subgroups of HS patients had significant differences in demographics, risk factors, and comorbid conditions.

Pulmonary and Critical Care Medicine

Chrissian AA, Abbas H, Chaddha U, **Debiane LG**, DeBiasi E, Filsoof D, **Hashmi MD**, Morton C, Naselsky WC, Pannu J, Ronaghi R, Salguero BD, Salmon C, Stewart SJ, and Channick CL. American Association of Bronchology and Interventional Pulmonology Essential Knowledge in Interventional Pulmonology Series: Selected Topics in Malignant Pleural Disease. *J Bronchology Interv Pulmonol* 2025; 32(1). PMID: 39704161. Full Text

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The goal of the American Association of Bronchology and Interventional Pulmonology Essential Knowledge in Interventional Pulmonology Series is to provide clinicians with concise, up-to-date reviews

of important topics in the field of interventional pulmonology. This 3-year alternating rotation of primary topics will start with a focus on selected topics in malignant pleural disease. In this article, we update the reader on malignant pleural effusion in 3 parts: part 1-diagnosis, focusing on imaging and fluid biomarkers; part 2-management, with review of multimodal approaches, cost considerations, and evolving targeted therapies; and part 3-pleural mesothelioma. These reviews complement the Essential Knowledge in Interventional Pulmonology Lecture Series presented at the 2023 AABIP Annual Conference, available for viewing on the AABIP website (https://aabip.memberclicks.net/essential-knowledge-in-interventional-pulmonology-series).

Radiation Oncology

Choi JI, Freedman GM, Guttmann DM, Ahmed K, Gao W, **Walker EM**, Harris EE, Gonzalez V, Ye J, Nead K, Taunk N, Tadros AB, Dang CT, Daroui P, and Novick K. Executive Summary of the American Radium Society Appropriate Use Criteria: Regional Nodal Irradiation for Breast Cancer. *Cancer Clin Trials* 2024. PMID: Not assigned. Full Text

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Objectives: Recent literature has provided additional data to further individualize treatment recommendations on regional nodal irradiation (RNI) patient selection and delivery techniques, but controversies surrounding optimal RNI utilization remain, including radiation technique, modality selection, and internal mammary lymph node (IMN) inclusion. The American Radium Society (ARS) Breast Appropriate Use Criteria (AUC) Committee performed a systematic review and developed a consensus guideline to summarize recent data and provide evidence-based recommendations. Methods: A multidisciplinary panel comprised of 15 members representing radiation oncologists, medical oncologists, and surgical oncologists specializing in the treatment of breast cancer conducted an analysis of the medical literature from January 1, 2011 to April 1, 2024. Modified Delphi methodology was used to rate the appropriateness of treatments for variants across 3 key questions. Results: Patients with intermediate-risk breast cancer, such as limited nodal involvement or large primary tumor size, are reasonable candidates for RNI, although a subset of patients with overall favorable clinicopathologic features may be considered for treatment de-escalation. Data on the use of advanced radiation techniques for RNI were limited in scope and strength, and the panel agreed that careful patient selection is needed when using these tools. Evidence suggests that the IMN should be included when delivering RNI given the absolute benefit demonstrated in multiple randomized trials. Conclusion: A systematic review and evidence-based summary of recommendations are provided in these consensus guidelines from the ARS Breast AUC Committee to provide current comprehensive guidance on the optimal management of non-metastatic breast cancer patients being considered for RNI.

Radiation Oncology

Kaljee L, **Antwi S**, **Dankerlui D**, Harris D, Israel B, **White-Perkins D**, **Aboah VO**, Aduse-Poku L, **Larrious-Lartey H**, Brush B, Coombe C, Patman L, Cawthorne N, Chue S, Rowe Z, **Mills C**, **Fernando K**, Daniels G, **Walker EM**, and **Jiagge E**. Cancer Clinical Trial Participation: A Qualitative Study of Black/African American Communities' and Patient/Survivors' Recommendations. *JNCI Cancer Spectr* 2024; Epub ahead of print. PMID: 39585656. Full Text

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BACKGROUND: Black/African Americans experience a disproportionate cancer burden and mortality rates. Racial/ethnic variation in cancer burden reflects systemic and healthcare inequities, cancer risk factors, and heredity and genomic diversity. Multiple systemic, socio-cultural, economic, and individual factors also contribute to disproportionately low Black/African American participation in cancer clinical trials. METHODS: The Participatory Action for Access to Clinical Trials project utilized a community-based participatory research (CBPR) approach inclusive of Black/African American community-based organizations (CBOs), Henry Ford Health (HFH), and the University of Michigan Urban Research Center. The project aims were to understand Black/African Americans' behavioral intentions to participate in cancer clinical trials and to obtain recommendations for improving participation. Audio-recorded focus group data were transcribed, coded, and searches were conducted to identify themes and subthemes. Representative text was extracted from the transcripts. RESULTS: Six community focus group discussions (70 participants) and six HFH patient/survivor focus group discussions (29 participants) were completed. General themes related to trial participation were identified including: 1) systemic issues related to racism, health disparities, and trust in government, health systems, and clinical research; 2) firsthand experiences with healthcare and health systems; 3) perceived and experienced advantages and disadvantages of clinical trial participation; and 4) recruitment procedures and personal decision-making processes. Specific recommendations on how to address barriers were obtained. CONCLUSIONS: CBPR is effective in bringing communities equitably to the table. To build trust, health systems must provide opportunities for patients and communities to jointly identify factors affecting cancer clinical trial participation, implement recommendations, and address health disparities.

Sleep Medicine

House SC, Byars-Winston A, Zarate S, Azurdia DE, Birren B, **Cheng P**, Diggs-Andrews K, Lee SP, Martinez-Hernandez K, McGee R, Prunuske A, Ramirez K, and Sorkness CA. Guiding principles for culturally responsive facilitation: Lessons learned from delivering culturally aware mentor training to STEMM faculty. *J Divers High Educ* 2024; 17(6):998-1004. PMID: Not assigned. Full Text

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Diversifying the academic workforce requires equitable and inclusive training environments. Essential to achieving this goal is understanding the relevance of racial and cultural identities in our interactions and a willingness and ability to engage in frank discussions about race and racism. Grounded in reflective practice, somatic abolitionism, and social justice education theory, this practice brief articulates six guiding principles for culturally responsive facilitation within diversity, equity, and inclusion workshops for adult learners. We use our collective experience implementing a mentorship education intervention, Culturally Aware Mentoring, with faculty in science, technology, engineering, mathematics, and medicine to illustrate these principles. (PsycInfo Database Record (c) 2024 APA, all rights reserved)

Surgery

Aspiras O, **Hutchings H**, Dawadi A, **Wang A**, **Poisson L**, **Okereke IC**, and Lucas T. Medical mistrust and receptivity to lung cancer screening among African American and white American smokers. *Psychol Health Med* 2024; 1-12. Epub ahead of print. PMID: 39608370. Full Text

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Although medical mistrust is associated with lower cancer screening uptake among racial minorities, such as African Americans, potential impacts on cancer screening among White Americans are generally understudied. In this study, we examined links from medical mistrust to lung cancer screening among African American (N = 203) and White American (N = 201) smokers. Participants completed the Group-Based Medical Mistrust Scale and viewed a brief online educational module about lung cancer risks,

etiology, and screening. Thereafter, participants reported their receptivity to lung cancer screening using a Theory of Planned Behavior (TPB) measurement framework (attitudes, normative beliefs, perceived control, and intentions). Medical mistrust predicted lower screening receptivity across all TPB measures for both racial groups. Although medical mistrust was higher among African Americans, there were no race differences in screening receptivity. However, there was some evidence that race moderates the relationship between medical mistrust and screening attitudes. While greater mistrust predicted more negative attitudes among both races, this effect was stronger among White Americans than African Americans. Findings suggest that group-based medical mistrust is a barrier to lung cancer screening for both African Americans and White Americans and illustrates the need to address medical mistrust as a barrier to screening for both racial minority and nonminority populations.

Surgery

Chahrour M, **Chamseddine H**, **Shepard A**, **Nypaver T**, **Weaver M**, **Boules T**, Hoballah JJ, **Hosn MA**, and **Kabbani L**. Endoscopic Vein Harvest Is Associated with Worse but Improving Outcomes in Infrainguinal Bypass. *J Vasc Surg* 2024; Epub ahead of print. PMID: 39743157. Full Text

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OBJECTIVE: The impact of great saphenous vein harvest technique on infrainguinal bypass outcomes remains a matter of debate, with no robust evidence favoring a specific technique over the other. This study aims to compare the outcomes of open vein harvest with endoscopic vein harvest in patients undergoing infrainguinal bypass surgery. METHODS: Patients who underwent an infrainguinal bypass from a femoral origin using a single-segment great saphenous vein between 2011 and 2023 were identified in the Vascular Quality Initiative infrainguinal bypass module. Only patients undergoing a bypass for peripheral artery disease were included, and those undergoing in-situ bypass were excluded. Patients were then classified according to their vein harvest technique into open vein harvest and endoscopic vein harvest groups. Three-to-one nearest-neighbor propensity score matching without replacement was performed to ensure balance of covariates between the two comparison groups. Kaplan-Meier and Cox-regression analysis were used to estimate long-term event rates and evaluate the association of vein harvest technique with the primary outcomes of primary patency, primary-assisted patency, secondary patency, re-intervention, amputation, and major adverse limb events, defined as the composite outcome of amputation and/or re-intervention. RESULTS: 7,929 patients who underwent open vein harvest were matched to 2,643 patients who underwent endoscopic vein harvest. All baseline characteristics, demographics, and operative details were balanced after propensity score matching. Endoscopic vein harvest had a significantly lower rate of surgical site infections (1.8% vs 2.9%, p=0.003), whereas other peri-operative outcomes including graft infection (p=0.12), myocardial infarction (p=0.16), stroke (p=0.13), and return to operating room (0.14) were similar between the two groups. At 1-year follow up, open vein harvest patients had a significantly higher primary patency (71% vs 65%, p<0.001), primary-assisted patency (86% vs 81%, p<0.001), and secondary patency (90% vs 85%, p<0.001), and significantly lower rates of amputation (6% vs 9%, p<0.001), re-intervention (20% vs 25%, p<0.001), and major adverse limb events (25% vs 30%, p<0.001) compared to endoscopic vein harvest patients. The primary patency of endoscopic vein harvest bypasses significantly increased from 59% to 70% between 2011 and 2020 (p=0.042). While open vein harvest had a significantly higher primary patency compared to endoscopic vein harvest in 2011-2012 (72% vs 59%, p=0.006), this difference diminished over time with no significant difference observed in the most recent interval (2019-2020) studied (73% vs 70%, p=0.214). CONCLUSION: While endoscopic vein harvest is associated with a lower post-operative wound complication rate, open vein harvest conferred superior long-term outcomes of patency, re-intervention,

and limb salvage over the study period. Nonetheless, endoscopic vein harvest has demonstrated improvements in primary patency over the years, significantly narrowing the gap in this outcome between the two harvest methods.

Surgery
Chamseddine H, **Shepard A**, Constantinou C, **Nypaver T**, **Weaver M**, **Boules T**, **Kavousi Y**, **Onofrey K**, **Peshkepija A**, **Halabi M**, and **Kabbani L**. Pre-operative Smoking Cessation Improves Carotid Endarterectomy Outcomes in Asymptomatic Carotid Stenosis Patients. *J Vasc Surg* 2024; Epub ahead of print. PMID: 39608415. Full Text

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OBJECTIVE: Smoking cessation has been suggested as having the potential to improve the outcomes of carotid endarterectomy (CEA) and mitigate the risk of long-term stroke in patients with asymptomatic carotid stenosis (ACS). This study aims to compare the peri-operative and long-term outcomes of CEA in ACS patients across different smoking status groups. METHODS: All patients receiving an elective CEA for ACS between 2013 and 2023 were identified in the Vascular Quality Initiative (VQI). Patients with an ipsilateral carotid stenosis <70% and those receiving a concomitant coronary artery bypass graft (CABG) were excluded. Patients were then classified according to their smoking status: never smokers, former smokers (defined as those who have stopped smoking more than 30 days prior to their operation), and current smokers. Patient characteristics and outcomes were compared using the χ(2) or Fischer's exact test as appropriate for categorical variables and the ANOVA or Kruskal-Wallis test as appropriate for continuous variables. Cox-regression analysis was used to study the association between smoking status and the primary outcomes of long-term stroke and major adverse cardiac events (MACE) defined as the composite outcome of stroke, MI, and/or mortality. RESULTS: A total of 77,664 patients received a CEA for ACS, of which 19,416 (25%) patients were never smokers, 39,374 (51%) patients were former smokers, and 18,874 (24%) patients were current smokers. Patients in the three groups had similar rates of perioperative stroke (p=0.79), myocardial infarction (p=0.07), mortality (p=0.23), and MACE (p=0.17). At 18-month follow up, former and never smokers had similar rates of stroke (former 0.9% vs never 0.8%, p=0.92), with former smokers exhibiting a lower stroke risk than current smokers (former 0.9% vs current 1.5%, p=0.001). At 18 months, former smokers had a significantly lower rate of MACE compared to current smokers (former 11.8% vs current 13.2%, p=0.03), but a higher rate compared to never smokers (former 11.8% vs never 8.7%, p<0.001). On multivariate Cox-regression analysis, compared to current smokers, former smokers were independently associated with a lower risk of stroke (HR 0.68, 95% CI 0.53-0.87, p=0.002), mortality (HR 0.79, 95% CI 0.74-0.84, p<0.001), and MACE (HR 0.77, 95% CI 0.70-0.83, p<0.001). No difference in long-term stroke risk was observed between former and never smokers (HR 1.06, 95% CI 0.82-1.38, p=0.65). CONCLUSION: This study demonstrates that preoperative smoking cessation in ACS patients significantly reduces the risk of stroke, mortality, and MACE following CEA compared to continued smoking, aligning their outcomes more closely with those of never smokers. Optimizing ACS patients prior to surgery should include smoking cessation counseling. Vascular surgeons play a critical role in encouraging smoking cessation, as their guidance can significantly improve patient outcomes following CEA.

Surgery
Chamseddine H, **Shepard A**, Constantinou C, **Nypaver T**, **Weaver M**, **Boules T**, **Kavousi Y**, **Onofrey K**, **Peshkepija A**, **Halabi M**, and **Kabbani L**. Preoperative smoking cessation improves carotid endarterectomy outcomes in asymptomatic carotid stenosis patients. *J Vasc Surg* 2024; Epub ahead of print. PMID: 39608415. Full Text

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OBJECTIVE: Smoking cessation has been suggested as having the potential to improve the outcomes of carotid endarterectomy (CEA) and mitigate the risk of long-term stroke in patients with asymptomatic carotid stenosis (ACS). This study aims to compare the perioperative and long-term outcomes of CEA in patients with ACS across different smoking status groups. METHODS: All patients receiving an elective CEA for ACS between 2013 and 2023 were identified in the Vascular Quality Initiative (VQI). Patients with an ipsilateral carotid stenosis <70% and those receiving a concomitant coronary artery bypass graft were excluded. Patients were then classified according to their smoking status: never smokers, former smokers (defined as those who have stopped smoking more than 30 days prior to their operation), and current smokers. Patient characteristics and outcomes were compared using the $\chi(2)$ or Fischer exact test as appropriate for categorical variables and the analysis of variance or Kruskal-Wallis test as appropriate for continuous variables. Cox regression analysis was used to study the association between smoking status and the primary outcomes of long-term stroke and major adverse cardiac events (MACE) defined as the composite outcome of stroke, myocardial infarction, and/or mortality. RESULTS: A total of 77,664 patients received a CEA for ACS, of which 19,416 patients (25%) were never smokers, 39,374 patients (51%) were former smokers, and 18,874 patients (24%) were current smokers. Patients in the three groups had similar rates of perioperative stroke (P = .79), myocardial infarction (P = .07), mortality (P = .23), and MACE (P = .17). At 18-month follow-up, former and never smokers had similar rates of stroke (former 0.9% vs never 0.8%; P = .92), with former smokers exhibiting a lower stroke risk than current smokers (former 0.9% vs current 1.5%; P = .001). At 18 months, former smokers had a significantly lower rate of MACE compared with current smokers (former 11.8% vs current 13.2%; P = .03), but a higher rate compared with never smokers (former 11.8% vs never 8.7%; P < .001). On multivariate Cox regression analysis, compared with current smokers, former smokers were independently associated with a lower risk of stroke (hazard ratio [HR], 0.68; 95% confidence interval [CI], 0.53-0.87; P = .002), mortality (HR, 0.79; 95% CI, 0.74-0.84; P < .001), and MACE (HR, 0.77; 95% CI, 0.70-0.83; P < .001). No difference in long-term stroke risk was observed between former and never smokers (HR, 1.06; 95% CI, 0.82-1.38; P = .65). CONCLUSIONS: This study demonstrates that preoperative smoking cessation in patients with ACS significantly reduces the risk of stroke, mortality, and MACE following CEA compared with continued smoking, aligning their outcomes more closely with those of never smokers. Optimizing patients with ACS prior to surgery should include smoking cessation counseling. Vascular surgeons play a critical role in encouraging smoking cessation, as their guidance can significantly improve patient outcomes following CEA.

Surgery
Chang DD. Bioengineered vessels used for vascular repairs in trauma. *Artif Organs* 2024; Epub ahead of print. PMID: 39673243. Full Text

Clinical trials demonstrate favorable outcomes of bioengineered vessels as graft conduits for reparation of traumatic vascular injuries compared with benchmarked synthetic conduits.

Surgery
Choi WJ, **Ivanics T**, Rajendran L, Li Z, Gavira F, Jones O, Gravely A, Claasen M, Yoon PD, Ladak F, Rana M, Gotlieb N, Dini Y, Naccarato K, McCluskey S, Ferreira R, Msallak H, Chow J, Abreu P, Rabindranath M, Selvanathan C, Muaddi H, Magyar CTJ, Englesakis M, Beecroft R, Vogel A, O'Kane G, Hansen B, and Sapisochin G. Comparative analysis of treatment modalities for solitary, small (≤3 cm) hepatocellular carcinoma: A systematic review and network meta-analysis of oncologic outcomes. *Surgery* 2024; 108917. Epub ahead of print. PMID: 39609218. Full Text

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BACKGROUND: Solitary hepatocellular carcinoma measuring ≤3 cm represents approximately 30% of hepatocellular carcinoma cases, yet treatment guidelines lack robust evidence. This study compares oncologic outcomes after ablation, liver resection, and liver transplantation for solitary, small hepatocellular carcinoma. METHODS: We systematically searched databases up to 7 February 2022, for studies including adults with solitary hepatocellular carcinoma ≤3 cm treated by any ablation, liver resection, or liver transplantation. We excluded non-hepatocellular carcinoma cancers, recurrent/metastatic diseases, and alternative therapies. A frequentist network meta-analysis assessed 5-year overall survival and recurrence-free survival using only adjusted effect estimates while accounting for bias risk. RESULTS: We identified 80 studies (4 randomized controlled trials, 72 retrospectives, and 4 prospective cohorts) with 28,211 patients. In the network meta-analysis for 5-year overall survival (26 studies), liver transplantation was associated with the lowest mortality hazard (hazard ratio, 0.47; 95% confidence interval, 0.31-0.73, referenced to liver resection), followed by liver resection (reference), whereas ablation had the greatest mortality hazard (hazard ratio, 1.32; 95% confidence interval, 1.16-1.49, referenced to liver resection). For 5-year recurrence-free survival (19 studies), liver transplantation had the best outcome (hazard ratio, 0.36; 95% confidence interval, 0.20-0.63, referenced to liver transplantation), followed by liver resection (reference), with ablation showing the least favorable outcome (hazard ratio, 1.67; 95% confidence interval, 1.45-1.93, referenced to liver resection). CONCLUSIONS: This network meta-analysis provides the evidence for comparing treatment modality outcomes for solitary, small (≤3 cm) hepatocellular carcinoma. LT emerges as the superior choice for achieving a better 5-year OS, followed by liver resection, then ablation. When feasible to preserve liver function, liver resection can be prioritized. Ablation with close surveillance should be reserved for individuals unfit for surgery.

Surgery

Choron RL, Piplani C, Kuzinar J, Teichman AL, Bargoud C, Sciarretta JD, Smith RN, Hanos D, Afif IN, Beard JH, Dhillon NK, Zhang A, Ghneim M, Devasahayam R, Gunter O, Smith AA, Sun B, Cao CS, Reynolds JK, Hilt LA, Holena DN, Chang G, Jonikas M, Echeverria-Rosario K, Fung NS, Anderson A, Fitzgerald CA, Dumas RP, Levin JH, Trankiem CT, Yoon J, Blank J, Hazelton JP, McLaughlin CJ, Al-Aref R, Kirsch JM, Howard DS, Scantling DR, Dellonte K, Vella MA, Hopkins B, Shell C, Udekwu P, Wong EG, Joseph B, Lieberman H, Ramsey WA, Stewart CH, Alvarez C, Berne JD, Nahmias J, Puente I, **Patton J**, **Rakitin I**, Perea L, Pulido O, Ahmed H, Keating J, Kodadek LM, Wade J, Reynold H, Schreiber M, Benjamin A, Khan A, Mann LK, Mentzer C, Mousafeiris V, Mulita F, Reid-Gruner S, Sais E, Foote CW, Palacio CH, Argandykov D, Kaafarani H, Bover Manderski MT, Moko L, Narayan M, and Seamon M. Pancreaticoduodenectomy in trauma patients with grade IV-V duodenal or pancreatic injuries: a post hoc analysis of an EAST multicenter trial. *Trauma Surg Acute Care Open* 2024; 9(1):e001438. PMID: 39717488. Full Text

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INTRODUCTION: The utility of pancreaticoduodenectomy (PD) for high-grade traumatic injuries remains unclear and data surrounding its use are limited. We hypothesized that PD does not result in improved outcomes when compared with non-PD surgical management of grade IV-V pancreaticoduodenal injuries. METHODS: This is a retrospective, multicenter analysis from 35 level 1 trauma centers from January 2010 to December 2020. Included patients were ≥15 years of age with the American Association for the Surgery of Trauma grade IV-V duodenal and/or pancreatic injuries. The study compared operative repair strategy: PD versus non-PD. RESULTS: The sample (n=95) was young (26 years), male (82%), with predominantly penetrating injuries (76%). There was no difference in demographics, hemodynamics, or blood product requirement on presentation between PD (n=32) vs non-PD (n=63). Anatomically, PD patients had more grade V duodenal, grade V pancreatic, ampullary, and pancreatic ductal injuries compared with non-PD patients (all $p<0.05$). 43% of all grade V duodenal injuries and 40% of all grade V pancreatic injuries were still managed with non-PD. One-third of non-PD duodenal injuries were managed with primary repair alone. PD patients had more gastrointestinal (GI)-related complications, longer intensive care unit length of stay (LOS), and longer hospital LOS compared with non-PD (all $p<0.05$). There was no difference in mortality or readmission. Multivariable logistic regression analysis determined PD to be associated with a 3.8-fold greater odds of GI complication ($p=0.010$) compared with non-PD. In a subanalysis of patients without ampullary injuries (n=60), PD patients had more anastomotic leaks compared with the non-PD group (3 (30%) vs 2 (4%), $p=0.028$). CONCLUSION: While PD patients did not have worse hemodynamics or blood product requirements on admission, they sustained more complex anatomic injuries and had more GI complications and longer LOS than non-PD patients. We suggest that the role of PD should be limited to cases of massive destruction of the pancreatic head and ampullary complex, given the likely procedure-related morbidity and adverse outcomes when compared with non-PD management. LEVEL OF EVIDENCE: IV, Multicenter retrospective comparative study.

Surgery
Choron RL, Rallo M, Piplani C, Youssef S, Teichman AL, Bargoud CG, Sciarretta JD, Smith RN, Hanos DS, Afif IN, Beard JH, Dhillon NK, Zhang A, Ghneim M, Devasahayam RJ, Gunter OL, Smith AA, Sun BL, Cao C, Reynolds JK, Hilt LA, Holena D, Chang G, Jonikas M, Echeverria K, Fung N, Anderson A, Dumas RP, Fitzgerald CA, Levin J, Trankiem C, Yoon JJ, Blank J, Hazelton J, McLaughlin CJ, Al-Aref R, Kirsch JM, Howard DS, Scantling DR, Dellonte K, Vella M, Hopkins B, Shell C, Udekwu PO, Wong EG, Joseph BA, Lieberman H, Ramsey W, Stewart C, Alvarez C, Berne JD, Nahmias J, Puente I, **Patton JP**, **Rakitin I**, Perea LL, Pulido OR, Ahmed H, Keating J, Kodadek L, Wade J, Henry R, Schreiber M, Benjamin A, Khan A, Mann LK, Mentzer C, Mousafeiris V, Mulita F, Reid-Gruner S, Sais E, Foote C, Palacio-Lascano C, Argandykov D, Kaafarani H, Bover Manderski M, Narayan M, and Seamon MJ. The impact of post-operative enteral nutrition on duodenal injury outcomes: A post hoc analysis of an EAST multicenter trial. *J Trauma Acute Care Surg* 2024; Epub ahead of print. PMID: 38745354. Full Text

BACKGROUND: Leak following surgical repair of traumatic duodenal injuries results in prolonged hospitalization and oftentimes nil per os(NPO) treatment. Parenteral nutrition(PN) has known morbidity; however, duodenal leak(DL) patients often have complex injuries and hospital courses resulting in barriers to enteral nutrition(EN). We hypothesized EN alone would be associated with 1)shorter duration

until leak closure and 2)less infectious complications and shorter hospital length of stay(HLOS) compared to PN. METHODS: This was a post-hoc analysis of a retrospective, multicenter study from 35 Level-1 trauma centers, including patients >14 years-old who underwent surgery for duodenal injuries(1/2010-12/2020) and endured post-operative DL. The study compared nutrition strategies: EN vs PN vs EN + PN using Chi-Square and Kruskal-Wallis tests; if significance was found pairwise comparison or Dunn's test were performed. RESULTS: There were 113 patients with DL: 43 EN, 22 PN, and 48 EN + PN. Patients were young(median age 28 years-old) males(83.2%) with penetrating injuries(81.4%). There was no difference in injury severity or critical illness among the groups, however there were more pancreatic injuries among PN groups. EN patients had less days NPO compared to both PN groups(12 days[IQR23] vs 40[54] vs 33[32],p = <0.001). Time until leak closure was less in EN patients when comparing the three groups(7 days[IQR14.5] vs 15[20.5] vs 25.5[55.8],p = 0.008). EN patients had less intra-abdominal abscesses, bacteremia, and days with drains than the PN groups(all p < 0.05). HLOS was shorter among EN patients vs both PN groups(27 days[24] vs 44[62] vs 45[31],p = 0.001). When controlling for predictors of leak, regression analysis demonstrated EN was associated with shorter HLOS(β -24.9, 95%CI -39.0 to -10.7,p < 0.001). CONCLUSION: EN was associated with a shorter duration until leak closure, less infectious complications, and shorter length of stay. Contrary to some conventional thought, PN was not associated with decreased time until leak closure. We therefore suggest EN should be the preferred choice of nutrition in patients with duodenal leaks whenever feasible. LEVEL OF EVIDENCE: IV.

Surgery

Hartgerink C, **Toiv A**, **Sarowar A**, **Todd E**, **Nagai S**, **Muszkat Y**, **Beltran N**, and **Jafri SM**. Safety and Efficacy of Everolimus Use to Preserve Renal Function in Intestinal and Multivisceral Transplantation Patients. *Transplant Proc* 2024; 56(10):2250-2254. PMID: 39603963. Full Text

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BACKGROUND: As calcineurin inhibitors are associated with renal impairment post intestinal transplant, use of everolimus (EVR) may provide renal-sparing benefits. METHODS: We performed a retrospective analysis focused on EVR use and renal function after intestinal or multivisceral transplant. No prisoners were used in the study. This study is compliant with the Helsinki Congress and the Declaration of Istanbul. RESULTS: A total of 28 patients, 18 patients who underwent isolated intestinal transplant, and 10 patients who underwent multivisceral transplant, were included in this study. For 13 patients that never received EVR, the average change in estimated glomerular filtration rate (eGFR) compared to baseline at the time of transplant were as follows: 1 year post-transplant = -18.1%; 2 years = -43.7%; 3 years = -44.1; and 5 years = -43.3%. For 15 patients who received EVR after transplant, average duration of EVR therapy was (579.60 ± 784.15) days with 87% of patients ultimately removed from medication due to side effects. In the EVR group, the average change in eGFR compared to baseline were as follows: 1 year post-transplant = -37.5%; 2 years = -43.5%; 3 years = -54.2%; and 5 years = -42.9%. After the initiation of EVR, the average change in eGFR compared to eGFR at time of EVR initiation was as follows: 1 year = +5.9%; 2 years = -1.57%; 3 years = -5.01%; and 5 years = -1.79%. CONCLUSIONS: This study suggests that EVR can play an important role in preserving renal function in intestinal and multivisceral transplant recipients, but tolerance of EVR is highly variable in this patient population.

Surgery

Kaljee L, **Antwi S**, **Dankerlui D**, Harris D, Israel B, **White-Perkins D**, **Aboah VO**, Aduse-Poku L, **Larrious-Lartey H**, Brush B, Coombe C, Patman L, Cawthorne N, Chue S, Rowe Z, **Mills C**, **Fernando K**, Daniels G, **Walker EM**, and **Jiagge E**. Cancer Clinical Trial Participation: A Qualitative Study of Black/African American Communities' and Patient/Survivors' Recommendations. *JNCI Cancer Spectr* 2024; Epub ahead of print. PMID: 39585656. Full Text

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BACKGROUND: Black/African Americans experience a disproportionate cancer burden and mortality rates. Racial/ethnic variation in cancer burden reflects systemic and healthcare inequities, cancer risk factors, and heredity and genomic diversity. Multiple systemic, socio-cultural, economic, and individual factors also contribute to disproportionately low Black/African American participation in cancer clinical trials. METHODS: The Participatory Action for Access to Clinical Trials project utilized a community-based participatory research (CBPR) approach inclusive of Black/African American community-based organizations (CBOs), Henry Ford Health (HFH), and the University of Michigan Urban Research Center. The project aims were to understand Black/African Americans' behavioral intentions to participate in cancer clinical trials and to obtain recommendations for improving participation. Audio-recorded focus group data were transcribed, coded, and searches were conducted to identify themes and subthemes. Representative text was extracted from the transcripts. RESULTS: Six community focus group discussions (70 participants) and six HFH patient/survivor focus group discussions (29 participants) were completed. General themes related to trial participation were identified including: 1) systemic issues related to racism, health disparities, and trust in government, health systems, and clinical research; 2) firsthand experiences with healthcare and health systems; 3) perceived and experienced advantages and disadvantages of clinical trial participation; and 4) recruitment procedures and personal decision-making processes. Specific recommendations on how to address barriers were obtained. CONCLUSIONS: CBPR is effective in bringing communities equitably to the table. To build trust, health systems must provide opportunities for patients and communities to jointly identify factors affecting cancer clinical trial participation, implement recommendations, and address health disparities.

Surgery

Loveless IM, Kemp SB, **Hartway KM**, Mitchell JT, Wu Y, **Zwernik SD**, **Salas-Escabillas DJ**, **Brender S**, **George M**, **Makinwa Y**, **Stockdale T**, **Gartrelle K**, **Reddy RG**, Long DW, **Wombwell A**, **Clark JM**, **Levin AM**, **Kwon D**, **Huang L**, **Francescone R**, **Vendramini-Costa DB**, Stanger B, Alessio A, Waters AM, Cui Y, Fertig EJ, Kagohara LT, **Theisen B**, **Crawford HC**, and **Steele NG**. Human pancreatic cancer single cell atlas reveals association of CXCL10+ fibroblasts and basal subtype tumor cells. *Clin Cancer Res* 2024; Epub ahead of print. PMID: 39636224. Full Text

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PURPOSE: Pancreatic ductal adenocarcinoma (PDAC) patients with tumors enriched for the basal-like molecular subtype exhibit enhanced resistance to standard of care treatments and have significantly worse overall survival (OS) compared to patients with classical subtype enriched tumors. It is important to develop genomic resources, enabling identification of novel putative targets in a statistically rigorous

manner. EXPERIMENTAL DESIGN: We compiled a single cell RNA sequencing (scRNAseq) atlas of the human pancreas with 229 patient samples, aggregated from publicly available raw data. We mapped cell-type specific scRNAseq gene signatures in bulk RNAseq (n=744) and spatial transcriptomics (ST) (n=22) and performed validation using multiplex immunostaining. RESULTS: Analysis of tumor cells from our scRNAseq atlas revealed nine distinct populations, two of which aligned with the basal subtype, correlating with worse OS in bulk RNAseq. Deconvolution identified one of the basal populations to be the predominant tumor subtype in non-dissociated ST tissues and in vitro tumor cell and patient-derived organoid lines. We discovered a novel enrichment and spatial association of CXCL10+ cancer associated fibroblasts (CAFs) with basal tumor cells. We identified that besides immune cells, ductal cells also express CXCR3, the receptor for CXCL10, suggesting a relationship between these cell types in PDAC tumor microenvironment. CONCLUSIONS: We show that our scRNAseq atlas (700,000 cells), integrated with ST data, has increased statistical power and is a powerful resource, allowing for expansion of current subtyping paradigms in PDAC. We uncovered a novel signaling niche marked by CXCL10+ CAFs and basal tumor cells that could be explored for future targeted therapies.

Surgery
Manivannan A, Pillai A, Liapakis A, Parikh ND, Kumar V, Verna EC, **Salgia R**, **Wu T**, **Lu M**, and **Jesse MT**. Influence of Acuity Circles on Hepatocellular Carcinoma and the Interaction of Gender and Race in Liver Transplantation. *Clin Transplant* 2024; 38(12):e70045. PMID: 39620868. Full Text

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The impact of liver transplant allocation policy using acuity circles (ACs) on interactions between race and gender on waitlist mortality or receipt of deceased donor liver transplant (DDLT) is unknown. Using data from the United Network for Organ Sharing (UNOS), we examined adults listed for DDLT from April 3, 2017, to October 4, 2022 (30 months pre- and post-AC). Fine-Gray sub-distribution hazard model explored AC indicators by race and gender interactions and their effect on receipt of DDLT or waitlist mortality. Also explored was AC's impact on hepatocellular carcinoma (HCC) diagnosis and receipt of DDLT or waitlist mortality. 59 592 patients (30 202 pre-AC, 29 390 post-AC) included. For both receipt of DDLT and waitlist mortality, there were no 3-way (AC by race by gender) interactions, indicating that the effects of race and gender on DDLT or waitlist mortality were consistent pre- and post-AC. Irrespective of AC implementation, Black and Hispanic women were less likely to receive DDLT and had an increased risk of waitlist mortality compared to White women. White, Black, and Hispanic men had lower waitlist mortality risk and greater likelihood of receiving DDLT compared to their female race/ethnic counterparts. Patients with HCC had a significantly greater chance for DDLT than non-HCC, although post-AC this effect was attenuated. Patients with HCC were also at greater risk of waitlist mortality pre- and post-AC compared to those without HCC however, the waitlist mortality post-AC was attenuated only for those patients without HCC. To our knowledge, this is the first study to show the interaction of gender and race on waitlist mortality and access to transplantation since the implementation of AC, showing continued disparate outcomes for women both within and across racial groups.

Surgery
Pearl ES, **Murray MF**, **Haley EN**, **Snodgrass M**, **Braciszewski JM**, **Carlin AM**, and **Miller-Matero LR**. Weight and shape overvaluation and its relation to anxiety, depression, and maladaptive eating symptoms for patients up to 4 years after bariatric surgery. *Surg Obes Relat Dis* 2024; Epub ahead of print. PMID: 39710526. Full Text

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BACKGROUND: Weight and shape overvaluation (WSO; undue influence of weight and shape on self-evaluation) is common among individuals undergoing bariatric surgery. Little is known about how WSO relates to poorer outcomes for patients remote from surgery. OBJECTIVES: To examine associations between WSO with anxiety and depression symptoms and various maladaptive eating behaviors in patients up to 4 years post-bariatric surgery. SETTING: Henry Ford Health, United States. METHODS: Patients who underwent surgery between 2018 and 2021 were invited to complete the study between 2021 and 2022. Participants (N = 765) completed anxiety and depression symptom and eating behavior measures. RESULTS: Participants endorsed moderate WSO (M = 3.62, standard deviation = 1.87), which was positively related to anxiety (r = .37) and depression (r = .20) symptoms; eating in response to anger/frustration (r = .26), anxiety (r = .28), and depression (r = .31); and addictive eating behaviors (r = .26); and was significantly associated with the presence of loss-of-control (odds ratio [OR] = 1.39), binge (OR = 1.39), and graze (OR = 1.24) eating. WSO also was related to more frequent grazing (r = .23) but not loss-of-control or binge eating frequency for participants who endorsed behavior presence. CONCLUSIONS: Findings underscore that links between WSO, psychiatric distress, and maladaptive eating behaviors persist up to 4 years after bariatric surgery. These domains should be assessed at bariatric follow-ups, and assessment of WSO may help providers identify patients at risk for poorer outcomes. Findings should be used to inform temporal modeling of how WSO may predispose patients to poorer bariatric outcomes.

Surgery

Salas-Escabillas DJ, **Hoffman MT**, **Brender SM**, **Moore JS**, **Wen HJ**, **Benitz S**, **Davis ET**, **Long D**, **Wombwell AM**, Chianis ERD, Allen-Petersen BL, **Steele NG**, Sears RC, Matsumoto I, DelGiorno KE, and **Crawford HC**. Tuft cells transdifferentiate to neural-like progenitor cells in the progression of pancreatic cancer. *Dev Cell* 2024; Epub ahead of print. PMID: 39721583. Full Text

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Pancreatic ductal adenocarcinoma (PDA) is partly initiated through the transdifferentiation of acinar cells to metaplasia, which progresses to neoplasia and cancer. Tuft cells (TCs) are chemosensory cells not found in the normal pancreas but arise in cancer precursor lesions and diminish during progression to carcinoma. These metaplastic TCs (mTCs) suppress tumor progression through communication with the tumor microenvironment, but their fate during progression is unknown. To determine the fate of mTCs during PDA progression, we created a dual recombinase lineage trace model, wherein a pancreas-specific FlpO was used to induce tumorigenesis, while a tuft-cell specific Pou2f3(CreERT/+) driver was used to induce expression of a tdTomato reporter. We found that mTCs in carcinoma transdifferentiate into neural-like progenitor cells (NRPs), a cell type associated with poor survival in patients. Using

conditional knockout and overexpression systems, we found that Myc activity in mTCs is necessary and sufficient to induce this tuft-to-neuroendocrine transition (TNT).

Surgery

Varban OA, Petersen S, Stricklen A, Kindel T, Noria S, Edwards MA, Petrick A, Obeid N, Finks JF, and **Carlin AM**. Impact of same-day sleeve gastrectomy surgery on postoperative emergency department visits: analysis from the Michigan Bariatric Surgery Collaborative. *Surg Obes Relat Dis* 2024; Epub ahead of print. PMID: 39730271. Full Text

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BACKGROUND: Same-day discharge after sleeve gastrectomy (SDDSG) is being performed in select patient populations with increased regularity since 2020. OBJECTIVES: To evaluate the impact of SDDSG on emergency department (ED) visits. SETTING: Academic and private practice bariatric surgery programs participating in a statewide quality improvement collaborative. METHODS: Using a statewide bariatric specific data registry, all patients undergoing SDDSG between 2020 and 2023 were identified (n = 984). Rates of 30-day ED visits and complications were compared between SDDSG and a 2:1 propensity-matched cohort with a 1-2-day hospital length of stay (n = 1968). RESULTS: The mean age and body mass index of SDDSG patients were 41.7 years and 45.9, respectively. When compared to the matched cohort, SDDSG patients had higher rates of ED visits (9.2% versus 6.2%, P = .0029), were more likely to present to ED earlier (10.3 days versus 12.9 days, P = .0118), and were less likely to require hospital admission (87.8% versus 71.1%, P < .0037), even though the overall complication rates were similar (4.7% versus 3.7%, P = .2087). The most common reason for an ED visit after SDDSG was nausea, vomiting, and dehydration (58.9% versus 66.9%, P = .2294), and the most common day to present to the ED was Friday (20.0% versus 20.7%, P = .9061), which was similar between groups. CONCLUSIONS: Despite having similar complication rates, patients undergoing SDDSG were more likely to present to the ED after surgery when compared to a matched cohort of patients with a 1-2-day hospital stay.

Urology

Al Hashimi M, Pinggera GM, Mostafa T, Shah R, Sahin B, Chung E, **Rambhatla A**, Cayan S, Alipour H, Ragab M, Raheem O, Arafa M, Alnajjar H, Kadioglu A, Hegde AV, Harraz A, and Agarwa A. The Role of Different Modalities of Regenerative Therapies in the Treatment of Erectile Dysfunction: A Global Survey and Global Andrology Forum Expert Recommendations. *World J Mens Health* 2024; Epub ahead of print. PMID: 39743219. Full Text

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PURPOSE: There is increased interest in regenerative therapies (RTs) to treat erectile dysfunction (ED). However, the need for society's guidelines has led to varied practices. This study aims to investigate current global practices, address the heterogeneity in treatment protocols and evaluations, and establish expert recommendations in clinical practice. MATERIALS AND METHODS: Senior experts from the Global Andrology Forum (GAF) created a 32-question survey to evaluate the clinical aspects of various RT modalities and compare them with each other and with phosphodiesterase type 5 inhibitors (PDE5is). The survey was distributed worldwide to ED specialists through online Google Forms, the GAF website, international professional societies, and direct emails. The responses were analyzed and are presented as percentage frequencies. Additionally, an expert consensus on recommendations for RT use was reached at via a modified Delphi method. RESULTS: Out of 163 respondents from 39 countries, the majority (80.1%) were using low-intensity shockwave therapy (LISWT), followed by platelet-rich plasma (PRP) 61.3% and stem cell therapy (SCT) 17.8%. Efficacy comparisons revealed no perceived significant differences among RT modalities (p=0.124). Compared to PDE5is, the efficacy of LISWT and PRP was considered lower by the respondents, while SCT was rated better by almost half of those who used SCT. The duration of improvement varied (p=0.279), with most improvements lasting 1 to 6 months. The treatment protocols used for LISWT were mainly consistent but varied widely for PRP and SCT. Adverse effects were minimal, particularly for LISWT (p<0.001). The costs varied significantly (p<0.001), with SCT being the most expensive. The evidence for efficacy was rated as primarily moderate to strong for LISWT but poor for PRP and SCT (p=0.027). CONCLUSIONS: Most respondents utilized LISWT, followed by PRP, with SCT being the least commonly utilized. The high break heterogeneity in treatment protocols and evaluation of RT underscores the need for further studies and guidelines to establish best practices.

Urology

Chiarelli G, **Davis M**, **Stephens A**, **Finati M**, **Cirulli GO**, **Morrison C**, Sood A, Carrieri G, Briganti A, Montorsi F, Lughezzani G, Buffi N, **Rogers C**, and **Abdollah F**. Racial Disparities in Future Development of Lethal Prostate Cancer Based on Midlife Baseline Prostate-Specific Antigen. *Prostate* 2024; e24834. Epub ahead of print. PMID: 39651707. Full Text

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BACKGROUND: Previous studies found that Midlife Baseline PSA (MB PSA) predicts the risk of developing lethal prostate cancer (PCa), although the cohorts were homogenous in terms of racial compositions. We aimed to investigate racial disparities in the predictive value of MB PSA for lethal PCa in a diverse, contemporary, North American population. METHODS: Our cohort included White and Black men aged 40-59 years, who underwent MB PSA through our health system. Cumulative incidence curves depicted lethal PCa stratified by race and MB PSA above/below the median. We utilized time-dependent Receiver Operating Characteristic (ROC) curves and Area Under the ROC Curve (AUC) to compare the

performance of MB PSA in predicting lethal PCa based on race. Multivariable regression (MVA) was used to examine the impact of the MB PSA in predicting lethal PCa by race. RESULTS: We included 112,967 men, of whom 27% were Black. The cumulative incidence estimate with MB PSA values equal to the median at 15 years of follow-up was 0.13 (0.04, 0.32) for White men and 0.55 (0.24, 1.11) for Black men. AUCs comparison showed no statistically significant differences in the predictive role of MB PSA for lethal PCa between White and Black men. At MVA, using White patients with PSA ≤ median as the reference group, the HR of lethal PCa for White men with PSA > median aged 40-44, 45-49, 50-54, and 55-59 was respectively 2.98 (1.59-5.57), 3.01 (1.89-4.81), 5.10 (3.38-7.70), and 3.38 (2.32-4.92). While for Black men was respectively 5.50 (2.94-10.27), 4.19 (2.59-6.78), 9.79 (6.37-15.04), and 7.53 (5.03-11.26) (all $p < 0.001$). CONCLUSION: Our findings indicate that for the same MB PSA and within the same age category, Black men have a greater risk of developing lethal PCa than White men. A separate cut-off should be created for MB PSA, if this is to be used to guide PSA screening in clinical practice.

Urology

Chiarelli G, **Stephens A**, **Finati M**, **Cirulli GO**, **Tinsley S**, **Wang Y**, Kolanukuduru K, Sood A, Carrieri G, Briganti A, Montorsi F, Lughezzani G, Buffi N, **Rogers C**, and **Abdollah F**. Active surveillance follow-up for prostate cancer: from guidelines to real-world clinical practice. *World J Urol* 2024; 42(1):646. PMID: 39589591. Full Text

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PURPOSE: To assess active surveillance (AS) adherence for prostate cancer (PCa) in a "real-world" clinical practice. MATERIALS AND METHODS: We utilized our institutional database which was built by interrogating electronic medical records for all men who got diagnosed with PCa from 1995 to 2022. Our cohort included all patients aged < 76 years, with PCa Gleason Grade (GG) 1 or 2, ≤ cT2c, PSA ≤ 20 ng/ml at diagnosis, enrolled on AS, and with at least one biopsy after diagnosis. Patients were separated into two groups based on the monitoring intensity. Patients with at least 1 PSA/year and at least 1 biopsy every 4 years were categorized as adherent to guidelines. Univariable and Multivariable logistic regression analyses were used to examine the impact of covariates on non-adherence to guidelines. Competing risks cumulative incidence was used to depict prostate cancer-specific mortality (PCSM). RESULTS: A total of 546 men met the inclusion criteria. Overall, 63 (11%) patients were adherent to guidelines (Group 1), while 483 (89%) were not (Group 2). Median PSAs/year and median biopsies/year were 2.3 (2.0-2.7) and 0.4 (0.3-0.6) for Group 1, and 1.2 (0.7-1.8) and 0.2 (0.1-0.2) for Group 2, respectively (both $p < 0.0001$). At multivariable analysis, Black men had a 2.20-fold higher risk of being in Group 2 than White men ($p < 0.05$). Patients with cT2 (OR:0.24, CI:0.11-0.52) and those with CCI ≥2 (OR:0.40, CCI:0.19-0.82) were less likely to be in Group 2, when compared to cT1 stage and CCI = 0, respectively (both $p < 0.05$). At 10 years, the cumulative incidence estimate of PCSM for the entire cohort was 2.1%. CONCLUSION: We found substantial deviations from AS monitoring guidelines, particularly in biopsy frequency, which did not seem to compromise PCSM in patients with stable PSA. Notably, our findings suggest that strict adherence to guidelines, especially in patients with cT2 at diagnosis, remains crucial.

Urology

Dasgupta S, Le TS, Rambhatla A, **Shah R**, and Agarwal A. Medical treatment prior to micro-TESE. *Asian J Androl* 2024; Epub ahead of print. PMID: 39716721. Full Text

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Except in cases of hypogonadotropic hypogonadism, the use of medical therapy before microsurgical testicular sperm extraction (micro-TESE) is controversial. In some studies, hormone therapy has been shown to improve the possibility of sperm retrieval during micro-TESE and even lead to the presence of sperm in the ejaculate in some cases, thereby obviating the need for micro-TESE. However, their routine use before micro-TESE in cases of nonobstructive azoospermia (NOA) being associated with hypergonadotropic hypogonadism and eugonadism (normogonadotropic condition) has not been supported with robust evidence. In this review, we discuss different types of medical therapy used before micro-TESE for NOA, their risks and benefits, and the available evidence surrounding their use in this setting.

Urology

Finati M, **Stephens A**, **Cirulli GO**, **Chiarelli G**, **Tinsley S**, **Morrison C**, Sood A, Buffi N, Lughezzani G, Salonia A, Briganti A, Montorsi F, Busetto GM, **Rogers C**, **Carrieri G**, and **Abdollah F**. Association of race and area of deprivation index with prostate cancer incidence and lethality: results from a contemporary North American cohort. *JNCI Cancer Spectr* 2024; 8(6). PMID: 39576690. Full Text

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BACKGROUND: Socioeconomic and demographic factors contribute to disparity in prostate cancer (PCa) outcomes. We examined the impact of Area of Deprivation Index (ADI) and race on PCa incidence and lethality in a North American cohort. METHODS: Our cohort included men who received at least 1 prostate-Specifig Antigen (pSA) test within our Health System (1995-2022). An ADI score was assigned to each patient based on their residential census block, ranked as a percentile of deprivation relative to the national level. Individuals were further categorized into quartiles, where the fourth one (ADI 75-100) represented those living in the most deprived areas. We investigated PCa incidence and lethality, using cumulative incidence estimates and competing-risk regression. An ADI × Race interaction term examined whether the relationship between ADI and outcomes varied based on race. RESULTS: We included 134 366 patients, 25% of whom were non-Hispanic Black (NHB). Median (IQR) follow-up was 8.8 (5-17) years. At multivariate analysis, individuals from the third quartile (ADI 50-74, 95% CI = 0.83 to 0.95) and the fourth quartile (ADI ≥75, 95% CI = 0.75 to 0.86) showed significant reduced hazard ratios for PCa incidence, when compared with the first quartile (ADI <25, all P < .001). In contrast to the overall cohort, PCa incidence increased with ADI in NHB men, who were persistently at higher hazard for both PCa incidence and lethality than non-Hispanic White (NHW), across all ADI strata (all P < .001). CONCLUSIONS: Living in more deprived areas was associated with lower PCa incidence and higher lethal disease rate. Conversely, PCa incidence increased with ADI for NHB, who consistently showed worse outcomes than NHW individuals, regardless of ADI.

Urology

Levin AM, **Okifo O**, **Buhl K**, **Ouchi T**, **Parker B**, **Tan J**, **Datta I**, **Dai X**, **Chen Y**, **Palanisamy N**, **Veenstra J**, **Carskadon S**, **Li J**, **Ozog D**, **Keller CE**, **Chitale D**, **Bobbitt KR**, **Crawford HC**, **Steele N**, **Mi QS**, and **Jones LR**. Higher expression of mir-31-5p is associated with reduced risk of head and neck keloid recurrence following surgical resection. *Laryngoscope Investig Otolaryngol* 2024; 9(6):e70040. PMID: 39664781. Full Text

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OBJECTIVE: In this study, we aimed to evaluate mir-31-5p as a prognostic biomarker of keloid disease (KD) recurrence using a retrospective, treatment naïve, surgical cohort of head and neck KD cases from Henry Ford Health. METHODS: Using a tissue microarray, mir-31-5p expression was measured with miRNAscope, and mir-31-5p cell positivity was determined with QuPath. Logistic regression was used to test the association between mir-31-5p positive cells and KD recurrence at 1 year. In an independent dataset, associations between mir-31-5p and messenger RNA (mRNA) expression were assessed. Ingenuity Pathway Analysis identified target genes and pathways impacted by mir-31-5p. RESULTS: Of the 58 KD patients, 42 (72%) received adjuvant triamcinolone injections, and 8 recurred (14%). mir-31-5p was expressed in 48 (83%) specimens. Increasing mir-31-5p expression was associated with decreased risk of recurrence (p = .031), with an odds ratio of 0.86 (95% CI 0.75-0.98) for each 20% increase in mir-31-5p cellular positivity. This effect persisted with triamcinolone treatment (odds ratio 0.82; 95% CI 0.71-0.95; p = .015). mir-31-5p correlated with gene expression enriched in KD pathways, including mRNA splicing and autophagy. CONCLUSION: Taken together, our data supports the association between mir-31-5p expression and KD recurrence. Its potential as a prognostic biomarker should be further investigated. LEVEL OF EVIDENCE: Level 2.

Urology

Puri D, Meagher MF, Wu Z, Franco A, Wang L, Margulis V, Bhanvadia R, **Abdollah F**, **Finati M**, Antonelli A, Ditonno F, Singla N, Broenimann S, Simone G, Tuderti G, Rais-Bahrami S, Moon SC, Ferro M, Tozzi M, Porpiglia F, Amparore D, Correa A, Helstrom E, Gonzalgo ML, Mendiola DF, Perdonà S, Tufano A, Eilender BM, Mehrazin R, Yong C, Ghoreifi A, Sundaram CP, Djaladat H, Autorino R, and Derweesh IH. The impact of post-nephroureterectomy surgically induced chronic kidney disease on survival outcomes. *BJU Int* 2024; Epub ahead of print. PMID: 39663586. Full Text

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OBJECTIVE: To investigate the prevalence, predictors and impact of surgically induced chronic kidney disease (CKD-S) on survival outcomes in patients with upper tract urothelial carcinoma (UTUC) following radical nephroureterectomy (RNU). METHODS: Utilising the ROBUUST 2.0 registry, a multicentre retrospective analysis was conducted in patients with UTUC undergoing RNU between 2006 and 2022 who did not have baseline chronic kidney disease (CKD) stages 3-5. We calculated the prevalence of postoperative CKD-S3a (estimated glomerular filtration rate [eGFR] 59-45 mL/min/1.73 m(2)) and CKD-S3b (eGFR <45 mL/min/1.73 m(2)) as measured by the Chronic Kidney Disease Epidemiology Collaboration 2021 equation. The analytical cohort was stratified by postoperative CKD stage [no CKD-S [eGFR ≥60 mL/min/1.73 m(2)]; CKD-S3a [eGFR 59-45 mL/min/1.73 m(2)] and CKD-S3b [eGFR <45 mL/min/1.73 m(2)]). The primary outcome was all-cause mortality (ACM). Predictors for development of CKD-S3a/3b and ACM/cancer-specific mortality (CSM) were analysed using logistic and Cox regression, respectively. Kaplan-Meier analysis was used to analyse overall survival (OS) and cancer-specific survival (CSS) among postoperative CKD groups. RESULTS: We analysed 1862 patients; 34.7% (646) and 39.6% (738), respectively, developed CKD-S3a and CKD-S3b. Predictors of CKD-S3b included increasing age (odds ratio [OR] 1.03, P = 0.029), decreasing preoperative eGFR (OR 1.06, P < 0.001) and receipt of neoadjuvant (OR 2.07, P = 0.006) and adjuvant chemotherapy (OR 1.41, P = 0.012). Worsened ACM was associated with CKD-S3b (hazard ratio 1.42, P = 0.032), but not CKD-S3a (P = 0.766). Development of CKD-S3a (P = 0.812) and CKD-S3b (P = 0.316) were not associated with CSM. The 5-year OS rate was significantly worse in CKD-S3b (no-CKD 71%, CKD-S3a 70%, CKD-S3b 59%; P = 0.017). No differences between CKD-S groups were noted for 5-year CSS (no-CKD 78%, CKD-S3a 77%, CKD-S3b 82%; P = 0.44). CONCLUSIONS: A significant proportion of UTUC patients undergoing RNU developed CKD-S. Development of CKD-S3b was associated with worse ACM. Increasing age, preoperative eGFR, and chemotherapy were associated with developing CKD-S3b. Our findings call for further exploration and refinement of nephron-preserving surgical strategies and non-nephrotoxic systemic therapy to improve survival outcomes in UTUC.

Conference Abstracts

Anesthesiology
Daher LA, **Ayyar I**, **Polanco A**, Baribeau V, **Clark C**, **Uribe-Marquez S**, **Londono CG**, **Park A**, **Mitchell J**, and **Guruswamy J**. Motion Analysis: An Objective Assessment of Novel Arterial Line Placement Protocol. *Anesth Analg* 2024; 139(5):296-298. Full Text

L.A. Daher, Henry Ford Health, United States

Introduction: Arterial line placement is a challenging skill for anesthesiology residents to master. Previous efforts have demonstrated the utility of analyzing data from motion trackers to objectively assess performance across procedural skills.1-2 While motion tracking has been previously used to assess radial artery access in interventional radiologists, the approach and equipment used was different from that traditionally used by anesthesiologists.3 Furthermore, this study was performed without guidance, with a skill trainer that required manual pulsation with a bulb device, potentially resulting in variability in rate and pulse pressure within and between attempts. Therefore, we developed and tested a standardized protocol for ultrasound guided arterial lines, integrating a machine-automated pulsatile arterial line simulator, and incorporating equipment commonly used by anesthesiologists. Our hypothesis was that our motion analysis would detect differences in performance between novices and experts. Methods: A Viper tracking system equipped with electromagnetic motion sensors (Polhemus Ltd, Colchester, VT), was used to record motion during the ultrasound-guided insertion of an arterial line. Sensor 1 was attached to the dorsum of the participant's dominant hand and sensor 2 was attached to the base of a Butterfly ultrasound probe (Butterfly Inc, Burlington, MA). An integrated arterial catheter (Arrow brand-Teleflex Medical, Carrington, NC) was used in this protocol as it is commonly used in anesthesiology for arterial line placement. The participants completed two trials of an arterial line procedure from image identification through cannulation on a pulsatile arterial line trainer (Simulab, Seattle, WA) using a heart rate of 80 BPM, a moderate pulse strength, and a standardized starting position and approach. Participants imaged the vessel, cannulated the vessel, passed the guidewire, advanced the catheter, and then removed the needle. All trials were recorded and de-identified for analysis. The 4 metrics measured were path length (total distance travelled), rotational sum (degrees rotated), translational motions (individual movements), and time from beginning to end of procedure. Data was collected on 10 novices (anesthesiology residents) and 3 experts (attending anesthesiologists) using identical protocols. Comparisons were made between novices and experts for each parameter measured using 2-tailed t-tests with unequal variance; significance was considered as $p < 0.05$. Results: Path length was not significantly different between novices and experts ($p = 0.021$). The remaining parameters were all significantly higher in novices than experts including rotational sum ($p = 0.034$), translational motions ($p = 0.027$), and time ($p=0.021$). Conclusions: In this protocol, novices could be reliably differentiated from experts based on rotational sum, translational motions, and time required to complete the procedure. Path length was not significantly different across cohorts. A non-significant difference in path length was potentially due to the lack of gross motor movements required to complete the procedure. More specifically, a lack of hand movement outside of the small procedural field and lack of sliding in the ultrasound probe. Meanwhile, greater rotational sum and translational motions in novices likely reflect their need for significantly more minor optimizations in angle needling with their dominant hand, probe fanning and rotation to image the needle tip, and overall redundancy in motion for both sensors after failing to effectively cannulate on first needle pass. Experts completing the procedure in less time suggests greater efficiency and familiarity with procedural flow. Future studies should aim to identify whether intermediate level trainees can be differentiated from novices and experts within this protocol. They should also explore the impact of naturally variable parameters such as artery depth and diameter, which convey significant variety in difficulty in clinical practice. Lastly, goal-directed moti n metric feedback should be explored as a tool to expedite learning curves in arterial line placement and mitigate skill decay. (Figure Presented).

Anesthesiology
Daher LA, **Dionisio O**, **Baribeau V**, **Clark C**, **Was J**, **Londono CG**, **Uribe-Marquez S**, Lodico D, and **Mitchell J**. Motion Augmented eXperience (MAX) Feedback Enhances POCUS Performance as Compared to Traditional Expert Feedback, a Pilot Study. *Anesth Analg* 2024; 139(5):299-301. Full Text

L.A. Daher, Henry Ford Health, United States

Introduction: Point of care ultrasound (POCUS) encompasses a wide range of assessment and management techniques utilizing ultrasound (US) imaging to provide real-time information to better diagnose and manage patients in emergency, military, and remote situations. In addition, Simulation Based Mastery Learning (SBML) with Deliberate Practice (DP) has been the cornerstone of teaching complex technical skills.1 Traditionally, feedback was based on direct expert observations of performance and checklist-based evaluations. However, this type of feedback suffers from a ceiling effect and may not completely capture performance and areas for improvement. Motion tracking technologies have been employed to track advancements of technical skills in both physicians and military medics.2-4 As part of a comprehensive one-week POCUS training course for Navy Medics, we have begun providing Motion Augmented eXperience (MAX) Feedback to course participants to enhance their performance. We hypothesize that providing this MAX Feedback data to course participants could enhance performance beyond traditional expert feedback. Methods: The primary outcome of this pilot study was to compare MAX feedback and traditional expert feedback. Our research team tracked motion data for rapid ultrasound for shock and hypotension (RUSH) exams performed by 11 course participants; 8 Navy Combat Medics and 3 Submarine Independent Duty Corpsmen. The participants were randomized to either receive MAX Feedback or traditional expert feedback. Motion tracking was done by attaching a sensor (Polhemus ltd, Colchester, VT) to an ultrasound probe (Butterfly IQ +, Burlington, MA) to track the movements of each participant as they completed their RUSH exam. Each trial was timestamped and segmented by individual view for analysis. Each trial was also rated by an expert, who also verified image adequacy before allowing progression to the next view in sequence. The motion metrics analyzed were path length, rotational sum, translational sum, and time. Expert evaluations included image finding, image fine tuning, final image accuracy, speed, global rating, and best and worst image obtained. Each participant completed 2 exams at the end of each daily training session and these results were averaged to produce daily performance results. Each day, prior to conducting RUSH exams, the participants received either feedback based on both expert rating and their motion performance (MAX Feedback) or based on expert feedback alone (Traditional expert feedback). We compared Initial RUSH exam performance on the first 2 exams of the course to the final 2 exams of the week to assess for differences in skill progression. Results: The average MAX feedback path length was 1,109cm as compared to 2,186 cm in the traditional feedback group, p value = 0.0000059. For average rotation, MAX feedback path rotation sum was 9,618 degrees compared to 18,819 in the traditional feedback group, p value = 0.0000592. For translational motion, number of translational motion was 207 in MAX feedback compared to 316 in the traditional feedback group, p value = 0.00041. As for the time comparison, MAX feedback group had 136 seconds as compared to 165 seconds compared to traditional feedback group, p value 0.057. Therefore, MAX Feedback significantly outperformed Traditional Feedback in all motion parameters measured except time with all p values < 0.0005 except Time (p = 0.057). Conclusions: MAX Feedback has enhanced our ability to quantify continued performance improvements over conventional methods, leading to shortened learning curves and improved immediate procedural performance. The end goal of MAX Feedback training is to allow trainees to use POCUS accurately and efficiently in diagnostic and management decisions in a timely manner thus ensuring retention of training. In this pilot study, MAX Feedback results in significantly improved motion performance over traditional expert feedback at the end of a 1-week POCUS training course. The impact of MAX Feedback versus standard expert feedback in our com rehensive POCUS training program for now requires full scale investigation on larger cohorts of trainees, focus on other skills, and comparison to other performance metrics. Follow up is also planned to assess whether MAX Feedback enhances durability of training and skill retention over conventional expert feedback. (Figure Presented).

Anesthesiology

Khan A, Savir S, Yunus R, Rehman TA, Saeed S, Jackson C, Sharkey A, Neves S, Mahmood F, **Mitchell J**, Matyal R, and Winterton D. Virtual Reality for Invasive Procedural Training: Results from a Feasibility Study. *Anesth Analg* 2024; 139(5):949-951. Full Text

A. Khan, Beth Israel Deaconess Medical Center, Harvard Medical School, United States

Introduction: Current invasive procedural training for central venous access (CVA) relies on manikin-based simulator sessions. Given the evolution towards preclinical proficiency for skills acquisition, there is a pressing need for innovative training modalities to prepare the upcoming generation of physicians.[1] Virtual Reality (VR) is one potential technology that has been tested for training residents in certain specialties. [2,3] In this study our objective was to initiate the use of a novel VR technology for residents undergoing CVA training and assess its feasibility in comparison to the established manikinbased simulation training in our curriculum. Methods: This feasibility study was conducted from December 2022 to August 2023 in a single-center setting. We utilized the Vantari Virtual Reality Software (Sydney, Australia) on an Oculus Quest 2 VR Headset with Fast-Switch LCD Display and built-in 3D positional audio (Reality Labs; MetaPlatforms, Inc, Melo Park, CA). (FIGURE 1) We conducted a pilot of the VR technology among pre-internship medical graduates, medical interns, and PGY2s (CA1s), assessing their feedback compared with standard manikin-based simulation training with a survey distributed through Microsoft Forms (Microsoft, Redmond, WA). (FIGURE 2) Results: 17 volunteers including 5 medical graduates (PGY0), 5 interns (PGY1), and 7 first year anesthesia residents (PGY2) completed a training session on the VR simulator. (FIGURE 3) Seventy percent (n=3, strongly agree; n=9 agree) of participants found the VR equipment simple to operate and intuitive. 82.3% of participants (n=14) felt that the scenario mirrored real-life situations, with responses split between 'strongly agree' (3 participants) and 'agree' (11 participants). A significant majority, 70% (n=12), expressed confidence in their ability to use the VR training equipment independently, without the need for a supervising provider. While using the VR simulator, adverse effects were minimal. The reported adverse effects were nausea (5%), dizziness after extended use (5%), and headache after prolonged usage (5%). 76% (n=13) stated that they would like to use the simulator again. Of the 17 participants, 94% (n=16) agreed or strongly agreed that the VR simulator helps understand the different steps required for a proper central line placement. 65% (n=9) felt it developed awareness of proper ergonomics of equipment and ultrasounds (US). 41% (n=7) of participants agreed that the VR simulator helps the trainee to develop needle tracking skills. For comparison, traditional manikin training received slightly lower scores for understanding procedural steps (84.5% n=14), comparable rates for developing spatial awareness; (69.2% n=5), and higher rates for enhancing motor skills of proper utilization of instruments and US (70.5% n=6). Approximately 82% (n=14) of participants either agreed (n=11) or strongly agreed (n=3) that the VR scenario felt very realistic, simulating the environment of an OR. When participants were asked about their training preferences, 41% (n=7) showed a preference for the manikin, 18% (n=3) preferred VR, and 41% (n=7) viewed both as equally beneficial. Conclusions: Although manikin-based is the current standard method of training in our institution and many others, there are specific areas we have identified for potential enhancement. While it effectively enables the practice of US skills such as needle tracking and probe handling, it is often lacks a comprehensive, standardized, and structured portrayal of procedural steps. Moreover, it falls short in replicating a true-tolife environment crucial for a comprehensive simulation. VR on the other hand, provides an opportunity to simulate the milieu of the operating room, including ambient sounds, distractions, and the workspace. Beyond its capability to fully immerse a trainee in the simulation - the portability, cost-effectiveness, and accessibility render it a promising tool for invasive procedural training.[3] Our feasibility study suggests that while the current state of VR trainin models is inadequate when used independently, VR serves as a valuable supplement to standard manikin training. A larger multi-center observational study would be the next step to confirm our findings. The potential for future development in VR simulation, incorporating dynamic vital signs, patient anatomical variations, and common complications, could hold promise for significantly augmenting the efficacy of simulation training. (Figure Presented).

Anesthesiology
Wachtendorf L, Ahrens E, Munoz-Acuna R, Paschold BS, Redaelli S, Tenge T, Santer P, Robitaille M, Neves S, **Mitchell J**, Schaefer M, and Ma H. The Association Between Anesthesia Resident Training Level and The Incidence of Intraoperative Adverse Events: A Retrospective Cohort Study. *Anesth Analg* 2024; 139(5):748-750. Full Text

L. Wachtendorf, Beth Israel Deaconess Medical Center, Harvard Medical School, United States

Introduction: In the emergency department, endotracheal intubations performed by less experienced physicians are associated with higher rates of adverse events such as hypotension and hypoxemia [1]. In

the perioperative setting, anesthesia resident training level has been linked to differential risks of post-extubation desaturation [2]. However, it is unclear whether the training level of the anesthesia resident is associated with differential risks of intraoperative adverse events such as hypoxemia and hypotension in patients undergoing surgery. In this study, we hypothesized that anesthesia resident training level is associated with differential risks in the occurrence of intraoperative adverse events. Methods: This retrospective cohort study included 62,807 adult patients who underwent non-ambulatory, non-cardiac, non-transplant surgery with anesthesia care provided by an anesthesia resident as the primary provider under attending supervision at an academic healthcare center in the United States of America between 2009 and 2020 (Figure 1). The primary exposure was the training level of the anesthesiologist (CA-1 versus CA-2 versus CA-3). The primary outcome was a composite of intraoperative adverse events, defined as the occurrence of either arterial hypotension (mean arterial pressure <55 mmHg for ≥5 cumulative minutes) [3] or hypoxemia (peripheral oxygen saturation of <90% for an episode of >2 cohering minutes) [4]. We assessed the association between anesthesia resident training level and intraoperative adverse events using multivariable logistic regression adjusted for several patient- and procedural characteristics. Results: 22,078 (35.2%) patients received anesthesia care from CA-1 residents, while 19,961 (31.8%) and 20,768 (33.0%) patients received care from CA-2 and CA-3 anesthesia residents, respectively. Patients who received anesthesia care from CA-3 compared to CA-1 residents were on average older, had a higher comorbidity burden, and underwent more complex procedures (Table 1). Intraoperative adverse events occurred in 20.5% (n=12,887) of patients, while 18.0% (n=11,304) of patients experienced hypotension, and 3.3% (n=2,055) of patients experienced intraoperative hypoxemia. Compared to CA-1 residents, the risk of intraoperative adverse events was decreased if CA-2 residents provided anesthesia care (ORadj 0.92; 95%CI 0.88-0.97; P=0.003; Figure 2) and lowest if CA-3 residents provided anesthesia care (ORadj 0.84; 95%CI 0.80-0.89; P<0.001; Figure 2). This association was driven by lower rates of intraoperative hypotension among CA-2 (ORadj 0.91; 95%CI 0.87-0.97; P=0.001; Figure 2) and CA-3 residents (ORadj 0.83; 95%CI 0.79-0.88; P<0.001; Figure 2), respectively, while no differences were observed in the risk of hypoxemia across different training levels (CA-2 versus CA-1: ORadj 1.02; 95%CI 0.90-1.16; P=0.72 and CA-3 versus CA-1: ORadj 0.97; 95%CI 0.85-1.10; P=0.61; Figure 2). Conclusions: We observed a lower risk of intraoperative hypotension in anesthesia residents at higher training levels compared to early-career anesthesia residents. Based on our data, future studies are warranted to investigate underlying mechanisms and the potential relevance for patient outcomes after surgery as well as for anesthesia residency training and supervision. (Table Presented).

Anesthesiology
Yanko F, Phillips M, Miller C, **Mitchell J**, **Chhina A**, and Ballard H. A Multi-Institutional Targeted Needs Assessment of Leadership Skills: A Pilot Study. *Anesth Analg* 2024; 139(5):309-312. Full Text

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Introduction: Excellence in medical care transcends clinical expertise, requiring physicians to possess essential leadership skills. The importance of leadership skills is recognized by several Accreditation Council for Graduate Medical Education (ACGME) Anesthesiology milestones including Situational Awareness and Crisis Management, Reflective Practice and Commitment to Personal Growth, Interpersonal and Team Communication, among others.1 While leadership qualities are not innate, they can be honed with training and supportive experiences.2,3 Despite the escalating demand for leadership training, graduate medical education often neglects this vital aspect. The aim of this study was to assess leadership needs among anesthesia trainees and junior faculty across multiple institutions to inform the development of a leadership curriculum. We hypothesized that there would be significant differences in desired leadership domains and teaching methods between groups. Methods: We used an electronic cross-sectional survey design to investigate the need for a leadership curriculum in anesthesia education. The survey measured demographic information, as well as previous leadership experience and training. The participants were then asked about the importance of validated leadership domains using Kazley's Masters of Health Administration Collaborative Leadership Model, by utilizing a seven-point Likert scale. Participants were also asked about preferred learning modalities using the same Likert scale. Descriptive statistics were used to report participants' demographic information and experience. Cronbach's Alpha was calculated to test the internal reliability of the survey instrument. Chi square tests were used to detect

differences in proportions between groups. Results: Sixty-four participants, from five different institutions, comprising residents (38), fellows (13), and junior attendings (8), responded to the survey, yielding an overall response rate of 92%. A summary of participants demographic data is provided in Table 1. Notably less than 20% of any participant group had received any formal leadership education. Even though 50% of the attendings held leadership roles, none had formal leadership training. On average, participants rated themselves “slightly satisfied” with their leadership abilities. The 27-item survey was shown to have a high level of internal validity with a Cronbach's alpha of 0.94 and average interitem covariance of 0.49. There were no significant differences in the preferred leadership domains and learning modalities between groups (Table 2). In terms of competencies, all groups highly valued interpersonal communication, teamworking, emotional intelligence, ability for honest self-assessment, problem solving and decision making. Presentation skills, writing skills, human resource navigation, and billing and coding competencies were regarded as less important. In terms of learning modalities, there was not a clear preference for a single modality (Table 3). Case-based studies and small group sessions were valued highly by all three groups of learners. Reflective writing and online slide decks were the least preferred learning modalities. Conclusions: In this multi-institutional survey, we found an overall lack of leadership training and self-reported ability in all groups. Training in interpersonal communication, teamworking, and emotional intelligence was thought to be most helpful. This study highlights a pressing need for a leadership curriculum in anesthesia education, unveiling disparities in perceived abilities and training preferences. The absence of formal training reported by junior attendings in leadership roles signals a significant oversight. Evaluation of learning modalities stresses the importance of diverse instructional approaches as no single approach appeared to be superior. These insights lay the groundwork for targeted curriculum development, aspiring to cultivate effective and adaptable leaders within the anesthesia profession. (Table Presented).

Cardiology/Cardiovascular Research
Al-Suraimi A, **Almajed MR**, **Heil H**, **O'Neill B**, **Villablanca P**, **Parikh S**, **Gonzalez PE**, **Lee J**, **Zweig B**, **Wyman J**, **Frisoli T**, **O'Neill W**, and **Wang D**. Isolated Mitral Regurgitation Versus Multivalvular Disease in Patients Undergoing Mitral Valve Transcatheter Edge-toEdge Repair: A Comparison of Cardiac Function and Structure. *JACC Cardiovasc Interv* 2024; 17(4):S60-S60. Full Text

[Al-Suraimi, A.; Almajed, M. R.; O'Neill, B.; Villablanca, P.; Parikh, S.; Gonzalez, P. Engel; Lee, J.; Zweig, B.; Wyman, J.; Frisoli, T.; O'Neill, W.; Wang, D.] Henry Ford Hosp, Detroit, MI USA. [Heil, H.] Wayne State Univ, Detroit, MI USA.

Cardiology/Cardiovascular Research
Jebbawi LA, **McClafferty A**, **Parikh S**, **Khan A**, and **Ford H**. SUCCESSFUL ABLATION OF ATRIAL FLUTTER THROUGH A TRANS-BAFFLE APPROACH IN A PATIENT WITH MUSTARD REPAIR OF D-TRANSPOSITION OF THE GREAT ARTERIES(D-TGA). *J Am Coll Cardiol* 2024; 83(13):2944. Full Text

Background Atrial switch repair in d-TGA is a substrate for atrial tachyarrhythmias (AT). Due to complex anatomical and hemodynamic changes, therapies are often challenging. Case A 54-year-old male with d-TGA and Mustard repair in 1974, presented with symptomatic atrial flutter (AF). Different treatments were discussed with the patient, who opted for catheter ablation. Decision-making AT isthmus-dependent reentry is most common (77%) in this population. Ablation can be achieved through aortic retrograde approach or via a transbaffle approach. Both pose considerable technical challenges, requiring a precise understanding of the anatomy of the surgically modified chambers. During the procedure, AF was induced with a cycle length (CL) of 270 ms. Using the CARTO system, an electroanatomic map of the morphological left atrium was performed where entrainment mapping showed a long PPI-TCL. Guided by intracardiac echocardiogram, a transbaffle puncture was performed to access and map the systemic right atrium. Entrainment showed a PPI-TCL of 0ms around the systemic tricuspid valve. Ablation was performed from the valve plane to the left superior pulmonary vein. Local electrograms were eliminated with bidirectional block confirmation. Conclusion With the unsatisfactory outcomes of rhythm control, pacing, and cardioversion in atrial switch-related AT, catheter ablation can be therapeutic. An understanding of AT mechanisms, altered anatomy, and procedural adaptation is key to achieve success. [Formula presented]

Cardiology/Cardiovascular Research

Siems C, Cogswell R, Masotti M, Schultz J, **Cowger J**, Shaffer A, and John R. Impact of left ventricular assist device complications on heart transplant outcomes under the 2018 heart transplant allocation policy. *J Thorac Cardiovasc Surg* 2024; 167(3):1049-1059.e1045. Full Text

R. John, Division of Cardiothoracic Surgery, Department of Surgery, 420 Delaware St SE, MMC 207, Minneapolis, MN, United States

Objective: The study objective was to determine the impact of left ventricular assist device complications on post–heart transplant survival before and after the 2018 US heart transplant allocation policy change. Methods: Adult patients (age >18 years) supported by left ventricular assist devices at the time of listing or transplantation in the United Network for Organ Sharing between October 18, 2015, and December 31, 2021, were included. Left ventricular assist device complications were defined by status at transplant (nonelective 1A in the prior era or new era status 2 or 3). Post-transplant survival (primary analysis) and baseline characteristics were compared among those with and without left ventricular assist device complications and by allocation era using multivariable Cox regression analyses. Results: The primary analysis included 4160 patients with left ventricular assist devices who underwent heart transplant (prior era n = 2458, new era n = 1702). Patients who underwent heart transplant with left ventricular assist device complications were on left ventricular assist device support longer under the new era (498 days vs 423 days P < .001). Post-transplant survival was highest in the prior era among those without left ventricular assist device complications. Patients who underwent transplantation in the prior era with a complication and in the new era without complications were not statistically different. Left ventricular assist device complications in the new era were associated with the highest post-transplant mortality (status 2 adjusted hazard ratio, 1.87, 95% confidence interval, 1.31-2.67, P < .001, status 3 adjusted hazard ratio, 1.50, 95% confidence interval, 1.11-2.04, P = .009). Conclusions: Left ventricular assist device complications in the new era are associated with increased post-transplant mortality. As a heart allocation score is being considered, modeling time on left ventricular assist device support to promote heart transplant before development of left ventricular assist device–related complications may improve outcomes for patients with left ventricular assist devices.

Cardiology/Cardiovascular Research

Singh G, **Zhang K**, Grewal PK, Taggart AKP, Coughlin S, **Lanfear DE**, and **Sabbah HN**. A model of atrial fibrillation in dogs with chronic heart failure. *Eur J Heart Fail* 2024; 26:11-11. Full Text

[Singh, G.; Zhang, K.; Lanfear, D. E.; Sabbah, H. N.] Henry Ford Hosp, Detroit, MI USA. [Grewal, P. K.; Taggart, A. K. P.; Coughlin, S.] Novartis Biomed Res, Cambridge, MA USA.

Background: Atrial fibrillation (AF) is the most common rhythm disorder in humans, affecting an estimated 38 million people Worldwide and is particularly common in patients with heart failure (HF) where it contributes to early mortality. Various large animal models of lone AF exist but a robust model of AF in the setting of chronic HF is lacking. We evaluated the ease of induction, duration, and reproducibility of AF in a well-established coronary microembolization model of HF with reduced ejection fraction (EF) as a potential pre-clinical tool for assessing the safety and efficacy of novel therapies targeting AF in HF patients. Methods: 17 anesthetized HF dogs (LV EF <35%) weighing between 21.0 and 28.2 kg were studied. A Josephson quadripolar electrophysiology catheter positioned in the high right atrium (RA) was used. The RA was stimulated for 60 sec at increments of 100 beats/min, starting from a rate of 400 beats/min up to a rate of 600 beats/min. If sustained AF induction was not seen, an atrial extra-stimuli technique (up to 5 extra-stimuli) was used at a drive train of 600 msec (30 cycles). After AF was induced, the duration of AF was assessed for up to 600 seconds; if AF did not terminate spontaneously within 600 seconds, AF was terminated by Direct Current cardioversion at 100J. A second AF induction was performed consecutively for confirmation and an average of both AF inductions was used for all parameters. This process was repeated 2 additional times at 2 hour intervals to assess reproducibility. AF induction threshold and duration were each assigned a score of 1 to 8 such that a combined score of 16 would indicate low AF induction threshold and long AF sustainability whereas a score of 2 would indicate high threshold for AF induction and low AF sustainability. Results: Data are shown in the Table. On average, the induction threshold was approximately 500 beats/min and typical AF duration was 300 to

400 seconds, indicating relatively low AF threshold and substantial duration. The pacing threshold for AF induction, AF duration, and combined score were relatively stable across all 3 timepoints (baseline, 2 hours, and 4 hours) with no statistically significant differences. Conclusions: These results point to a robust model of AF induction in dogs with chronic HF characterized by low AF induction threshold and high sustained AF duration that are easily quantifiable and relatively stable. This model may represent a useful pre-clinical tool for evaluating the efficacy of therapies targeting AF in the setting of HF.

Center for Integrative Medicine

Kulas M. GRAVES' HYPERTHYROIDISM SYMPTOMS AND LABS MANAGED WITH AURICULAR ELECTROACUPUNCTURE VAGAL NERVE STIMULATION AND TRADITIONAL CHINESE MEDICINE: A CASE REPORT. *J Integr Complement Med* 2024; 30(8):A25. Full Text

M. Kulas, Henry Ford Health, United States

Introduction: This case report offers insight into the effects of multimodal auricular acupuncture vagal nerve stimulation (aaVNS) therapy interspersed with Traditional Chinese Medicine protocols (TCM) for management of Graves' hyperthyroidism symptoms following chemotherapy (CT) and radiation therapy (RT) of large B cell non-Hodgkin's lymphoma. Case: A mid-50's Caucasian female suffering from moderate mixed presentation insomnia, palpitations, anxiety, daytime flushing, night sweats, and fatigue. Measurable thyroid levels showed an oscillation between hyper-, hypothyroid, and Grave's disease for at least two years prior to initiation of acupuncture. Traditional acupuncture point prescriptions were utilized, as well as aaVNS with diaphragmatic breathing due to dysautonomia symptoms. Results: Physical symptoms surrounding sleep, palpitations, and flushing were significantly improved within the first three months. Thyroid stimulating hormone (TSH), free T4, free T3, and thyroid stimulating immunoglobulin (TSI) levels normalized when patient was in otherwise good health but demonstrated regression of disease markers when prone to opportunistic infections. Conclusions: Data from other studies suggest mixed conclusions if acupuncture as a stand-alone treatment can impact thyroid levels. This case presents a unique look at measurable thyroid changes utilizing a multimodal approach of auricular vagal stimulation, diaphragmatic breathing, and traditional acupuncture.

Dermatology

Hamzavi I, Coulter J, Balaji A, Franco L, Darnell S, Law E, Kurosky S, Adiri R, Elbuluk N, and Hauber B. PCR163 Treatment Priorities and Unmet Need Among Adults and Adolescents With Non-Segmental Vitiligo in the United States. *Value Health* 2024; 27:S538. Full Text

Objectives: To quantify treatment priorities and unmet need among adults and adolescents with vitiligo in the United States (US). Methods: An adaptive self-explicated preference-elicitation survey was administered to adults (age ≥18 years) and adolescents (age 12-17 years) with non-segmental vitiligo. The preference-elicitation included 26 attributes related to treatment efficacy, safety, and mode of administration. Relative importance (RI) of each attribute was estimated using latent class analysis (LCA). Satisfaction with the 10 most important attributes for each patient was elicited using rating scales. RI and satisfaction were combined to estimate unmet need using a modified outcome-driven innovation approach which defines unmet need as high RI combined with low satisfaction. Results: The sample comprised adults (N=321) and adolescents (N-201) who received vitiligo care from 83 sites across the US. They had a mean (SD) age of 26 (9.1) and 14 (1.6) years, respectively. More than 50% of participants self-identified as non-White; 50% were female. Fitzpatrick skin types were 23.9% Type I-II (pale white, fair), 43.6% III-IV (darker white, light brown), and 32.4% V-VI (brown, black). LCA identified three preference segments: Efficacy (N=182,34.9%), most important attributes were amount of repigmentation on the entire body (RI=5.16) and reducing the emotional burden of vitiligo (RI=5.00); Mode of Administration (MOA) (N=159,30.5%), most important attributes were having an oral (RI=4.80), systemic (RI=5.03) treatment; Safety (N=181,34.7%), most important attributes were avoiding cardiovascular events (RI=4.53), cancer (RI=4.38), or shingles (RI=4.42). Among the full sample, the greatest areas of unmet need were reducing the emotional burden of vitiligo and having access to an oral systemic (rather than topical) treatment. Conclusions: Treatment preferences among people with vitiligo are heterogeneous. In addition to repigmentation, reducing the emotional burden of vitiligo is a key

treatment goal for patients. An effective oral systemic treatment could help address unmet need in this patient population.

Dermatology

Lebwohl M, Bukhalo M, **Stein-Gold L**, Pelle M, Glick B, Llamas-Velasco M, Sanchez-Rivera S, Zhan T, Drogaris L, Espaillat R, and Bissonnette R. 51675 Safety and efficacy of risankizumab in adult patients with moderate-to-severe plaque psoriasis with non-pustular palmoplantar involvement: changes in PPASI and PASI from Phase 3b IMMprint trial. *J Am Acad Dermatol* 2024; 91:AB306. Full Text

Introduction: Risankizumab (RZB) is an IL-23 inhibitor approved for the treatment of moderate-to-severe psoriasis (PsO). We assessed the improvement in palmoplantar psoriasis area and severity index (PPASI) and PASI in patients with moderate-to-severe non-pustular palmoplantar PsO (PPPsO). Methods: In IMMprint (NCT04713592), a phase 3b, double-blind, placebo-controlled study, patients (≥18 years) were randomized 1:1 to receive RZB 150mg (week 0, 4 and 16) or placebo (PBO). Starting at week 16, all patients received open-label RZB 150mg (PBO/RZB vs. RZB/RZB) every 12 weeks till week 40 with final evaluation at week 52. PPASI and PASI were assessed by Mixed-effect Model Repeat Measurement (MMRM) to handle missing data in Period A, and Observed Cases (OC) in Period B. Results: The change from baseline in PPASI (RZB vs. PBO, nominal p-value) was -11.3 vs. -6.1, $p < 0.001$ at week 16 and -16.9 vs. -17.2 (RZB/RZB vs. PBO/RZB) at week 52. The percent change from baseline in PPASI was -51.8 vs. -27.6, $p <0.001$ at week 16 and -76.1 vs. -78.7 (RZB/RZB vs. PBO/RZB) at week 52. The change from baseline in PASI was -7.6 vs. -2.3, $p < 0.001$ at week 16 and -10.3 vs -9.4 (RZB/RZB vs. PBO/RZB) at week 52. The percent change from baseline in PASI among baseline ≥ 12 was -68.1 vs. -15.9, $p < 0.001$ at week 16 and -89.7 vs. -87.1 (RZB/RZB vs. PBO/RZB) at week 52. Conclusions: Treatment with RZB led to improved clinical responses in the patients with PPPsO with no new safety signal.

Diagnostic Radiology

Ali SA, **Ahmad Adil S**, **Harris K**, **Kamran W**, **Elatrache M**, **Zuchelli T**, and **Piraka C**. Navigating Obstacles: A Case Report on Endoluminal Treatment of Afferent Limb Syndrome Post-Whipple Procedure for Cholangiocarcinoma. *Am J Gastroenterol* 2024; 119(10):S2596. Full Text

S.A. Ali, Henry Ford Hospital, Detroit, MI, United States

Introduction: Afferent limb syndrome (ALS) is a rare complication of the Whipple pancreaticoduodenectomy (0.3%-1%). While optimal treatment is not established, surgical revision is a traditional approach for malignant ALS. Recently, endoscopic or radiologic interventions, such as stenting or percutaneous biliary drainage, have emerged as palliative alternatives. Case Description/Methods: This is a 74-year-old man with history of metastatic cholangiocarcinoma stage IIB status post neoadjuvant therapy followed by Whipple procedure. Course was complicated by obstructive jaundice due to partially obstructing afferent limb jejunal mass seen on enteroscopy, biopsy-proven to be recurrent cholangiocarcinoma. The resultant severe stricture could not be traversed endoscopically hence an internal-external percutaneous transhepatic cholangiography (PTC) drain was inserted, complicated by persistent leak around the insertion site requiring several tube exchanges. He was later admitted for jaundice & poor oral intake. Abdominal imaging re-demonstrated the mass with an abrupt transition point (Figure 1). A cholangiogram revealed dilated small bowel loop in the afferent limb concerning for ALS. Based on imaging, there was no good window for an endoscopic ultrasound-guided jejuno- or gastrojejunostomy to bypass the obstruction. Therefore, a 22 mm x 6 cm uncovered metal Wallflex stent (Boston Scientific, Marlborough, MA) was inserted across the site (Figure 1B), which improved his symptoms & oral intake without further PTC leaks. Discussion: Malignant ALS post-Whipple negatively impacts outcomes & quality of life in a population with already limited life expectancy. Diagnosis can be a challenge as it may not present with typical gastrointestinal (GI) obstruction symptoms, requiring clinical suspicion & imaging (commonly computerized tomography as upper GI series may not detect its presence). Management requires a multidisciplinary approach with surgeons, therapeutic endoscopists, &/or interventional radiologists. Our case underscores the importance of prompt recognition to allow for an early intervention. Palliative surgical revision is limited by low success rates given overall poor patient condition or from tumor burden causing kinks. Percutaneous approaches introduce risk of retrograde

biliary infection, & in this case failed due to downstream obstruction. Endoluminal interventions, despite technical difficulty, emerge as promising alternatives which warrant further prospective trials comparing outcomes with other modalities. (Figure Presented).

Emergency Medicine

Daher LA, **Ayyar I**, **Polanco A**, Baribeau V, **Clark C**, **Uribe-Marquez S**, **Londono CG**, **Park A**, **Mitchell J**, and **Guruswamy J**. Motion Analysis: An Objective Assessment of Novel Arterial Line Placement Protocol. *Anesth Analg* 2024; 139(5):296-298. Full Text

L.A. Daher, Henry Ford Health, United States

Introduction: Arterial line placement is a challenging skill for anesthesiology residents to master. Previous efforts have demonstrated the utility of analyzing data from motion trackers to objectively assess performance across procedural skills.1-2 While motion tracking has been previously used to assess radial artery access in interventional radiologists, the approach and equipment used was different from that traditionally used by anesthesiologists.3 Furthermore, this study was performed without guidance, with a skill trainer that required manual pulsation with a bulb device, potentially resulting in variability in rate and pulse pressure within and between attempts. Therefore, we developed and tested a standardized protocol for ultrasound guided arterial lines, integrating a machine-automated pulsatile arterial line simulator, and incorporating equipment commonly used by anesthesiologists. Our hypothesis was that our motion analysis would detect differences in performance between novices and experts. Methods: A Viper tracking system equipped with electromagnetic motion sensors (Polhemus Ltd, Colchester, VT), was used to record motion during the ultrasound-guided insertion of an arterial line. Sensor 1 was attached to the dorsum of the participant's dominant hand and sensor 2 was attached to the base of a Butterfly ultrasound probe (Butterfly Inc, Burlington, MA). An integrated arterial catheter (Arrow brand-Teleflex Medical, Carrington, NC) was used in this protocol as it is commonly used in anesthesiology for arterial line placement. The participants completed two trials of an arterial line procedure from image identification through cannulation on a pulsatile arterial line trainer (Simulab, Seattle, WA) using a heart rate of 80 BPM, a moderate pulse strength, and a standardized starting position and approach. Participants imaged the vessel, cannulated the vessel, passed the guidewire, advanced the catheter, and then removed the needle. All trials were recorded and de-identified for analysis. The 4 metrics measured were path length (total distance travelled), rotational sum (degrees rotated), translational motions (individual movements), and time from beginning to end of procedure. Data was collected on 10 novices (anesthesiology residents) and 3 experts (attending anesthesiologists) using identical protocols. Comparisons were made between novices and experts for each parameter measured using 2-tailed t-tests with unequal variance; significance was considered as $p < 0.05$. Results: Path length was not significantly different between novices and experts ($p = 0.021$). The remaining parameters were all significantly higher in novices than experts including rotational sum ($p = 0.034$), translational motions ($p = 0.027$), and time ($p=0.021$). Conclusions: In this protocol, novices could be reliably differentiated from experts based on rotational sum, translational motions, and time required to complete the procedure. Path length was not significantly different across cohorts. A non-significant difference in path length was potentially due to the lack of gross motor movements required to complete the procedure. More specifically, a lack of hand movement outside of the small procedural field and lack of sliding in the ultrasound probe. Meanwhile, greater rotational sum and translational motions in novices likely reflect their need for significantly more minor optimizations in angle needling with their dominant hand, probe fanning and rotation to image the needle tip, and overall redundancy in motion for both sensors after failing to effectively cannulate on first needle pass. Experts completing the procedure in less time suggests greater efficiency and familiarity with procedural flow. Future studies should aim to identify whether intermediate level trainees can be differentiated from novices and experts within this protocol. They should also explore the impact of naturally variable parameters such as artery depth and diameter, which convey significant variety in difficulty in clinical practice. Lastly, goal-directed moti n metric feedback should be explored as a tool to expedite learning curves in arterial line placement and mitigate skill decay. (Figure Presented).

Emergency Medicine

Daher LA, **Dionisio O**, **Baribeau V**, **Clark C**, **Was J**, **Londono CG**, **Uribe-Marquez S**, Lodico D, and **Mitchell J**. Motion Augmented eXperience (MAX) Feedback Enhances POCUS Performance as Compared to Traditional Expert Feedback, a Pilot Study. *Anesth Analg* 2024; 139(5):299-301. Full Text

L.A. Daher, Henry Ford Health, United States

Introduction: Point of care ultrasound (POCUS) encompasses a wide range of assessment and management techniques utilizing ultrasound (US) imaging to provide real-time information to better diagnose and manage patients in emergency, military, and remote situations. In addition, Simulation Based Mastery Learning (SBML) with Deliberate Practice (DP) has been the cornerstone of teaching complex technical skills.1 Traditionally, feedback was based on direct expert observations of performance and checklist-based evaluations. However, this type of feedback suffers from a ceiling effect and may not completely capture performance and areas for improvement. Motion tracking technologies have been employed to track advancements of technical skills in both physicians and military medics.2-4 As part of a comprehensive one-week POCUS training course for Navy Medics, we have begun providing Motion Augmented eXperience (MAX) Feedback to course participants to enhance their performance. We hypothesize that providing this MAX Feedback data to course participants could enhance performance beyond traditional expert feedback. Methods: The primary outcome of this pilot study was to compare MAX feedback and traditional expert feedback. Our research team tracked motion data for rapid ultrasound for shock and hypotension (RUSH) exams performed by 11 course participants; 8 Navy Combat Medics and 3 Submarine Independent Duty Corpsmen. The participants were randomized to either receive MAX Feedback or traditional expert feedback. Motion tracking was done by attaching a sensor (Polhemus ltd, Colchester, VT) to an ultrasound probe (Butterfly IQ +, Burlington, MA) to track the movements of each participant as they completed their RUSH exam. Each trial was timestamped and segmented by individual view for analysis. Each trial was also rated by an expert, who also verified image adequacy before allowing progression to the next view in sequence. The motion metrics analyzed were path length, rotational sum, translational sum, and time. Expert evaluations included image finding, image fine tuning, final image accuracy, speed, global rating, and best and worst image obtained. Each participant completed 2 exams at the end of each daily training session and these results were averaged to produce daily performance results. Each day, prior to conducting RUSH exams, the participants received either feedback based on both expert rating and their motion performance (MAX Feedback) or based on expert feedback alone (Traditional expert feedback). We compared Initial RUSH exam performance on the first 2 exams of the course to the final 2 exams of the week to assess for differences in skill progression. Results: The average MAX feedback path length was 1,109cm as compared to 2,186 cm in the traditional feedback group, p value = 0.0000059. For average rotation, MAX feedback path rotation sum was 9,618 degrees compared to 18,819 in the traditional feedback group, p value = 0.0000592. For translational motion, number of translational motion was 207 in MAX feedback compared to 316 in the traditional feedback group, p value = 0.00041. As for the time comparison, MAX feedback group had 136 seconds as compared to 165 seconds compared to traditional feedback group, p value 0.057. Therefore, MAX Feedback significantly outperformed Traditional Feedback in all motion parameters measured except time with all p values < 0.0005 except Time (p = 0.057). Conclusions: MAX Feedback has enhanced our ability to quantify continued performance improvements over conventional methods, leading to shortened learning curves and improved immediate procedural performance. The end goal of MAX Feedback training is to allow trainees to use POCUS accurately and efficiently in diagnostic and management decisions in a timely manner thus ensuring retention of training. In this pilot study, MAX Feedback results in significantly improved motion performance over traditional expert feedback at the end of a 1-week POCUS training course. The impact of MAX Feedback versus standard expert feedback in our com rehensive POCUS training program for now requires full scale investigation on larger cohorts of trainees, focus on other skills, and comparison to other performance metrics. Follow up is also planned to assess whether MAX Feedback enhances durability of training and skill retention over conventional expert feedback. (Figure Presented).

Emergency Medicine

Morse P, **Chouman A**, **Tamr A**, **Saleem A**, **Cunningham C**, and **Umanath K**. CMV Colitis in Immunocompetent Host. *Am J Gastroenterol* 2024; 119(10):S2432-S2433. Full Text

P. Morse, Wayne State School of Medicine, Detroit, MI, United States

Introduction: Cytomegalovirus (CMV) is a double-stranded DNA virus which causes disease in humans based on their immune status. Despite being a common infection in immunocompromised hosts, CMV colitis rarely occurs in the immunocompetent. Symptoms of CMV colitis are nonspecific, including diarrhea, abdominal pain, fever, and rectal bleeding. We present an immunocompetent patient who was identified as having biopsy proven CMV colitis. Case Description/Methods: A 55-year-old woman with a history of well-controlled type 2 diabetes and end-stage renal disease (ESRD) on dialysis presented to the hospital with painless hematochezia and diarrhea for two months with acute worsening in the last week. Imaging several weeks before presentation to the ED was suggestive of ischemic colitis, but no further studies were completed at that time. Her hemoglobin on presentation was 8.4 g/dL. The next day, her hemoglobin dropped to 6.5 g/dL requiring blood transfusion. The patient's white blood cell count was mildly decreased at 3.6 K/mL with a normal differential. She underwent esophagogastroduodenoscopy, which was normal, and colonoscopy, which showed diffuse inflammation and a colonic ulcer which was biopsied. Pathology showed features of ischemic colitis and stained positive for CMV. Serum CMV quantitation at this time was 1474 IU/mL. She started intravenous ganiciclovir, which was transitioned to oral valganciclovir at discharge. Upon outpatient follow up two weeks later, the patient reported compliance with the valganciclovir and resolution of her symptoms. Serum CMV quantitation was undetectable at this visit. Discussion: Here we present a patient with well-controlled diabetes and ESRD on dialysis who presented with CMV colitis. Despite multiple comorbidities, she was immunocompetent. Given the patient's positive biopsy staining for CMV, elevated serum CMV quantitation, and complete resolution of symptoms on valganciclovir, CMV colitis is the most likely diagnosis. Diabetes and ESRD on dialysis are known to be comorbid conditions with CMV colitis in immunocompetent hosts. Additionally, prior research indicates that being age 55 or over is also a risk factor. It is hypothesized that these comorbidities contribute to a weakening of the immune system, facilitating CMV colitis to develop in patients traditionally considered immunocompetent. Clinicians should consider CMV colitis in otherwise unexplained abdominal symptoms, particularly in patients with multiple comorbidities like diabetes, ESRD, and age 55 or greater.

Endocrinology and Metabolism

Bhan A, **Simon R**, **Aseel Y**, **Qiu S**, and **Rao SD**. The Utility of 24-hour Urine Calcium Excretion in Evaluating Kidney Stone (KS) Risk in Patients with Primary Hyperparathyroidism (PHPT). *J Bone Miner Res* 2024; 39:81. Full Text

S.D. Rao, Henry Ford Health, United States

There is currently a debate about the link between 24-hour urine calcium levels (24h-UCa) and the risk of kidney stone formation in patients with primary hyperparathyroidism (PHPT). The aim of this study was to assess the usefulness of measuring 24h-UCa excretion in assessing risk of kidney stones in PHPT patients. Additionally, we explored the prevalence of kidney stones among different genders, races and 24h-UCa levels. Of the 343 PHPT patients aged 21 to 91 years, 72 had kidney stones. The cohort consisted of 117 Blacks (101 females and 16 males) and 226 Whites (170 females and 56 males). The biochemical measurements included serum calcium (SCa), ionized calcium (iCa), serum creatinine (SCr), parathyroid hormone (PTH), and 24h-UCa. Hypercalciuria was defined by two criteria based 24-Uca: >400mg/day without regard to gender or >300 mg/day for men and >250 mg/day for women. Among the 343 PHPT patients, individuals without kidney stones were significantly older than those with kidney stones (Table 1). However, no significant differences were observed in biochemical variables between the groups with and without kidney stones. In both groups, the PTH levels were higher than the normal reference range, while the other variables were within the reference range (Table 1). The ANCOVA analysis revealed that 24h-UCa levels were significantly higher in men compared to women, and in Whites compared to Blacks, but not different between the patients with and without kidney stones. According to the Chi-Squared test results presented in Table 2, the prevalence of kidney stones was higher in Whites than in Blacks, and in men than in women. However, 24h-UCa levels did not significantly impact kidney stone prevalence (Table 2). In conclusion, the results suggest that although 24h-UCa levels may differ among genders and races, they might not be a crucial factor for evaluating kidney

stones in patients with PHPT. These results suggest that the differences in kidney stone prevalence among genders and races are likely independent of the levels of 24h-UCa. More studies are necessary to validate these outcomes and investigate other possible risk factors for kidney stones in PHPT patients.

Endocrinology and Metabolism

Costris AR, **Shiri L**, and **Honasoge M**. Denosumab Discontinuation and the Rebound Phenomenon: A Case Report. *J Bone Miner Res* 2024; 39:165. Full Text

A.R. Costris, Henry Ford Hospital, United States

Antiresorptive therapy with Denosumab increases bone mineral density (BMD) and lowers fracture risks across all skeletal sites. Progressive increase in BMD with long term use is thought to be due to preservation of modelling and intermittent increases in parathyroid hormone secretion. Nevertheless, upon discontinuation of therapy, there is a heightened likelihood of experiencing a rebound surge in bone turnover markers, potentially resulting in bone loss, and in individuals at high risk, possibly culminating in fractures. Prolonged use increases the risk of this rebound phenomenon in addition to other factors. We present the case of a 65-year-old woman diagnosed with osteoporosis at age 45 when she was diagnosed with breast cancer. BMD improved after treatment with Tamoxifen and Alendronate for 5 years. She then received Denosumab for 11 years with improvement in BMD: lumbar spine T-score of -1.7 with 11.2 % increase in BMD and femoral neck T-score of -1.9 with 20.3% increase in BMD. Denosumab was discontinued and bone markers were followed closely: Serum C-Telopeptide (CTx) at that time of discontinuation was 55 pg/mL (104-1008 pg/ mL). She received IV Zolendronic acid (ZDN) 6 months after cessation of Denosumab when her CTx was 163. There was a marked increase in bone remodeling 12 months after discontinuation of Denosumab despite IV ZDN given 6 months after discontinuation of Denosumab. BMD showed a mild decrease in spine BMD and a marked 14.5% decrease in femoral neck BMD. Oral weekly alendronate 70 mg was started, additional second dose of IV ZDN was administered, and oral bisphosphonate continued. Bone markers are showing a gradual decline. The expected 50-60% reduction of bone remodeling did not occur with IV ZDN suggesting some resistance to the antiresorptive effect of the most potent bisphosphonate. The rebound increase in bone remodeling following the cessation of Denosumab is believed to stem from the emergence of new osteoclasts from precursors, and/or the transition of osteoclasts into more aggressive osteomorphs. To safely discontinue Denosumab, clinicians should monitor bone markers closely and administer IV ZDN coinciding with activation of remodeling. Additional IV ZDN in combination with oral alendronate may be necessary if there is persistent increase in bone remodeling.

Endocrinology and Metabolism

Dave D, and **Rao SD**. Coexistent Toxic Nodular Goiter And Primary Hyperparathyroidism (PHPT), A Combo With Diagnostic And Management Implications. *J Endocr Soc* 2024; 8:A210. Full Text

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About 17-84% of patients with PHPT have concomitant thyroid disorders, but the prevalence of coexistent hyperthyroidism in PHPT varies 9-14 %. A vast majority had Graves' disease with only 3 cases of toxic multinodular goiter (MNG) and PHPT reported in the literature as of 2022 ([1]). We present a rare case of coexistent toxic MNG and PHPT. Case Description: A 68y woman presented with recent 23 kg unintended weight loss and palpitations, but no other symptoms. Denied having kidney stones or fractures. On examination she had fine tremors of hands, MNG without exophthalmos. An ultrasound showed multinodular MNG with cystic lesions. A diagnosis of toxic MNG was made. Laboratory results were: TSH (<0.01 uIU/mL), free T4 1,68 ng/dL (normal: 0.61-1.44 ng/ml), high serum Ca (11.0 - 11.4 mg/dl) over 4y, but PTH was unavailable prior to the visit when it was 107 pg/ml and 89 pg/ml after 3 months of antithyroid therapy. Despite clinical and biochemical euthyroidism after 3 months, serum Ca and PTH levels remained high (11.4 mg/dl and 89 pg/ml respectively). Because she had pulmonary embolism a few years ago, we deferred parathyroidectomy until complete remission of hyperthyroidism. Discussion: Hypercalcemia is the biochemical hallmark of PHPT but can occur in 2-10% of patients with hyperthyroidism alone but only 1% of those will have coexistent PHPT. When these two conditions coexist, hypercalcemia is moderate to severe, and an occasional patient may present with hypercalcemic

crisis (2). Prior to the availability of PTH assays, it was a challenge to diagnose coexistent PHPT. Hypercalcemia in hyperthyroidism responds to propranolol but not in PHPT, although the response is variable (3). With the availability of sensitive PTH assays, this maneuver is not necessary. In most cases, current PTH assays distinguish hypercalcemia of hyperthyroidism with suppressed PTH from coexistent PHPT in whom PTH level is non-suppressed or elevated. Monitoring serum Ca and PTH levels during therapy of hyperthyroidism would be useful as normalization of serum Ca and PTH has occasionally been reported (4). In our patient, serum Ca and PTH levels remained high with 3-months of methimazole and atenolol. The impact of both conditions on bone and mineral metabolism are profound, with fractures and kidney stones. Since kidney stones are uncommon in hyperthyroidism, presence of kidney stone in a hyperthyroid hypercalcemic patient should alert the possibility of PHPT. Similarly, significant decrease in bone density in such patient also raises the possibility of PHPT. Prompt diagnosis and appropriate treatment of both conditions is necessary to avoid irreversible complications.

Endocrinology and Metabolism

Garg S, Arya A, Kumari P, Nada R, Sachdeva N, Dahiya D, **Rao SD**, Mithal A, and Bhadada SK. Targeted Sequencing to Screen Germline and Somatic Variants, its Validation and Expression at Gene and Protein Levels in Indian Primary Hyperparathyroidism Patients. *J Bone Miner Res* 2024; 39:128. Full Text

S. Garg, Department of Endocrinology, PGIMER, India

Background: Primary hyperparathyroidism (PHPT) has been characterized by hypercalcemia with elevated parathyroid hormone. In India, the genetic causes of familial forms of PHPT have been known, however, there has been no comprehensive study of genetic analysis of sporadic and familial PHPT cases till now. Aim: To establish an Indian database of germline and somatic variants using 18 genes panel clinically relevant to parathyroid tumors Methods: Thirty histopathologically proven, PHPT patients and five controls were recruited between 2019-2023. A panel of 18 genes (MEN1, CDC73, CASR, CDKN1B, RET, GCM2, AP2S1, GNA11, PTH, CDKN1A, CDKN2B, CDKN2C, EZH2, ZFX, GATA3, CTNNB1, LRP5, and CCND1) clinically relevant to PHPT was designed for next generation sequencing. DNA extracted from both blood and tissue samples from patients and controls were prepared in two different pools of libraries and run on NovaSeq 6000 Illumina platform. Variant calling was performed to obtain germline and somatic variants as per ACMG guidelines which were validated through sanger sequencing. Besides, gene and protein expression of genes as well as in-silico functional characterization (Mutalyzer 3 and CharmGUI) was done. Results: The mean age of the patients recruited was 48.33 ± 15.70 years (28-70) with a sporadic: familial ratio of 25:5. Clinical manifestations were bone pain (n=20;66.6%), abdominal pain (n=15;50%), weakness and fatigue (n=21;70%), gall stone disease (n=6; 20%), renal stone disease (n=18;60%), fractures (n=10;33.3%), and osteoporosis (n=18;60%). Biochemically, the corrected serum calcium (11.68 ± 1.41 mg/dl), vitamin D (24.52 ± 13.53 ng/ml), serum PTH (811.3 ± 904.5 pg/ml), serum phosphorus (2.36 ± 0.76 mg/dL), serum alkaline phosphatase (267.7±237) and serum creatinine (0.96 ± 0.47 mg/dl) levels were fluctuated in PHPT patients in comparison to control. Out of total 197 germline and 108 somatic variations; the benign mutations reported were 190 (germline) and 103 (somatic) respectively. In germline, the pathogenic missense (c.T818C, exon 5) and frameshift insertion mutations (c.252dupT, exon 2; c.566dupA, exon3) were screened in MEN1 gene and VUS (possibly pathogenic) in GCM2 (c.T1102A, exon 5), LRP5 (c.C3919T, exon 18; c.G229A, exon 2) and RET (c.C1423T, exon 7) genes. In somatic, the pathogenic stopgain (c.C981G, exon7; c.C590T, exon 3); and missense (c.C496T, exon 3; c.T1673G, exon 10; c.G467A, exon 3) mutations were screened in MEN1 gene and further validated through sanger sequencing. Loss of function was observed in the MEN1 gene at gene and protein expression level. In-silico analysis showed truncated MEN1 protein in stopgain and frameshift insertions affecting structure and function of the protein. Conclusion: Two novel mutations have been reported in the blood and four in tissue samples of Indian PHPT patients. Approx. 17% of MEN1 mutations were screened in sporadic PHPT patients.

Endocrinology and Metabolism

Gomes KM, **Davydov E**, and **Lahiri SW**. Acute Hypercalcemic Renal Failure As A Presenting Manifestation Of Primary Hyperparathyroidism Due To Atypical Adenoma. *J Endocr Soc* 2024; 8:A187. Full Text

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Atypical parathyroid adenomas have uncertain malignant potential and are a rare cause of primary hyperparathyroidism. Compared to typical parathyroid adenomas, patients with atypical parathyroid adenomas have higher preoperative serum calcium and parathyroid hormone (PTH) levels. However pre-operative distinction between atypical parathyroid adenomas, typical adenomas and parathyroid carcinoma is challenging, and histological evaluation is needed for definitive diagnosis. A 59-year-old female with history of nephrolithiasis presented with syncope. Laboratory evaluation revealed a serum calcium of 21.3 mg/dL (8.2-10.2), creatinine of 2.35 mg/dL with GFR of 36 mL/min/1.723 m2, PTH of 3711 pg/mL (15-65), 25-hydroxy vitamin D of 12 ng/mL, phosphorus of 5.6 mg/ dL (2.5-4.5). She incidentally tested positive for COVID-19. CT abdomen/pelvis demonstrated bilateral obstructive renal calculi requiring stent placement. Despite treatment with intravenous normal saline, 4 mg of zoledronic acid, two doses of 300 units of calcitonin, and cinacalcet 30 mg twice daily, repeat calcium and creatinine were 17.9 mg/dL and 3.64 mg/dL, respectively, and hemodialysis was initiated. CT neck and chest identified a 2.0 x 2.3 x 3.8 cm hypodense nodule inferior to the left thyroid lobe. A parathyroid planar scan with SPECT/CT showed uptake within the hypodense nodule. Bone scan did not reveal any disease. The enlarged left parathyroid gland was removed. Intra-operatively, PTH decreased to 302 pg/mL. Pathological evaluation of the left inferior parathyroid gland revealed a 4.2 cm partially encapsulated hypercellular neoplasm weighing 7.3 grams with increased mitotic activity and focally thickened fibrotic capsule and no extracapsular or vascular invasion consistent with atypical parathyroid adenoma. On postop day 4, her calcium declined to 7.1 mg/dL and PTH was 383 pg/mL. Calcium supplementation was initiated due to concern for hungry bone syndrome. On postop day 14, calcium increased to 10.3 mg/ dL and supplementation was discontinued. Her calcium levels have remained normal without supplementation three months after surgery. Severe hypercalcemia causing renal failure is an uncommon manifestation of primary hyperparathyroidism. Preoperative differentiation of parathyroid carcinomas and parathyroid adenomas is difficult, but important since surgical management of these two distinct entities differs. Higher preoperative calcium and PTH levels and concomitant renal failure suggest parathyroid carcinoma. This case highlights the challenge of differentiating atypical parathyroid adenomas from parathyroid carcinoma since both conditions can present with severe hypercalcemia and renal failure. Further research on the risk of carcinoma and recurrence of hypercalcemia in atypical parathyroid adenoma is needed.

Endocrinology and Metabolism

Kumari P, Arya A, Garg S, Sachdeva N, Dahiya D, Saikia UN, **Rao SD**, and Bhadada SK. Transcriptome Analysis Identifies Novel EZH2 Target Genes And Altered Signaling Pathways In Primary Hyperparathyroidism. *J Bone Miner Res* 2024; 39:129-130. Full Text

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BACKGROUND Primary hyperparathyroidism (PHPT) is characterized by hypercalcemia and elevated parathyroid hormone levels. Epigenetic modifications identified as a regulator in parathyroid tumorigenesis. EZH2, a critical epigenetic modifier catalyzes trimethylation of lysine (K) 27 (H3K27me3) thereby regulate gene expression but its role is obscured in PHPT. This study was designed to analyze the gene and protein expression of EZH2 in PHPT patients followed by in-vitro identification of novel EZH2 target genes and pathways for the advanced therapeutic strategies. METHODOLOGY- 40 PHPT (30 parathyroid tumors, 10 aggressive parathyroid tumors) and 10 normal parathyroid tissues were recruited. Aggressive parathyroid tumors include minimally invasive parathyroid carcinoma (06) and carcinoma (04) cases. mRNA and protein expression for EZH2 was performed by qRT-PCR and immunohistochemistry. GSK343 against EZH2 was used for target gene identification in parathyroid cell line (PTHC-1) by using high-throughput mRNA sequencing (Novaseq6000 platform). Then, bioinformatics viz; STRING-cytohubba modules, kyoto encyclopedia of genes and genomics (KEGG) and Reactome was applied to identify EZH2 novel target genes and pathways. RESULTS-We found that EZH2 mRNA expression was significantly high in parathyroid tumors and highest in aggressive parathyroid tumors compared to controls [mean±S.E; (5.7±2.7 and 12.2±2.6 vs 1.0 ±0.3, p=0.005)]. EZH2 mRNA expression is weakly correlated with serum calcium (r=0.24, p=0.0002) and moderately with tumor weight (r=0.61,

p=0.005). Protein expression is also consistent with gene expression having 82% nuclear positivity in aggressive and 40% in parathyroid tumors compared to controls (negative staining). GSK343 treated cells showed inhibition of EZH2 mediated H3K27me3 with nanomolar potency. mRNA sequencing of GSK343 treated vs untreated cells identified ~4000 differential expressed genes (DEGs) using R-package with fold change (≥±1.5, p<0.05). The top upregulated genes are VDR, PTEN, ENO1 with (>5 fold change) and downregulated CDC6 with (-4 fold change). Functional enrichment identifies these top genes in enriched protein-protein networks with high confidence score >0.7 (STRING 12.0 software). Further, cell cycle and MAPK pathway predicted as highly enriched pathways in parathyroid tumors. CONCLUSIONS- We confirms elevated levels of H3K27me3-mediated EZH2 expression in parathyroid tumors, with the highest in aggressive parathyroid tumors. mRNA sequencing following GSK343 treatment identified potential EZH2 target genes (VDR, CDC6, PTEN, ENO1) and pathways (cell cycle, MAPK) with highest fold enrichment those could act as novel therapeutic targets in treatment of parathyroid tumors.

Endocrinology and Metabolism

Langnas E, **Chao S**, **Gomes KM**, and **Bhan A**. TERT Positive Thyroid Nodule in the Setting of Metastatic Melanoma. *J Endocr Soc* 2024; 8:A1089-A1090. Full Text

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Metastatic disease to the thyroid gland is uncommon with a reported incidence of up to 4% in post-surgical specimens. Lung cancer is the most common primary tumor site in autopsy series. Clinically, renal cell carcinoma is the most common primary tumor site. Metastatic melanoma to the thyroid gland is clinically rare, however, in autopsy series, it has been reported with incidence of up to 39%. A 61-year-old man presented to the endocrinology clinic for an incidentally detected thyroid nodule. He had recently presented with a chronic cough, prompting a chest x-ray that revealed pulmonary nodules. Subsequent computed tomography (CT) showed numerous bilateral lung nodules measuring up to 2.5 cm and an incidental thyroid nodule. Ultrasound of the thyroid identified a 2.7 cm mixed cysticsolid right thyroid nodule. No risk factors for thyroid cancer were identified. His TSH was 3.51uIU (0.45 - 5.33 uIU/mL). The thyroid nodule was biopsied, and pathology revealed atypical spindle cells with irregular nuclear membranes and scattered histiocytes. A further review with cytopathology suggested non-thyroidal origin of the cells. Molecular testing with AFIRMA reported a telomerase reverse transcriptase (TERT) promoter mutation at C228T. The sequencing was negative for TERT C250T, BRAF, RET PETC1 PTC3 and MTC. Due to concerns about metastatic disease, a positron-emission tomography (PET)-CT was conducted, revealing hypermetabolic lesions in numerous bilateral lung nodules, right thyroid nodule, porta hepatis lymph node, and a soft tissue nodule within the greater curvature of the gastric body. Subsequent biopsies of the right lung and gastric body confirmed the diagnosis of metastatic melanoma. On further questioning, it was found that the patient had a history of a skin lesion on his back that was excised several years ago with pathology reporting tumoral melanosis. Malignant melanoma has a poor prognosis due to high recurrence and metastatic rates. In melanoma TERT promoter mutations are the most common mutations in noncoding regulatory regions. TERT C228T mutations and C250T mutations are seen in malignant melanoma and studies have shown that TERT promoter mutations are associated with aggressive clinical behavior. These TERT promoter mutations can also be seen in various other cancers including primary thyroid cancers with a similar association with more aggressive thyroid tumor characteristics. Our case describes a patient with a thyroid nodule and molecular testing noting a TERT promoter mutation. Both primary thyroid cancer and metastatic disease to the thyroid should be considered in these cases. This case also highlights the importance of obtaining a thorough history of prior malignancy in patients with thyroid nodules to assess the risk of metastatic disease.

Endocrinology and Metabolism

Manas F, **Costris A**, **Simon R**, and **Bhan A**. Concurrent Thyroid and Lung Nodules: Unveiling Rare Pathways in Malignancy. *Thyroid* 2024; 34:A25-A26. Full Text

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Introduction: Thyroid cancer (TC) is the most common endocrine malignancy. Despite its frequency, distant metastases are seen in only 1% to 4% of patients. However, such metastatic events often carry a grim prognosis, becoming the primary driver of TC-related fatalities. Conversely, metastasis to the thyroid gland is rare, with breast, renal cell and lung being the most common primary sites. While instances of patients having two distinct primary malignancies exist, most cases involving multiple organs originate from a single primary source. This case series highlights patients with co-existing lung and thyroid nodules each exhibiting unique outcomes. Case series: We present three cases involving concurrent thyroid and lung masses. The first case involved bilateral lung nodules seen on CT ordered for evaluation of cough. A thyroid nodule was detected concurrently and an FNA showed atypical cells of undetermined origin. Further molecular testing showed a TERT mutation and concurrently a lung biopsy showed metastatic melanoma with an identical TERT mutation. The second case involved incidentally discovered lung nodules with lymphadenopathy in a non-smoker. Biopsy revealed adenocarcinoma with BRAF V 600 E mutation. PET-CT showed cervical lymphadenopathy and further evaluation revealed multiple thyroid nodules in the US. FNA biopsy of thyroid nodules showed papillary TC without BRAF V 600 E mutation. The third case had thyroid nodules and was diagnosed with papillary thyroid cancer after FNA biopsy. Her CT chest noted multiple bilateral pulmonary nodules with the largest in the left lower lobe. FNA of lung nodules confirmed metastatic PTC. Conclusions: A thorough review of existing literature revealed no consensus regarding the incidence of synchronous lung and thyroid nodules. Instances of TC metastases and a separate primary cancer spreading to the thyroid are both rare phenomena. Moreover, the presence of two distinct primary malignancies is uncommon. Our case series underscores the importance of obtaining proper tissue samples of both lung and thyroid masses identified concurrently to facilitate accurate diagnosis and treatment.

Endocrinology and Metabolism

Manas F, **Davydov E**, **Caines A**, **Estrada K**, and **Shill JE**. A Case Report Of Drug-Induced Liver Injury Secondary To Sublingual Estradiol In A Transgender Woman. *J Endocr Soc* 2024; 8:A532-A533. Full Text

F. Manas, Henry Ford Health System, Detroit, MI, United States

Drug-induced liver injury (DILI), the leading cause of acute liver failure in the United States, occurs in response to a medication or natural compound. Estrogens can lead to idiosyncratic DILI. According to LiverTox [livertox.nih. gov], estrogen has a likelihood score of A (highly likely) to cause DILI, whereas spironolactone has a likelihood score of D (rare). The current formulations of estrogens usually produce a mixed or cholestatic pattern of liver enzyme elevations, however very early, the ALT levels can be markedly elevated (5- to 20-fold). One can be asymptomatic. Often the liver injury resolves after removing the offending agent. We present a case of DILI with elevations of both alanine transferase (ALT) and aspartate transferase (AST), secondary to sublingual estradiol (E2). A 23-year-old transgender female presented for feminizing gender-affirming care. She was started on sublingual E2 2 mg once daily and spironolactone 100 mg orally twice daily. Approximately 14 weeks later, sublingual E2 was increased to 2 mg twice daily for a below-target E2 level, and spironolactone was decreased to 50 mg twice daily due to gas and nausea. Routine blood work three weeks later showed elevated liver function tests (LFTs) in a hepatocellular pattern with ALT of 216 IU/L (normal:<52IU/L), AST of 223 IU/L (normal:<35 IU/L), with normal total bilirubin and alkaline phosphatase. LFTs were normal six months prior. At the time of liver injury, she had consumed six alcoholic beverages in the previous fourteen days, and two doses of acetaminophen. She had no personal history of autoimmunity and no family history of liver disease. Acute hepatitis screen was normal. Abdominal US with liver Doppler was unremarkable. E2 and spironolactone were discontinued. Evaluation by hepatology lead to a diagnosis of DILI from sublingual E2, based on the temporal relationship between initiation of E2 and LFT elevation. Other potential causes of elevated LFTs were excluded. Although she reported alcohol use, the AST/ALT elevation was not in a classic 2:1 pattern. Three weeks after cessation of E2 and spironolactone, her LFTs normalized. Spironolactone was resumed along with E2 by patch, but due to skin-adherence issues she was transitioned to injectable E2 valerate. Her LFTs have remained normal since. This case illustrates a rare but potentially dangerous adverse event of DILI secondary to sublingual E2. Due to the low incidence of liver injury in various studies of individuals with gender incongruence on hormone therapy, current evidence does not support routine liver enzyme monitoring. Clinicians should be aware of the potential risk of liver injury and counsel

patients accordingly. As in this case, patients may be successfully rechallenged with the offending DILI medication. Further studies on different formulations of hormone therapy and their effects on the liver would be beneficial in this unique population.

Endocrinology and Metabolism
Manas F, **Estrada K**, and **Rao SD**. How to Manage Paget's Disease of Bone (PDB) in a Patient with Chronic Kidney Disease (CKD)? *J Bone Miner Res* 2024; 39:196. Full Text

F. Manas, Henry Ford Health System, United States

Introduction: PDB is a skeletal disorder characterized by localized accelerated bone remodeling in specific skeletal locations with abnormal osteoclasts. The usual onset is in the fifth decade of life, with a slight male predominance. Skull, spine, pelvis, and long bones of the lower extremity are the most common sites. Most patients are asymptomatic, and the diagnosis is usually made incidentally on a routine biochemistry showing elevated serum alkaline phosphatase (ALP) or an imaging study showing pagetic changes in bone. The most common clinical manifestation of PBD is pain in the involved bone(s). We report a case of asymptomatic polyostotic-PDB involving wight bearing bones with progressive rise in ALP in the context of CKD. Case Presentation: 64-year-old African American man with history of hypertension, hyperlipidemia, diabetes mellitus, vitamin D deficiency, and CKD-4, was referred for evaluation of PDB, which was discovered by the marked cortical and trabecular thickening of the proximal right femur, pelvic bones, and sacrum, consistent with PBD on X-rays done about ten years ago. There was progressive elevation in ALP from 200s to 700s IU/L (normal 40-140 IU/L) over 7-years. Marker of bone turnover, C-telopeptide was high at 2897 pg/ml (normal 40-840 pg/ml). There is a strong family history of PDB. He denied bone pain, headache, or hearing loss and fractures or kidney stones. Bone scan revealed increased radiotracer uptake involving the right scapula, sternum, spine (involving cervical, mid thoracic, and lumbar), sacrum, pelvis, and both femurs. Discussion: The treatment of PDB is indicated in symptomatic patients and in asymptomatic patients with significant biochemical abnormalities or imaging changes indicating risk of complications from untreated disease. Bisphosphonates are the standard treatment for PDB, but are contraindicated in patients with CKD-4-5. Hence, management of PBD can be challenging in patients with CKD. Denosumab is an appropriate alternative in patients with CKD, but there is insufficient data and clinical experience, and its role in the treatment of PDB remains to be defined.

Endocrinology and Metabolism
Manas F, and **Lahiri S**. Diffuse Parenchymal Micro-calcifications in the Thyroid Gland with or without Thyroid Nodule: Clinical Significance. *Thyroid* 2024; 34:A25. Full Text

F. Manas, Henry Ford Hospital, United States

Introduction: Microcalcifications are sub-centimetric punctate echogenic foci without posterior acoustic shadowing seen in ultrasonography (US). They may represent dystrophic calcification, intravascular tumor thrombi calcifications, or malignant papillae infarction. Fine needle aspiration (FNA) biopsy is warranted if microcalcifications are seen in thyroid nodules, especially in solid hypoechoic nodules. Microcalcifications without nodules can be seen in up to 2% of patients with papillary thyroid cancer (PTC) and have been reported in diffuse sclerosing variant PTC and classical PTC. They are a predictor of thyroid malignancy, even without a clear nodule, and are associated with multifocality, intrathyroidal lymphatic spread, and cervical lymph node metastasis. Description of the Case: A 30-year-old female presented with diffusely enlarged thyroid and finding of snowstorm appearance on US of the thyroid. She has a family history of Graves' disease. Her TSH was 2.49 (0.45-5.33uIU/mL) and thyroid peroxidase antibody was 21 (<9IU/mL). US of the neck revealed a heterogeneous nonenlarged thyroid gland with diffuse hyperemia and numerous punctate echoes. A discrete nodule was not visualized. Several lymph nodes with punctate echoes were seen around the right thyroid lobe. CT neck showed a 1.8 x 1.1 cm heterogeneous nodule with a large dystrophic calcification in the right thyroid lobe and several abnormal-appearing right level 2 to 4 lymph nodes. FNA of the dominant right neck lymph node was positive for PTC. Thyroglobulin in the washout from the lymph node FNA was 63,843 ng/mL. She underwent total thyroidectomy with central and right lateral neck dissection. Pathology revealed 1.8 cm conventional type

PTC in the right thyroid lobe, papillary thyroid microcarcinomas diffusely involving both thyroid lobes (greater than 20 foci), all welldifferentiated with papillary and follicular growth patterns, and 26 out of 74 regional lymph nodes with PTC (largest 1.8 cm). Chronic lymphocytic thyroiditis was also seen. Discussion: Diffuse microcalcifications in the thyroid gland, even without a clearly delineated thyroid nodule is an indicator of thyroid malignancy and can predict cervical lymph node metastasis. Current guidelines do not specifically address how to manage this sonographic finding. Further evaluation to assess cervical lymph nodes is warranted if diffuse parenchymal microcalcifications are seen on ultrasound.

Endocrinology and Metabolism

Manas F, **Nakdali R**, **Almajali DA**, **Bhan A**, and **Simon R**. Exploring the Clinical Landscape of Papillary Thyroid Microcarcinoma with Lymph Node Metastasis: A Single-Institution Case Series and Implications for Treatment Decisions. *J Endocr Soc* 2024; 8:A1024-A1025. Full Text

F. Manas, Henry Ford Hospital, Detroit, MI, United States

Introduction: Papillary thyroid microcarcinomas (PTMC) refer to papillary thyroid carcinomas with primary tumor size ≤ 1cm. Characterized by their indolent nature, PTMCs boast a mortality rate of less than 1%. Loco-regional spread occurs in approximately 2-6% of cases, while distant metastasis is observed in about 1-2%. Notably, the rate of recurrence after lymph node (LN) metastasis can reach up to 20%. The optimal management of PTMC remains controversial with some studies suggesting no discernible difference in clinical outcomes between patients undergoing active surveillance and those opting for surgical removal. There is limited research on thyroid cancer oncogenes that can predict the progression of PTMC outside of the thyroid gland. We report the clinical outcomes of a series of patients with PTMC who presented with LN metastasis at our institution.Case Series: We describe five patients diagnosed with papillary thyroid microcarcinoma with LN metastasis. All patients presented with a neck mass and evaluation by fine needle aspiration (FNA), showed papillary thyroid cancer. The tumor sizes ranged from 0.15 cm to 1 cm and all cases had extensive LN involvement, with sizes ranging from 0.7 to 4.5 cm. All patients received adjuvant RAI according to ATA guidelines. Molecular testing was not available for any of these patients.Discussion: Our case series offers valuable insight into the clinical outcomes of individuals with PTMC who underwent total thyroidectomy with LN dissection. We postulate that there are two separate groups of patients with PTMC. One group with indolent disease, which lends itself to careful follow-up, even without surgery, and the other group with aggressive disease at presentation. The challenge lies in the correct classification of the patient at baseline so that therapy is tailored to the type of cancer. We need better predictors of disease severity so that patients can be risk-stratified appropriately. The absence of clear guidelines regarding the optimal extent of surgery for PTMC adds complexity to treatment decisions. Nevertheless, our case series sheds light on the infrequent occurrence of PTMC with LN metastasis. It is noteworthy that despite the absence of a mutational profile for these patients, consistent with prior small-scale studies, no genetic alterations have been identified as reliable predictors of LN metastasis in PTMC. Our findings underscore the imperative for further investigative studies to enhance our ability to predict more aggressive cases of PTMC. By addressing the gap in knowledge, future research endeavors may contribute to the refinement of treatment strategies for individuals with PTMC.

Endocrinology and Metabolism

Nakdali R, and **Athimulam S**. Leydig Cell Tumor: A Rare Cause of Post-menopausal Hyperandrogenism. *J Endocr Soc* 2024; 8:A851. Full Text

R. Nakdali, Henry Ford Health, Detroit, MI, United States

Introduction: Ovarian steroid cell tumors are a rare subtype of sex-cord stromal tumors. Leydig cell tumors is a subtype of sex-stromal tumors that is found in < 1% of all ovarian tumors. They are typically benign, unilateral, and secrete androgens which causes virilization. Below we present the case of a postmenopausal woman who presented with signs of virilization and was diagnosed with an ovarian Leydig cell tumor. Case: A 62-year-old postmenopausal woman, with a history of partial hysterectomy with right oophorectomy presented to Endocrinology clinic for evaluation of thyroid nodules. However,

clinically she had signs of virilization noted by the provider on examination. She reported progressive androgenic alopecia, cystic acne, oily skin, hoarseness of voice and hirsutism, with increase hair growth over upper lip, chin and jaw line requiring daily shaving. She denied taking any supplements. She reported embarrassment of these physical changes and prior providers had attributed this to aging, therefore not prompting further testing. This caused significant emotional distress to the patient, leading to isolation. Biochemical testing confirmed elevated bioavailable testosterone (193.1 ng/dL) and total testosterone levels (579 ng/dL), with no evidence of hypercortisolemia. Magnetic resonance imaging (MRI) revealed a heterogenous soft tissue mass (2.9 x 2.1 x 2.1 cm) in the left ovary. She underwent a left salpingo-oophorectomy and pathology confirmed a welldifferentiated 2.4 cm Leydig cell tumor. Post-operatively, she reported improvement in facial and body hirsutism, reduced shaving frequency decrease in androgenic hair loss, with noticeable hair growth in her frontal scalp, and her skin became less oily with reduced acne. Post-operative labs confirmed cure of hyperandrogenism (Bioavailable testosterone < 2.6 ng/dL; Total testosterone: < 10ng/dL; and Free androgen index < 0.5%). She has been referred to genetics for evaluation. Discussion: Post-menopausal hyperandrogenism poses a diagnostic challenge as it can be mistaken for hormonal imbalances seen with aging. Often times, patients do not report symptoms due to embarrassment unless specifically addressed by provider. Initial testing consists of total and free testosterone and dehydroepiandrosterone sulfate (DHEAS) levels to assess the source of hyperandrogenism. Ruling out hypercortisolemia and assessment for ingestion of testosterone or DHEA supplements is vital. Pelvic ultrasound or cross-sectional imaging (CT or MRI) of abdomen and pelvis can identify structural abnormalities in the ovaries or adrenal glands. Prompt evaluation and management can alleviate significant distress to the patient. Leydig cell tumors represent a rare but important consideration in the differential diagnosis of postmenopausal hyperandrogenism, such as in our patient.

Endocrinology and Metabolism

Nakdali R, **Faber A**, and **Simon R**. From Chronic Inflammation to Metastatic Challenge: A Complex Intersection of Hidradenitis Suppurativa, Hypercalcemia, and Squamous Cell Carcinoma. *J Bone Miner Res* 2024; 39:80. Full Text

R. Nakdali, Henry Ford Hospital, United States

Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition that impacts hair follicles and often involves apocrine-rich, intertriginous skin regions. HS presents with relapsing, recurrent inflamed skin lesions that develop into draining abscesses, fibrosis, and disfiguration. Squamous cell carcinoma occurs in 4.6% of HS. Hypercalcemia associated with cutaneous carcinomas is rare in association with HS. We report a patient with parathyroid hormone-related protein (PTH-RP) driven hypercalcemia and squamous cell carcinoma arising from HS. A 66-year-old male presented to the hospital with decreased oral intake and confusion. His medical history was significant for atrial fibrillation and HS of the groin and perineum complicated by previous admissions for sepsis. He was admitted one month prior for sepsis due to an HS flare where he was incidentally noted to have new-onset hypercalcemia of 13.1 mg/dL. He was treated with IV fluids, calcitonin, and Zoledronic acid. The etiology of his hypercalcemia was not evaluated at that time. Workup this admission revealed leukocytosis of 40.8 k/UL, hypercalcemia of 15.1 mg/dL, ionized calcium of 1.94 mmol/L, low PTH of 2.0 pg/mL, elevated PTH-RP of 27 pg/mL, normal vitamin D and angiotensin converting enzyme. CT of the abdomen revealed irregular thickened skin with soft tissue gas within the perineum, scrotum and gluteal soft tissue, concerning for Fournier's gangrene. CT of the chest showed diffuse metastatic disease involving the right sixth and tenth ribs, para-aortic lymph nodes, pulmonary nodules, and likely malignant bilateral pleural effusions with incidental pulmonary emboli. He was admitted to ICU with septic shock and promptly started on broad spectrum antibiotics. Dermatology was concerned for potential transformation of his known HS into metastatic squamous cell carcinoma (SCC). This was confirmed on biopsy of perineal skin which revealed moderately to well-differentiated squamous cell carcinoma. His hypercalcemia was managed with IV fluids and Zoledronic acid. Unfortunately, the patient passed due to cardiac arrest one month later. This case demonstrates the significance of early recognition of hypercalcemia as a potential harbinger of cancer and the importance of considering transformation of chronic skin conditions into SCC in the setting of newly diagnosed hypercalcemia. In this case, humoral hypercalcemia of malignancy due to PTH-RP production from transformed HS into metastatic SCC was identified.

Endocrinology and Metabolism

Rothstein Costris A, **Davydov E**, and **Levy S**. Rare Case of Hyperparathyroidism in Third Trimester Pregnancy Requiring Urgent Parathyroidectomy. *J Endocr Soc* 2024; 8:A257-A258. Full Text

A. Rothstein Costris, Henry Ford Hospital, Detroit, MI, United States

Introduction: Primary hyperparathyroidism (PHPT) during pregnancy has risks to both the mother and her fetus. Complications include maternal pre-eclampsia, miscarriage, hyperemesis gravidarum, nephrolithiasis and pancreatitis. Fetal complications encompass hypocalcemia, tetany, intrauterine growth retardation and fetal demise. Though medical treatment is available, parathyroidectomy is the only definitive treatment. Traditionally, surgery is done in the second trimester of pregnancy. We report a case of a third trimester parathyroidectomy in a 29 yo female with PHPT. Case representation: A 29-year-old G1P0 woman at 28 weeks gestation presented with persistent nausea and vomiting, constipation, joint pain, and increased forgetfulness. She has moved to USA from Saudi Arabia and had not received prenatal care in the USA. She was found to have a PTH of 224 (15-65 pg/mL), Calcium of 13.5 (8.2-10.2 mg/dL), Ionized Calcium of 1.63 (1.00-1.35 mmol/L), and a corrected Calcium of 14.2 (8.7-10.1 mg/dL). Electrolyte abnormalities were also noticed, with a Potassium of 2.8 (3.5-5 mmol/L), Phosphorus of 1.7 (2.5-4.5 mg/dL) and Magnesium of 1.2 (1.8-2.3 mg/ dL). Vit. D levels were found to be extremely low <7 (20-40 ng/mL). Due to severe dehydration, persistent nausea, vomiting, and hypercalcemia, the patient received fluid resuscitation and Vit. D supplementation. A neck CT scan identified an 11 x 6 x 14 mm arterially hyperenhancing soft tissue structure at T1-T2, suggesting a probable parathyroid adenoma in the right paratracheal region. Management options included surgery or conservative therapy with fluids and Cinacalcet. A joint decision was made between Maternal Fetal Medicine, ENT and Endocrinology to proceed with parathyroidectomy. Surgical excision revealed an enlarged, hypercellular right inferior parathyroid gland (0.51g). Postoperative laboratory studies at 2 weeks showed normal PTH, Ca, Ionized Ca. Conclusion: It is preferable to conduct surgery for PHPT during the second trimester of pregnancy. However, when PHPT leads to severe symptoms, surgery might be considered in the third trimester. The severity of our patient's symptoms led to inability to tolerate oral intake, deeming surgery necessary. The multidisciplinary team agreed that surgery in the third trimester would be the best course of treatment as it will result in normocalcemia immediately. Second trimester parathyroidectomy is viewed as safer due to the completion of organogenesis and lower teratogenicity risks. Performance of surgery during the third trimester may lead to an increase in the risk of premature birth. However, untreated hypercalcemia may increase fetal loss and thus third trimester parathyroidectomy can be considered as a treatment option for PHPT in pregnancy. It is also imperative to discuss all options with the patient. In our case, the patient had opted for surgery which was successful.

Endocrinology and Metabolism

Rothstein Costris A, **Yaseen A**, and **Levy S**. A Case of Severe Myxedema Coma with Levothyroxine Allergy. *J Endocr Soc* 2024; 8:A970. Full Text

A. Rothstein Costris, Henry Ford Hospital, Detroit, MI, United States

Introduction: Myxedema coma is a life threatening condition with a mortality rate of 25-60%. Untreated, it can lead to fatal physiological changes. The treatment is thyroid hormone replacement therapy, alongside supportive care for complications. Clinical Case: A 65-year-old woman, who has been dealing with untreated hypothyroidism since 2012 and reported allergies to various levothyroxine brands, presented with falls, weakness, and exacerbated leg numbness. During the examination, she exhibited periorbital edema, non-pitting edema in the lower extremities, bradycardia, and hypothermia. The blood work revealed an elevation in TSH levels at 301 uIU/L (0.45-5.33 uIU/mL). The patient was administered IV Synthroid (200 mcg), Atropine, and Hydrocortisone due to concerns about myxedema coma. After four hours, the patient experienced angioedema and hypotension, necessitating intubation. This situation was complicated by a pulseless electrical activity (PEA) arrest. Following cardiopulmonary resuscitation and the administration of epinephrine, the patient achieved return of spontaneous circulation. The allergy team assessed the patient for potential anaphylactic shock from IV Synthroid. Subsequently, the patient was initiated onIV Liothyronine and Hydrocortisone, leading to improvement in mental status over a period of a few weeks, and no adverse effects were reported. Thyroid labs improved to TSH of 53 (0.45-

5.33 uIU/mL), FT3 of 3.3 (2.5-4.4 pg/mL) and total T3 of 133 (87-178 ng/dl). Upon discharge, the patient was prescribed Liothyronine, with plans to perform a Levothyroxine desensitization test in the outpatient setting. Conclusion: Myxedema coma is an endocrine emergency. Patients usually present with deteriorating mental status, hypothermia, and multiple organ system abnormalities. The diagnosis relies more on the clinical presentation and physical examination than on laboratory results. Thyroid replacement therapy serves as the cornerstone of treatment, with a preference for T4 due to its greater availability and lower likelihood of adverse events compared to Liothyronine, which may increase the risk of mortality at higher doses. Despite associated risks, incorporating low doses of Liothyronine is still considered in treatment plans, driven by concerns about reduced T4 to T3 conversion in myxedema patients. Hypersensitivity reactions to Levothyroxine are uncommon but may manifest as widespread hives, swelling, eczema-like skin rashes, elevated body temperature, and compromised liver function, with only one case reporting an anaphylactic reaction to Levothyroxine. In summary, the potential for experiencing an anaphylactic reaction to Levothyroxine exists, highlighting the need to contemplate alternative treatments, such as Liothyronine. Desensitization methods can be considered once the patient's condition is stable.

Endocrinology and Metabolism
Subramani R, Zahra S, and **Manas F**. Graves' Wrath on the Heart: A Focus on Pericardial Effusion. *J Endocr Soc* 2024; 8:A311-A312. Full Text

R. Subramani, Robert Packer Hospital, Sayre, PA, United States

Introduction: Hyperthyroidism, marked by an overproduction of thyroid hormones, is linked to various cardiovascular issues like high or normal output heart failure, arrhythmias, and tachycardia-related cardiomyopathy. Pericardial effusion is less common in hyperthyroidism compared to hypothyroidism. Here we report a 20 year old with pericardial effusion, later diagnosed with Grave's disease. Case Summary: A20-year-old female with a past medical history of anxiety, depression, and seizure disorder presented to the emergency department with chief complaints of dizziness, shortness of breath, palpitations, and chest pain. She complained of tremors, generalized weakness, and weight loss for the last two months. She denied any personal or family history of hypo- or hyper-thyroidism. No history of head or neck irradiation, anterior neck tenderness or pain, dysphagia or hoarseness. No history of recent viral infection. Examination revealed tachycardia with thyromegaly and pericardial friction rub but there was no neck tenderness, exophthalmos or lid lag. Blood work was remarkable for low TSH (<0.02 uIu/ml, normal: 0.27-4.2 uIu/ml) and elevated free T4 (>7.7nd/dl, normal:0.9-1.7ng/ dl) and total T3 (>651 ng/dl, normal 80-200 ng/dl). Rest of the blood work, including blood cultures and immunologic workup (antinuclear antibody, anti-neutrophil cytoplasmic antibody, and rheumatoid factor) was negative. EKG showed sinus tachycardia. CT chest confirmed thyromegaly and showed pericardial effusion. Ultrasound neck showed enlarged heterogeneous thyroid gland with relative increased vascularity. Echocardiography showed mild to moderate pericardial effusion with no tamponade physiology and normal ejection fraction. Anti thyroid peroxidase antibodies, thyroid stimulating immunoglobulin, and TSH receptor antibodies were markedly elevated. The patient was diagnosed with Grave's thyrotoxicosis with thyromegaly and pericardial effusion. Endocrinology was consulted and the patient was started on beta blockers for symptom control and anti-thyroid medication (methimazole). Discussion: Fabowale MO et al highlighted the potential role of immunological mechanisms in causing pericardial effusion, while Fonseca et al focused on pathophysiological changes involving both extravascular and intravascular proteins, coupled with reduced lymphatic drainage. Cardiac complications in Graves' disease tend to occur more frequently when the condition has been poorly managed for an extended period before seeking medical help. If symptoms persist despite achieving proper control, clinicians need to be watchful for potential cardiac complications.

Endocrinology and Metabolism
Taleb M, **Stephan J**, **Vo T**, and **Estrada K**. A Delayed Diagnosis of Diabetic Myonecrosis: Case Report. *J Endocr Soc* 2024; 8:A341. Full Text

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Background: Diabetic myonecrosis, also termed diabetic muscle infarction, isa raremicrovascular complicationofdiabetes mellitus (DM). Although it can manifest in patients with all types of DM, it is more common in type 1 DM. It presents with pain and swelling localized in a muscle group and is associated with significant morbidity. The most commonly affected area is the anterior thigh, followed by the posterior thigh or calf. Clinical Case: A 34-year-old woman presented with two months of left thigh pain and swelling. She had a history of long-standing type 1 DM complicated by end-stage kidney disease for which she had been initiated on peritoneal dialysis (PD) six months prior to presentation. Her localized symptoms started after a fall and persisted since then. Our patient's initial workup showed an elevated CPK level of 1340 IU/L (normal <178 IU/L), and limb radiographs were negative for fracture or dislocation. Her symptoms were attributed to musculoskeletal pain. She subsequently presented to the emergency departments multiple times with the same symptoms. On one presentation, she was diagnosed with nontraumatic rhabdomyolysis in the setting of hematuria and persistent left thigh pain. On another presentation, CT of the left femur was done and showed skin thickening, subcutaneous fat stranding, and edema without osseous abnormalities; she was diagnosed with complex regionalpainsyndrome (CRPS)anddischarged home on gabapentin, which did not improve her symptoms. Ultimately, she was admitted to the hospital with the inability to ambulate due to her persistent and severe symptoms. MRI of the left hip and femur showed signs of diffusemyositis and areas of myonecrosis consistent with diabeticmyonecrosis. Prior to initiation of PD, our patient's HbA1c had been well controlled at the target of <7%.Due to the high dextrose content in dialysate, she had an increase in her HbA1c to 9.0% within a span of three months despite no changes in her medications or diet. Once the diagnosis was established, aspirin was initiated and insulin regimen was adjusted for tighter glucose control. Two weeks after treatment our patient had resolution of her symptoms.Conclusion:We highlight a case of diabetic myonecrosis, a complication of DM, that can bemissed due to its rarity and nonspecific presentation. Index of suspicion should be high in patients with persistent unexplained musculoskeletal symptoms. Despite MRI being the diagnostic modality of choice, obtaining it was delayed due to multiple factors including initial radiologic findings negative for acute fractures and previous misdiagnosis of rhabdomyolysis and CRPS. Management of diabetic myonecrosis is centered around tight glycemic control. This highlights the importance of close monitoring of glycemic control when initiating a patient with diabetes mellitus on PD, given the constituents of the dialysate used, to prevent complications of diabetes.

Endocrinology and Metabolism

Yeni YN, **Oravec D**, **Yadav R**, **Drost J**, **Flynn M**, **Divine G**, and **Rao SD**. Textural and geometric measures derived from digital tomosynthesis discriminate patients with vertebral fracture from those without. *J Bone Miner Res* 2024; 39:152. Full Text

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Digital tomosynthesis (DTS) is a limited-angle tomographic imaging modality providing a stack image of an object at high resolution and low radiation exposure. The purpose of this study was to examine the extent to which DTS derived textural and geometric properties of vertebrae discriminate patients with and without vertebral fracture. Under IRB approval, 93 postmenopausal women (age ≥ 50 years) with no history of bone disease other than osteoporosis were enrolled. The patients with vertebral fracture (Fx, N = 39) and those without (NFx, N = 54) were not different in age (65 ± 8 vs 64 ± 7 years; p > 0.2), BMI (25.1 ± 3.3 vs 25.1 ± 3.7 kg/m2; p > 0.9) or race distribution (9\30 vs 8\46 Black\Nonblack; p > 0.3). Lumbar spine bone mineral density (BMD) and trabecular bone score (TBS) were measured, and vertebral fracture assessment was performed from DXA scans. DTS of the spine was performed using a clinical system (Sonialvision Safire II, Shimadzu Inc) with the participant in supine position and central X-ray tube fixed at the T12-L1 level. DTS images were reconstructed with a voxel spacing of 0.28 x 0.28 x 1 mm. Fractal dimension (FD, a measure of texture complexity) and lacunarity (λ, a measure of texture heterogeneity) were calculated for cancellous bone using FracLac and ImageJ software. Mean intercept length (MIL, a measure of feature size) and line fraction deviation (LFD, a measure of orientation) were measured and degree of anisotropy (DA) was calculated (maximum MIL/minimum MIL). In addition, vertebral width was calculated at the narrowest section of the mid-vertebra using coronal images. DTS values for fractured T12 and L1 vertebrae were imputed from unfractured levels using a mixed model regression of each DTS variable by vertebral level from a superset of 131 patients with no fracture. DTS

measurements of the T12 and L1 vertebrae were averaged for each subject. Differences between groups were assessed using t-tests or Wilcoxon tests based on data normality. Logistic regression models were constructed to examine the extent to which DTS predicts vertebral fracture status. BMD and TBS were higher, while DA and width were lower, in NFx than Fx ($p < 0.02$ to $p < 0.003$). Multiple logistic regression identified BMD, FD, λ, DA and width as significant predictors ($p < 0.02$ to $p < 0.001$) with AUC of ROC = 0.79 (compared to 0.67 for BMD alone) (Figure). These results support complementary use of DTS in assessment of bone quality and potentially of fracture risk.

Endocrinology and Metabolism

Yu K, **Athimulam S**, Saini J, Kaur R, Singh JRJ, Grebe KSK, Xue Q, and Bancos I. Serum Steroid Profiling For The Diagnosis Of Adrenocortical Carcinoma: A Prospective Cross-Sectional Study From A Tertiary Center. *J Endocr Soc* 2024; 8:A155. Full Text

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Context: Early diagnosis is essential to assure a better prognosis in patients with adrenocortical carcinoma (ACC). Guidelines suggested performing urine steroid profiling in patients with indeterminate adrenal tumors to make a noninvasive diagnosis of ACC. However, urine steroid profiling is notwidely available. Accuracy of clinically available serum steroids in diagnosing ACC has not been established. Objective: To determine the accuracy of 11-deoxycortisol, 17OH-progesterone, and 17OH-pregnenolone in diagnosing ACC. Design: Prospective single-center cohort study. Participants: Between 2015 and 2023, consecutive patients with adrenal mass were prospectively enrolled in the prospective registry and biobank study. Patients who agreed to contribute a fasting serumsamplewere included inthestudy. Exclusion criteria were congenital adrenal hyperplasia, exogenous glucocorticoid use, absence of unenhanced Hounsfield unitmeasurements (HU), and lack of established reference standard (histopathology, imaging characteristics, 2-year imaging follow up, or 5-year clinical follow up). Measures and Outcomes: measurements included 11-deoxycortisol, 17OH-progesterone, and 17OH-pregnenolone by liquid chromatography-mass spectrometry. Localized Generalized Matrix Learning Vector Quantization(LGMLVQ) analysiswasused todevelop serum steroid scoreand assessedwithareaunder receiver operating curve (AUROC). Results: Of 263 patients with adrenal masses, 44 (17%) were diagnosed with ACC, 161 (61%) with adrenocortical adenomas (ACAs), 27 (10%) with other adrenal malignancies, and 31 (12%) with other. HU ≥ 20 were demonstrated in allACCs, in all but one other adrenalmalignancy, and only in 58 (31%) ACAs. All 3 steroids were higher in patients with ACCs vs nonACCs, including when comparing ACCs with functioning ACAs, and with ACAs withHU ≥ 20 ($P<0.0001$ for all). LGMLVQ analysis yielded a serum steroid score that discriminated between ACC and non-ACC groups with a mean threshold fixed AUROC of 0.823. Serumsteroid score of 0.29 demonstrated amean false negative rate of 0% and a score of 0.61 demonstrated amean false positive rate of 0%. Conclusions: We showed that measurements of 11-deoxycortisol, 17OH-progesterone, and 17OH-pregnenolone could be valuable in diagnosing ACC. After appropriate validation, serumsteroid score could be integrated in clinical practice.

Endocrinology and Metabolism

Zahra S, Subramani R, Abbas M, Hasan KY, **Manas F**, and Bajracharya C. Breathless Struggle: Unraveling The Interplay Between DKA And Acute Respiratory Distress Syndrome. *J Endocr Soc* 2024; 8:A363-A364. Full Text

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Introduction: Diabetic Ketoacidosis (DKA) is a life threatening emergency with mortality rate of 0.15%-0.30%. Acute Respiratory Distress Syndrome (ARDS) is a rare complication of DKA which presents as a sudden onset of dyspnea and progressive hypoxia. It is an inflammatory process that damages the alveolar-capillary membrane leading to the fluid leakage into the alveolar space. The incidence of ARDS in DKA remains unknown. It is more commonly seen in adolescents and young adults. The exact pathogenesis of ARDS in DKA is currently unknown. Some proposed mechanisms are that a severe metabolic acidosis in DKA along with increased cytokines production due to long standing hyperglycemia leads to increased capillary membrane permeability allowing fluid to accumulate in the alveolar space.

TNF-a and IL-6 along with other pro-inflammatory cytokines are known to cause endothelial damage and increase pulmonary permeability leading to pulmonary edema. However most DKA patients with severe metabolic acidosis do not develop ARDS. Case Presentation:Case 1: A 19 year old male with uncontrolled type I diabetes mellitus presented with altered mental status. On examination, he was tachycardic and tachypneic with dry mucous membranes. Lab workup revealed leukocytosis, severe hyperglycemia, and severe anion gap metabolic acidosis with beta hydroxybutyrate level of 14.20 mmol/L (normal: 0.02-0.27 mmol/L). He was diagnosed with DKA and started on intravenous fluids, and insulin as per institutional DKA protocol. Approximately 12 hours post-admission, the patient experienced sudden-onset dyspnea with deteriorating hypoxia, necessitating emergent intubation and mechanical ventilation. Chest radiography displayed bilateral patchy ground-glass opacifications consistent with acute respiratory distress syndrome (ARDS). Despite the administration of 8 liters of intravenous fluids, the patient exhibited a negative net fluid balance of 2.3 liters, implicating fluid shift. Further investigations, including bronchoscopy and bronchoalveolar lavage, revealed an unobstructed airway, minimal secretions, and no evidence of hemorrhage or infection. Comprehensive infectious work-ups yielded negative results as well, reinforcing the diagnosis of DKA as the underlying cause of ARDS. Conclusion: Acute Respiratory Distress Syndrome is a rare but potentially fatal complication of Diabetic Ketoacidosis. Early recognition of this serious pulmonary complication of DKA and its prompt management is essential to prevent respiratory failure and mortality.

Gastroenterology

Abusuliman M, Abusuliman A, Aboeldahb M, Salem A, Meribout S, Mohamed I, Ibrahim AM, **Nimri F**, **Sheqwara J**, and **Jafri SM**. A Rare Case of T-cell Post-Transplant Lymphoproliferative Disorder (PTLD) Found Following a Diagnosis of Hemophagocytic Lymphohistiocytosis in a Patient With History of Liver Transplantation. *Am J Gastroenterol* 2024; 119(10):S2813. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Post-Transplant Lymphoproliferative Disorder (PTLD) encompasses various lymphoid proliferative disorders arising after hematopoietic or solid organ transplantation and ranging from polyclonal lesions to lymphomas. It mostly arises from B-cell origin and is linked to Ebstein-Barr Virus (EBV) in the setting of post-transplant immunosuppression. T-cell PTLD is rare, and its association with EBV is even rarer. We herein report a rare case of T-cell PTLD complicated by Hemophagocytic Lymphohistiocytosis (HLH) in a patient with history of liver transplant Case Description/Methods: A 43-year-old patient with history of alcoholic cirrhosis status post liver transplant presented with progressive bilateral lower limb weakness a year after transplant. A magnetic resonance imaging (MRI) of the spine showed cauda equina enhancements. Lumbar puncture showed inflammation and was positive for EBV. She was started on ganciclovir and bortezomib, but developed fever and pleural effusion; thoracentesis revealed exudate positive for Streptococci. Despite placement of chest tube and completion of antibiotic course, she continued to have febrile episodes with negative infectious workup except for EBV viremia. She had hemophagocytosis on bone marrow biopsy, and splenomegaly on computed tomography (CT), meeting the criteria for HLH. Her liver enzymes were elevated and CT of the liver showed bilateral multiple rounded lobular hypo-attenuating collections, the largest measuring 17 mm (Figure 1). She underwent a liver biopsy which showed EBV-positive monomorphic T-cell lymphoproliferative disorder, consistent with peripheral T-cell Lymphoma, not otherwise specified. The patient was started on CHEOP (cyclophosphamide, doxorubicin, etoposide, vincristine and prednisone) Her course was complicated with pancytopenia and recurrent attacks of fever. She eventually passed away 2 months later from septic shock Discussion: PTLD is a rare complication post solid organ transplant that is related to immune suppression. It is classically EBV related, B cell lymphoproliferation. The incidence of PTLD is higher post cardiac lung or multi organ transplant because of the higher doses of immune suppressants needed in these cases, with only 5-11% occur following liver transplant. Peripheral T-cell lymphoma is a rare PTLD subtype that is rarely associated with EBV. Vigilance post transplant is key to recognize these rare cases and guide the treatment strategy, which is usually directed towards reducing immune suppression and chemotherapy.

Gastroenterology
Abusuliman M, Abusuliman A, **Jamali T**, **Nimri F**, **Malick AN**, Salem A, Meribout S, and **Elatrache M**. A Rare Case of Carney-Stratakis Syndrome With a Large Gastrointestinal Stromal Tumor (GIST) Masquerading as a Pancreatic Mass. *Am J Gastroenterol* 2024; 119(10):S2629-S2630. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Carney-Stratakis syndrome (CSS), a rare familial syndrome of paraganglioma and gastrointestinal stromal tumor (GIST), is attributable to germline mutations in the succinate dehydrogenase genes SDHB, SDHC, and SDHD genes. It is a morbid disease with distinct clinical presentations and genetic heterogeneity that can contribute to underdiagnosis. We present a distinctive case of CSS in a 39-yearold woman. Case Description/Methods: A 39-year-old woman presented with worsening epigastric pain, loose clay-colored stool, early satiety and bloating. She had a history of endometriosis with excision of abdominal wall endometriosis and excision of a left paraganglioma. She has family history of paraganglioma, genetic testing performed on the patient during that time showed heterozygous c.136C .T (p.Arg46X) disease associated sequence variant in the SDHB gene which is associated with hereditary paraganglioma. Abdominal computed tomography (Figure 1) showed a large solid and cystic mass spanning along the entire length of the pancreas, extending to the left upper quadrant with mass effect on the greater curvature of the stomach, spleen, and splenoportal confluence; measuring 16.8 x 7.1 x 7.2 cm. Magnetic resonance of the abdomen showed a large heterogeneous mass within the lesser sac abutting the pancreatic neck measuring 12.1 x 8.6 x 8.0 cm. Urine and plasma metanephrines were within normal limit. Patient underwent Endoscopic Ultrasound-guided fine needle biopsy (EUS-FNB) of the lesion with a 22 gauge Franseen-tip needle. Morphology and immunoprofile of the sample were compatible with GIST, epithelioid variant. Staining and molecular analysis for SDHB showed partially loss nuclear stain. Considering the patient's known history of paraganglioma, she was diagnosed with CSS. Because the tumor was very extensive and not surgically resectable, treatment with Sunitinib was initiated. She was seen 2 months later with good general condition, with intermittent abdominal pain controlled with Ibuprofen. Genetic counselling for her 3 children was recommended. Discussion: CSS is a rare hereditary syndrome with a 50% risk of transmission to the offspring. GIST is integral to CSS diagnosis. While most GISTs arise from a mutation in KIT or platelet-derived growth factor receptor alpha, about 7.5% of GISTs involve SDH gene mutations, including those arising as part of CSS. In this case, EUS-guided FNB of the lesion provided a definitive diagnosis, benefiting both the patient and descendants who might share the condition. (Figure Presented).

Gastroenterology
Abusuliman M, Abusuliman A, **Rehman S**, Abosheaishaa H, Salem A, Elfert K, **Saleem A**, **Alomari A**, Meribout S, Ibrahim AM, and **Jafri SM**. Correlation Between Transient Elastography and Liver Biopsy in MASLD. *Am J Gastroenterol* 2024; 119(10):S1329-S1330. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: The escalating prevalence of metabolic syndrome has led to a parallel rise in NAFLD, thus identifying worsening fibrosis is crucial. Liver biopsy, though the gold standard, is invasive and prone to sampling error. Serologic markers and imaging modalities have limitations in distinguishing MASLD from MASH. Transient Elastography detects hepatic fibrosis effectively. Developing non-invasive methods to distinguish MASLD from MASH is crucial for disease monitoring. Our study aimed to evaluate the concordance of Fibroscan (transient elastography) in predicting degree of fibrosis when compared to Liver Biopsy in patients suspected of having MASLD. Methods: We evaluated patients with metabolic liver disease presenting to a single tertiary center between 2015 and 2020 who underwent confirmatory liver biopsy to assess diagnosis and degree of fibrosis. Baseline characteristics and procedural data were collected. Results: Forty-five patients were included in the study, Baseline characteristics are shown in Table 1. The Spearman correlation coefficient for the association between the estimate of fibrosis on liver biopsy versus the estimate of fibrosis on Fibroscan was 0.249 (P5 0.032), indicating a strong positive monotonic relationship between the 2 variables. The Spearman correlation coefficient for the association between the estimate of fibrosis on liver biopsy versus the estimate of fibrosis on Fib-4. was 0.341 (P = 0.004). The Spearman correlation coefficient for the association between the estimate of fibrosis on liver

biopsy versus the estimate of fibrosis on MASLD fibrosis score was 0.400 (P5 0.014). For F0-1, 94% of patients had the same degree of fibrosis on Fibroscan and liver biopsy, 6% had higher degrees of fibrosis on liver biopsy. There were 89% of patients with F2 had the same degree of fibrosis on Fibroscan and liver biopsy, 11% had higher degrees of fibrosis on liver biopsy. Eighty-seven percent of patients with F3 had the same degree of fibrosis on Fibroscan and liver biopsy, 13% had higher degrees of fibrosis on liver biopsy. For F4 100% of patients had the same degree of fibrosis on Fibroscan and liver biopsy. Conclusion: Fibroscan, Fib-4, and MASLD fibrosis score are all valuable methods to accurately estimate fibrosis in patients with MASLD with results comparable to liver biopsy. Fibroscan is a safe, non-invasive, and accurate method for predicting the degree of fibrosis compared to Liver Biopsy in patients suspected of having MASLD.

Gastroenterology
Abusuliman M, Abusuliman A, **Rehman S**, Salem A, Abosheaishaa H, Mohamed I, Aboeldahb M, Ibrahim AM, and **Jafri SM**. Pregnancy Outcomes Following Triple Organ (Small Bowel, Liver, and Pancreas) Transplantation. *Am J Gastroenterol* 2024; 119(10):S3043-S3044. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Compared to other solid organ transplants, intestinal transplant is relatively novel, and occurrences of successful pregnancies following this procedure are considerably less common. Literature shows only 10 documented cases of successful pregnancy after intestinal transplantation, and to date, only 1 of which was a triple organ (intestine, liver, pancreas) transplant.We present an extremely rare case of successful pregnancy post triple gastrointestinal organ transplant. Case Description/Methods: 20-year-old, 31-week-pregnant woman was evaluated by our Hepatology team for elevated liver enzymes on routine checkup. The patient had a history of small bowel, liver, and pancreas transplant at age 1 due to complicated gastroschisis at birth, and hospitalization from birth to age 4 years. She had no history of rejection and has had an uncomplicated post-transplant course. Prior to pregnancy, immune suppression was maintained with tacrolimus, sirolimus and prednisone. Sirolimus and prednisone were discontinued when the patient became pregnant, with continuation of tacrolimus 5 mg twice a day, with reported medication compliance. Labs showed elevated liver enzymes: aspartate aminotransferase= 275 IU/L, alanine transaminase =228 IU/L, total bilirubin= 1.8 mg/dL, and FK level < 2, despite reported compliance. Ultrasound imaging revealed normal liver transplant and normal directional flow. Virology panel came back negative. Prednisone 10 mg daily was added. The patient then developed acute kidney injury, Cr:1.37, pulmonary edema, and FK went supra-therapeutic reaching 13.7 so it was held at that time. The patient was diagnosed with preeclampsia with severe features and was taken for an uncomplicated C-section. The baby was admitted to pediatric intensive care unit for preterm labor with initial respiratory insufficiency that later improved with no complications, discharged home 3 weeks later.A month later, liver function tests (LFTs) were elevated with concern for rejection. The patient had a low tacrolimus level, reporting she was taking 3 mg daily instead of twice a day. High dose steroid (1 gm solumedrol for 3 days) was given, with improvement of LFTs after 2 doses. Tacrolimus was increased to 3 mg twice a day and sirolimus was restarted. The patient is currently on tacrolimus and sirolimus with normal LFTs. Discussion: Triple gastrointestinal organ transplant procedure is uncommon, and achieving a successful pregnancy afterward is even rarer. Challenges presented by pregnancy is to maintain stability of the graft, prevent infection, ensure good nutritional support and monitor fetal wellbeing and growth (see Table 1).

Gastroenterology
Abusuliman M, Abusuliman A, Saad N, **Rehman S**, Ibrahim AM, **Jamali T**, **Shamaa O**, **Jafri SM**, and **Elatrache M**. A Rare Case of Pulmonary Sclerosing Pneumocytoma Diagnosed by Endoscopic Ultrasound (EUS). *Am J Gastroenterol* 2024; 119(10):S2628-S2629. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Pulmonary sclerosing pneumocytoma (PSP), formerly known as pulmonary sclerosing hemangioma, is a rare benign lung tumor with malignant potential. It mostly affects middle- aged women of Asian descent and is usually incidentally found, as most patients do not exhibit obvious medical

symptoms. Cytological and immunohistochemical analysis is essential for definitive diagnosis of PSP. Analysis is typically performed on biopsy specimen obtained via image-guided fine needle aspiration (FNA) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). We present a case of a middle-aged woman diagnosed with PSP via Endoscopic Ultrasound (EUS)-guided FNA of a pulmonary nodule. To our knowledge, there are no reports of cases of PSP diagnosed with EUS-FNA. Case Description/Methods: A 54-year-old white woman, who is an ex-smoker with a family history of lung cancer, presented with right clavicle swelling after shoulder injury. A chest x-ray incidentally revealed a soft tissue mass seen on the lateral view just anterior to the xiphoid. Cross-sectional imaging of the chest showed a 14 mm para-mediastinal nodule extending to the mediastinal pleura in the medial basal segment of the right lower lobe in close proximity to the distal esophagus (Figure 1). Due to proximity to the esophagus, this area was felt to be accessible with EUS. Endosonographic examination revealed a 17 mm by 10 mm extramural well-defined hypoechoic lesion with a microcystic component outside the distal esophageal wall and abutting it. EUS-guided FNA of the lesion was performed. Histopathological examination revealed atypical alveolar type 2-like pneumocytes concerning for Sclerosing Pneumocytoma. The patient underwent wedge resection and is currently undergoing surveillance imaging. Discussion: PSP is a rare, slow-growing benign lung tumor with malignant potential. Most patients are asymptomatic on presentation. Diagnosis is frequently incidental, and a definitive diagnosis requires histopathological examination. EUS-FNA can be a safe and minimally invasive tool to aid in the diagnosis of this rare condition when it is in close proximity to the gastrointestinal tract. Our case highlights the utility of EUS-FNA in diagnosis and management of unique mediastinal and lung lesions outside of the GI tract. (Figure Presented).

Gastroenterology

Abusuliman M, Abusuliman A, **Saleem A**, **Alomari A**, Abosheaishaa H, **Nimri F**, **Jamali T**, and **El-Nachef N**. A Rare Presentation of Cytomegalovirus (CMV) Colitis as a Colonic Mass. *Am J Gastroenterol* 2024; 119(10):S1995. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Cytomegalovirus (CMV) infection affects the gastrointestinal tract in both immunocompromised and immunocompetent individuals. While commonly manifesting as ulcerative lesions, instances of CMV-induced mass lesions in the gastrointestinal tract are rare, and have only been described in a handful of cases. We herein report a rare presentation of CMV as a discrete colonic mass in a patient presenting with hematochezia. Case Description/Methods: A 54-year-old woman with end state renal disease on hemodialysis, hypertension, and sarcoidosis (on azathioprine), presented to the emergency roomwith rectal bleeding ongoing for a few months.A month prior she was hospitalized for diarrhea and abdominal pain. Abdominal computed tomography at the time was concerning for ischemic vs infectious colitis. She was scheduled for an outpatient colonoscopy. In the emergency room, the patient was hypotensive, and her hemoglobin dropped from 8.4 g/dl to 6.5 g/dl. She had a normal white blood cells and CD4 T-cell count. Computed tomography showed colitis from the cecum to the distal transverse colon. Stool studies ruled out C. difficile/common bacterial infections. She underwent a colonoscopy which showed 3 x 4 cm protruding mass in the ascending colon contiguous with the ileocecal valve. The lesion was villous and characterized by superficial ulceration, friability, and scarring, with an adjacent area of ulceration and erythema on a nearby colonic fold (Figure 1). Biopsies revealed severely active nonspecific colitis in the ascending and transverse colon with positive CMV staining. The patient was started on ganciclovir IV 1.25 mg/kg 3 times weekly (renal dose adjusted) for 3 weeks. On follow up 3 weeks later, her other symptoms resolved and CMV levels were undetected. She still complained of abdominal pain, so the decision was to continue Valganciclovir for 6 weeks with regular monitoring. Follow up 2 months later showed hemoglobin improvement to 11.4 g/dl, with resolution of all symptoms. Discussion: While colonic masses are commonly attributed to neoplasms, infectious causes like CMV must be considered. Gastrointestinal symptoms of CMV when present are usually in patients with low white blood cell and CD4 counts, with HIV/AIDS or transplantation being the 2 greatest risk factors, but suspicion should be considered in individuals on immunosuppressants for rheumatological conditions as well, even with normal counts. Identification of CMV warrants medical intervention, resulting in clinical improvement and potential resolution of the mass.

Gastroenterology

Abusuliman M, **Jamali T**, Abusuliman A, **Nimri F**, **Rehman S**, **Hammad T**, and **Pompa R**. One Lesion at a Thyme: Oligometastatic Thymoma to the Liver. *Am J Gastroenterol* 2024; 119(10):S2812-S2813. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Thymomas are rare slowly growing tumors that can infiltrate directly through contiguity. They account for 40% of all mediastinal masses, resulting from neoplastic transformation of thymus epithelial cells. They mostly affect the surrounding structures via direct invasion. Extra-thoracic metastasis of thymomas is exceedingly rare, and the exact incidence is not known. Available literature revealed a total of 50 cases of extra-thoracic metastasis of thymoma. Of these have been 18 cases with liver metastasis,10 with simultaneous liver and other organs metastasis, and only 8 with solely liver metastasis. We herein report the first endoscopic ultrasound (EUS)-guided biopsy of metastatic thymoma solely to the liver Case Description/Methods: An 89-year-old man presented to his primary physician with urinary retention. Computed tomography (CT) scan incidentally noted a 6.8 x 5.2 cm heterogeneous mass in the aortopulmonary window suspicious for primary mediastinal malignancy or metastatic disease and an indeterminate 1.9 cm lesion in the left hepatic lobe. Abdominal Magnetic resonance imaging confirmed a 1.9 cm lesion in the left hepatic lobe concerning malignancy (Figure 1B). The mediastinal mass was biopsied, and pathology showed features consistent with Thymoma type B2. Gastroenterology team were consulted for an endoscopic ultrasound-guided biopsy of the liver lesion. The lesion appeared hypoechoic, heterogenous, and solid with well-defined borders, 16 mm 320 mm in diameter (Figure 1A). Pathology findings were consistent with metastatic thymoma. PET-CT confirmed a hypermetabolic anterior mediastinal mass and segment III liver mass consistent with metastatic thymoma. Radiation therapy was recommended as the patient was a poor candidate for surgery or chemotherapy given his advanced age and comorbidities Discussion: Extra-thoracic dissemination of thymomas is an extremely rare occurrence of these already rare tumors (Table 1). EUS-guided liver biopsy is a useful tool for diagnosis and easy access to metastatic lesions in the liver, and also morphologically characterize the lesion, avoiding more invasive diagnostic methods.

Gastroenterology

Abusuliman M, Jamali T, Nimri F, **Chaudhary AJ**, **Saleem A**, **Faisal MS**, **Alomari A**, **Rehman S**, Elfert K, Salem A, Meribout S, Abosheaishaa H, Ibrahim AM, **Shamaa O**, **Salman Faisal M**, **Watson A**, **Pompa R**, **Dang D**, **Elatrache M**, **Piraka C**, **Singla S**, and **Zuchelli T**. Adverse Events Associated With LAMS With and Without Plastic Stents Placement During Different EUS-Guided Interventions. *Am J Gastroenterol* 2024; 119(10):S1139-S1141. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Endoscopic ultrasound (EUS) guided lumen apposing metal stent (LAMS) has been used increasingly in lieu of surgery for multiple conditions, due to the novelty of the intervention, data on adverse events (AE) is scarce. We conducted this study to better understand and quantify the AE rates associated with LAMS placement, and plastic stent placement along with LAMS. Methods: Patients who underwent attempted EUS-guided LAMS interventions from 2015 to 2023 were identified from a single quaternary care hospital (Henry Ford Hospital) endoscopic procedure database. Retrospective demographic, clinical, and procedure-related data (including AE data using a modified version of the American Society for Gastrointestinal Endoscopy lexicon for endoscopic AE) was collected from the medical record. Results: Out of 243 patients, 133 (54.7%) were male and 159 (65.4%) were white, with a mean age of 53.7 ± 15.9 years. The primary indication for lumen-apposing metal stents (LAMS) was pancreatic fluid collections in 170 (70%) patients, with cyst-gastrostomy being the most common intervention in 159 (65.4%) patients. The technical success rate of LAMS placement was 97.5%, while the clinical success rate, defined as an improvement in clinical outcomes, was 93%. A total of 96 (39.5%) patients experienced adverse events (AEs), with 48 (19.7%) having early AEs (occurring < 48 hours post-procedure) and 70 (28.8%) having late AEs (occurring >48 hours and < 30 days post-procedure). Abdominal pain was the most common early and late AE, affecting 28 and 25 patients, respectively. Plastic stents were placed alongside LAMS in 176 patients, of whom 85 (48.3%) experienced

complications. The combination of plastic stent placement and LAMS was associated with a significantly higher overall risk of AEs (48.3% vs. 29.9%, P=0.009) and a higher risk of delayed AEs (33% vs. 17.9%, P=0.021). Multivariate analysis revealed that LAMS dilation without plastic stent placement resulted in a significantly higher rate of stent occlusion compared to LAMS dilation with plastic stent placement (7.3% vs. 0.8%, P=0.021). Additionally, LAMS dilation alone was associated with a higher rate of abdominal pain than when combined with stent placement (14.5% vs. 5.5%, P=0.027). Conclusion: LAMS has been demonstrated to have high technical and clinical success rates. Pairing of LAMS dilation and plastic stent placement may have beneficial effects on stent occlusion. More studies are needed to investigate the safety profile of LAMS. (Table Presented).

Gastroenterology

Adil SA, **Chaudhary AJ**, **Tang J**, and **El-Nachef N**. Infliximab-Associated Takotsubo Cardiomyopathy in a Patient With Ulcerative Colitis. *Am J Gastroenterol* 2024; 119(10):S2536. Full Text

S.A. Adil, Henry Ford Health, Shelby Township, MI, United States

Introduction: Tumor Necrosis Factor-alpha (TNF-α) inhibitors have been associated with heart failure, myocarditis, and acute myocardial infarction (MI). Takotsubo (stress-induced) cardiomyopathy (TC) is characterized by transient regional systolic dysfunction and mimics MI but without evidence of obstructive coronary artery disease. While emotional stressors are commonly implicated in TC, there is increasing recognition of pharmacological triggers. Data, however, is scarce on the association of anti-TNF therapy with TC. Here, we present a case of a 53-year-old woman with ulcerative colitis admitted to our hospital with TC, thought to be related to infliximab. Case Description/Methods: A 53-year-old woman with a history of left sided ulcerative colitis for 2 years had recently undergone escalation of therapy for colitis due to breakthrough symptoms despite maximum mesalamine therapy. She was started on infliximab 5mg/kg and underwent standard induction doses at week 0,2,6 and received 1 maintenance dose which resulted in clinical remission. However, she presented to the emergency department 19 days after her fourth infusion with complaints of chest pain, dyspnea, and diaphoresis. On arrival, her vital signs and electrocardiogram were normal, but her highsensitivity troponin levels were elevated, peaking at 2180 ng/L. A computed tomography scan was negative for pulmonary embolism, while an echocardiogram revealed regional wall motion abnormalities concerning for TC. Subsequent cardiac catheterization demonstrated non-obstructive coronary artery disease and a diagnosis of TC was confirmed. Upon review of her clinical and medication history, the inpatient cardiology team felt infliximab was a possible culprit for her presentation, although a definitive relationship could not be established. After discharge, she followed up with her gastroenterologist, who discontinued infliximab and started her on vedolizumab therapy for her ulcerative colitis. Discussion: TNF-α inhibitors are widely used in the management of inflammatory bowel disease (IBD) but are seldom implicated in cardiovascular adverse events. In our case, the temporal relationship between the initiation of infliximab and the development of TC raises suspicion for a potential association. Although rare, it is important for clinicians to remain cognizant of potential cardiovascular adverse events in patients with IBD who are undergoing biologic therapy, especially if they have existing cardiac risk factors. Switching to a different drug class should be considered.

Gastroenterology

Al-Nabolsi A, **Chaudhary AJ**, **Jamali T**, **Caines AN**, and **Elatrache M**. Esophagitis in a Post-Liver Transplant Patient: A Case of Cytomegalovirus and Herpes Simplex Virus-1 Coinfection. *Am J Gastroenterol* 2024; 119(10):S2222-S2223. Full Text

A. Al-Nabolsi, Corewell Health Farmington Hills, Dearborn, MI, United States

Introduction: Infectious esophagitis is the third most common cause of esophagitis, after gastroesophageal reflux disease and eosinophilic esophagitis. Common infectious organisms include candida, herpes simplex virus (HSV) and cytomegalovirus (CMV). While the occurrence of CMV esophagitis is rare in CMV infected patients, there remains minimal reported cases regarding CMV/HSV esophagitis coinfection. We present a rare case of CMV/HSV esophagitis successfully treated with antivirals. Case Description/Methods: A 59-year-old woman with history of primary sclerosing cholangitis,

who underwent orthotopic liver transplantation from a CMV seropositive donor 6 years ago, and achalasia secondary to scleroderma, treated with esophageal perusal endoscopic myotomy (EPOEM) one year ago, presented with a one-week history of dysphagia. The patient's immunosuppressive therapy at the time of presentation included prednisone, tacrolimus, and mycophenolate. The patient had negative CMV serology prior. An esophagogastroduodenoscopy (EGD) revealed severe esophagitis with extensive serpiginous and confluent non-bleeding ulceration (Figure 1A, B, C). Biopsies from the ulcer bed as well as ulcer edges confirmed CMV and herpes simplex virus-1 (HSV-1) co-infection. CMV quantitation in the blood was 9,523 IU/mL, subsequently becoming undetectable following treatment with valganciclovir. Mycophenolate was temporarily discontinued during treatment for CMV and HSV esophagitis. A repeat EGD performed 2 months later showed esophageal ulcers with no recent bleeding stigmata (Figure 1D). Biopsies revealed candida esophagitis with ulceration, and notably, CMV/HSV testing was negative. Discussion: CMV/HSV co-infection in the esophagus is very rare and can be associated with higher complication rates including perforation and bleeding. Thus, in immunocompromised hosts with esophagitis, a high index of suspicion for these conditions can help with targeting of appropriate biopsies of the esophagus to yield accurate and early diagnoses, allowing for rapid treatment.

Gastroenterology

Alhaj Ali S, **Dawod S**, **Alomari A**, **Omeish H**, **Cobty K**, **Shamaa O**, **Todd S**, **Williams C**, and **Jafri SM**. Hepatology Management of Adults with Fontan Circulation: An Interdisciplinary Protocol. *Am J Gastroenterol* 2024; 119(10):S1235-S1236. Full Text

S. Alhaj Ali, Henry Ford Hospital, Detroit, MI, United States

Introduction: The Fontan procedure is a palliative treatment for complex congenital heart disease that reduces cardiac output and raises venous pressure, leading to hepatic and cardiac complications. This study describes the clinical course and current management of adult patients with Fontan circulation under an interdisciplinary protocol. Methods: A retrospective review was done on adult patients with Fontan circulation after data collection on fibrosis evaluation, laboratory/imaging surveillance, and clinical follow-up. Monthly meetings helped establish the protocol and review challenging cases. Data was analyzed for describing hepatic, oncologic, cardiac, and renal outcomes. Results: Forty-three patients were included, average age 30.4 ± 7.2 years. Lateral tunnel (60.5%) and extracardiac (30.2%) Fontan were predominant; 46.5% were fenestrated. Indications included arterial malposition (25.6%), tricuspid atresia (23.3%), and hypoplastic left heart (20.9%). Elevated liver enzymes and total bilirubin were noted in 23% and 13.9%, respectively. Transient elastography (TEG) was done on 31 patients showing median stiffness of 14.3 kPa, with 51.7% having F4 fibrosis and 37.9% F3. All patients underwent liver Ultrasound or Magnetic resonance imaging within the last 2 years, revealing cirrhosis in 34.9% and congestion in 23.3%. Despite lacking imaging evidence of fibrosis, 21 had F2 or higher fibrosis on TEG. Liver biopsies in 13 patients showed congestion (53.8%), no/mild fibrosis (23.1%), and cirrhosis (15.9%). 4 patients had congestion without advanced fibrosis, despite advanced TEG or imaging findings. Cirrhotic complications included varices (11.9%) and ascites (7%). There were no cases of hepatocellular carcinoma or hepatic encephalopathy, and 1 patient was referred for liver transplant evaluation. Median ejection fraction was 55%. Heart catheterizations were done in 79.1%, 35.3% of whom had high Fontan pressures. Over half (53.9%) required repeat catheterization and 16.3% got additional heart surgery. 1 patient was referred for heart transplant. None developed chronic kidney disease (CKD). Conclusion: Our results show that fibrosis evaluation via TEG screening and laboratory/imaging surveillance may be confounded by congestive hepatopathy, commonly necessitating liver biopsy. Frequent heart catheterizations are crucial for surveillance in those with advanced fibrosis or congestion. Risk of liver or heart transplant as well as CKD remains low. An interdisciplinary protocol is imperative to establish clearer guidelines on surveillance techniques/intervals to reduce morbidity. (Table Presented).

Gastroenterology

Ali SA, **Ahmad Adil S**, **Harris K**, **Kamran W**, **Elatrache M**, **Zuchelli T**, and **Piraka C**. Navigating Obstacles: A Case Report on Endoluminal Treatment of Afferent Limb Syndrome Post-Whipple Procedure for Cholangiocarcinoma. *Am J Gastroenterol* 2024; 119(10):S2596. Full Text

S.A. Ali, Henry Ford Hospital, Detroit, MI, United States

Introduction: Afferent limb syndrome (ALS) is a rare complication of the Whipple pancreaticoduodenectomy (0.3%-1%). While optimal treatment is not established, surgical revision is a traditional approach for malignant ALS. Recently, endoscopic or radiologic interventions, such as stenting or percutaneous biliary drainage, have emerged as palliative alternatives. Case Description/Methods: This is a 74-year-old man with history of metastatic cholangiocarcinoma stage IIB status post neoadjuvant therapy followed by Whipple procedure. Course was complicated by obstructive jaundice due to partially obstructing afferent limb jejunal mass seen on enteroscopy, biopsy-proven to be recurrent cholangiocarcinoma. The resultant severe stricture could not be traversed endoscopically hence an internal-external percutaneous transhepatic cholangiography (PTC) drain was inserted, complicated by persistent leak around the insertion site requiring several tube exchanges. He was later admitted for jaundice & poor oral intake. Abdominal imaging re-demonstrated the mass with an abrupt transition point (Figure 1). A cholangiogram revealed dilated small bowel loop in the afferent limb concerning for ALS. Based on imaging, there was no good window for an endoscopic ultrasound-guided jejuno- or gastrojejunostomy to bypass the obstruction. Therefore, a 22 mm x 6 cm uncovered metal Wallflex stent (Boston Scientific, Marlborough, MA) was inserted across the site (Figure 1B), which improved his symptoms & oral intake without further PTC leaks. Discussion: Malignant ALS post-Whipple negatively impacts outcomes & quality of life in a population with already limited life expectancy. Diagnosis can be a challenge as it may not present with typical gastrointestinal (GI) obstruction symptoms, requiring clinical suspicion & imaging (commonly computerized tomography as upper GI series may not detect its presence). Management requires a multidisciplinary approach with surgeons, therapeutic endoscopists, &/or interventional radiologists. Our case underscores the importance of prompt recognition to allow for an early intervention. Palliative surgical revision is limited by low success rates given overall poor patient condition or from tumor burden causing kinks. Percutaneous approaches introduce risk of retrograde biliary infection, & in this case failed due to downstream obstruction. Endoluminal interventions, despite technical difficulty, emerge as promising alternatives which warrant further prospective trials comparing outcomes with other modalities. (Figure Presented).

Gastroenterology
Ali SA, **Kostecki P**, **Khan MZ**, and **Bhan A**. A Rare Case of Primary Gastrointestinal Mantle Cell Lymphoma Hiding in Plain Sight as Colon Polyps. *Am J Gastroenterol* 2024; 119(10):S1917-S1918. Full Text

S.A. Ali, Henry Ford Hospital, Detroit, MI, United States

Introduction: Mantle cell lymphoma (MCL) is an aggressive subtype of B cell non-Hodgkin lymphoma that constitutes only a small fraction (0.4%) of all primary gastrointestinal lymphomas. Patients with MCL have a high relapse rate and poor prognosis. Case Description/Methods: A 71-year-old man presented with 6 months of non-specific symptoms including abdominal discomfort, altered bowel habits, and weight loss. Although he had a normal colonoscopy 4 years prior, a repeat endoscopic examination revealed significant lymphomatous polyposis, with hundreds of non-bleeding polyps localized from the rectum to the distal ascending colon. Histopathological assessment of the polyps revealed a lymphoid infiltrate consistent with MCL. Cytogenetic analysis of bone marrow aspirate along with imaging revealing extensive mesenteric and retroperitoneal adenopathy and a mildly enlarged spleen confirmed the MCL diagnosis. The patient underwent 6 cycles of bendamustine and rituximab followed by maintenance rituximab therapy every 2 months. Throughout and after treatment, serial imaging showed markedly reduced adenopathy, and colonoscopy performed 2 months post-treatment (prior to maintenance therapy) demonstrated completely normal colon without evidence of any residual polyps. One month after completing initial chemotherapy, an incidental complex renal lesion was diagnosed as clear-cell renal cell carcinoma (World Health Organization / International Society of Urologic Pathologists grade 1, 4 cm, limited to the kidney), and the patient underwent successful partial nephrectomy after completion of chemotherapy. Discussion: Our case underscores the imperativeness of thorough endoscopic evaluation in patients with non-specific gastrointestinal symptoms to ensure early detection and effective management of rare colonic cancers. This is particularly important with classic “red-flag” symptoms and features suggesting malignancy and despite normal recent colonoscopies (as in our patient who had a normal colonoscopy 4 years prior). The case further highlights how quickly the rare condition of

gastrointestinal MCL can arise, necessitating swift immunohistochemical, imaging, and cytogenetic analysis to identify this aggressive condition. Even with a delayed presentation and diagnosis, diligent and timely treatment can still result in significant disease remission. The co-occurrence of gastrointestinal MCL with renal cell carcinoma introduces additional complexity to the case and suggests a potential association warranting further study (see Figure 1).

Gastroenterology
Ali SA, **Shamaa O**, **Omeish H**, **Mullins K**, and **Heidemann D**. Open Access Colonoscopy: Assessing the Outcomes of a Novel Electronic Medical Record Best Practice Alert (BPA) in Reducing Inappropriate Colonoscopy Referrals. *Am J Gastroenterol* 2024; 119(10):S281-S282. Full Text

S.A. Ali, Henry Ford Hospital, Detroit, MI, United States

Introduction: In our prior study, we established that open access colonoscopy (OAC) for colon cancer screening is burdened by high inappropriate referral rates, leading to delayed patient care, increased resource use, & lower colonoscopy completion rates for rejected patients. Our group initiated a quality improvement project involving an electronic medical record (EMR) best practice alert (BPA) that notifies providers if specific criteria prohibiting OAC are met. This study assesses the BPA's outcomes after implementation. Methods: Starting April 2023, an EMR BPA was launched at our primary care clinic. Upon ordering OAC, if a patient meets prohibitive criteria, the BPA (seen in Figure 1) notifies the provider to cancel the order & either refer to gastroenterology (GI) or order stool testing. If the order remains, a text box appears for an optional explanation. High-risk patients have only the GI referral option. Concurrently, we liberalized OAC guidelines, raising hemoglobin A1c (HbA1C) & body mass index (BMI) thresholds. Data from January to March 2024 was collected post-BPA refinement, & a random sample of 200 patients was chart reviewed to assess outcomes. Results: From January to March 2024, the BPA was triggered 508 times. Mean age was 61.1 years. Common BPA triggers were hypokalemia ≤3.3 mmol/L (18.5%), HbA1C ≥9.5% (18.5%), hemoglobin ≤10 g/ dL (15.5%), age ≥80 years (15.5%), BMI ≥50 kg/m2 (13.5%), & blood pressure ≥180/110 (8%). Most common alternatives were referral to GI (53%), stool testing (2%), or neither (45%). Those who ordered neither mostly proceeded with the order without any reason/changes (54.4%), or canceled it (24.4%). For “high risk” patients where the BPA triggered (n=51), only 52.9% were referred to GI. There were 5 cases where the BPA inaccurately fired, 19 cases where OAC referral was still accepted by GI despite BPA accuracy, & 20 cases where referral was rejected for another individualized reason. Only 11% of the sample completed any colon cancer screening & 9% completed a colonoscopy; mean time from referral to colonoscopy was 77.1 days. Conclusion: The BPA appears to reduce inappropriate referrals but effectiveness is limited by provider awareness & inability to factor in personalized patient factors. Low completion rates may be due to demographic challenges like missed appointments or socioeconomic barriers, as well as the recent nature of the data. This suggests a need for longer BPA implementation to fully assess its impact on referral appropriateness & completion rates. (Table Presented).

Gastroenterology
Alluri S, **Lloyd J**, and **Caines AN**. The Dark Side of Slimming: Weight Loss Supplement Induced Liver Injury. *Am J Gastroenterol* 2024; 119(10):S2885. Full Text

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Introduction: Drug-induced liver injury (DILI) is a significant and underrecognized cause of acute liver failure, with weight loss supplements being a notable culprit due to unregulated ingredients and widespread use. Diversity of causative agents in DILI results in a sundry of clinical presentations that often mimic other liver diseases, making diagnosis complex. This case report delves into the diagnostic challenges and clinical implications of DILI. Case Description/Methods: A young African American woman with history of hypertension and obesity, presented with 1 week of new-onset jaundice, pruritus, and vomiting. She denied alcohol use, personal or family history of liver disease, or new medications apart from weight loss supplements purchased online 2 months prior. Initial lab work revealed ALT 1593, AST 1309, Tbili 12.5, ALP 191, and INR 1.65. Infectious, metabolic workup was negative, with positive antimitochondrial antibody (AMA) of 86 U/mL, and negative Anti- smooth muscle antibody (16 U/mL) .

Subsequent imaging with US and MRCP showed no structural abnormality. Liver biopsy done to differentiate drug induced liver injury (DILI), drug induced autoimmune liver disease, and autoimmune related liver disease and/or overlap syndrome. Biopsy showed diffuse mixed inflammation typical of acute hepatocellular injury rather than the focal lymphocytic biliary injury characteristic of PBC. Patient was diagnosed with DILI secondary to herbal/ dietary supplements (HDS) based on the drug exposure timeline, histologic findings, and the negative workup for alternative etiologies. Supplement was discontinued, however due to prolonged jaundice and lack of spontaneous recovery, glucocorticoids were initiated in Hepatology clinic 2 months later . Subsequent labs at 4 month follow up, showed significant improvement to ALT 36, AST 52, ALP 61 , Tbili 0.9, and INR 1.3. Discussion: This case highlights the need for awareness of DILI, which is often underreported and can lead to severe outcomes. With the rise in access to weight loss supplements, coupled with minimal patient education on associated risks, providers must be thorough in history taking and workup. The patient's positive AMA titer, though an uncommon finding in DILI, is important to recognize as it may indicate a predisposition to autoimmune liver disease, guiding future monitoring. Although histopathology is not a standard diagnostic criterion for DILI, it proved imperative in establishing diagnosis in our case, emphasizing its value in clinical practice.

Gastroenterology
Alluri S, and **Matin T**. Isolated Colonic Polypoid Ganglioneuromas in Patient With Neurofibromatosis Type 1. *Am J Gastroenterol* 2024; 119(10):S2058. Full Text

S. Alluri, Henry Ford Health, West Bloomfield, MI, United States

Introduction: Ganglioneuromas are rare, benign neurogenic tumors arising from the peripheral nervous system, which can occur in the mediastinum, retroperitoneum, adrenal gland, and uncommonly, the GI tract. Intestinal ganglioneuromas are typically diagnosed in adolescents and young adults and can manifest as polypoid, multifocal, or diffuse involvement of the intestinal tract. While patients are often asymptomatic, large lesions can cause significant downstream effects such as Gastrointestinal bleeding, motility issues and obstruction, making recognition imperative. Diffuse ganglioneuromatosis has been associated with syndromic conditions such as MEN2B and Cowden, however association with Neurofibromatosis 1 (NF1) remains largely undocumented. Case Description/Methods: We report the case of a 60-year-old African American woman with history of neurofibromatosis type 1 (NF1), who presents for colonoscopy after reporting several months of intermittent constipation. She was diagnosed with NF1 at the age of 22 with disease manifestations including Lisch nodules, and cutaneous and cervical neurofibromas. Colonoscopy unexpectedly revealed an 11 mm sessile polyp in the cecum, and 2 sessile polyps in the sigmoid colon, which were removed via cold snare polypectomy. Histopathology revealed Ganglioneuroma and lipomas with immunostaining positive for s100 protein supporting diagnosis of ganglioneuroma (GN). Discussion: Intestinal ganglioneuromas can be categorized as polypoid, multifocal, or diffuse with the latter 2 having had documented association with NFI. However, association with NF1 and solitary lesions has been sparsely documented in literature. In our peculiar case, an older woman with history of NF1 presented with 3 isolated polypoid ganglioneuromas in sigmoid colon and cecum. While the incidence and risk of malignant transformation of ganglioneuromas is low, it is important to be mindful of this pathology in order to provide definitive management with surgical removal. Recognition can be delayed due to non-specific presenting symptoms and lack of screening guidelines in patients with NF1. While association is more well established with MEN2B and Cowden, testing for these conditions along with NF1 should be considered based on concomitant clinical findings in patient's without history of systemic syndromes.

Gastroenterology
Alluri S, **Singh B**, **Sarowar A**, **Ramanan S**, **Rehman S**, and **Jafri SM**. Patterns and Predictors of Outcomes in Total Parenteral Nutrition Associated Liver Disease. *Am J Gastroenterol* 2024; 119(10):S1386. Full Text

S. Alluri, Henry Ford Health, West Bloomfield, MI, United States

Introduction: Total parenteral nutrition (TPN) is used as a life-saving intervention in patients who are unable to tolerate alternative nutrition. However, elevated liver enzymes in patients requiring TPN are a

significant predictor of morbidity and have been associated with increased mortality rates as well. Given the complexity and clinical implications of TPN associated liver disease, bridging the gap in understanding and management of this phenomenon is pivotal. Our study aims to elucidate patterns and predictors of liver enzyme elevation in this patient population, with a focus on clinical management and outcomes. Methods: A retrospective chart review was conducted of all adults (18 years or older) at our center (2014-2024) with history of elevated liver enzymes (Alanine transaminase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), and Total Bilirubin) while on TPN. Data on basic patient demographics, indication for TPN, Duration of TPN therapy and Liver enzyme elevation, changes in TPN formulation, and mortality were collected. Results: A total of 111 patients with history of elevated liver enzymes (ALT, AST, ALP, and Total Bilirubin) while on TPN were included, 48 (43.2%) were male, 63 (56.8 %) were females, and 87 (78.4%) were White. Most common indications for TPN initiation were prolonged malnutrition in 41 (36.9) patients, and short gut syndrome in 39 (35.1) patients. Mortality occurred in 52 (46.8%) of patients. Indication for TPN (P=0.82) and Duration of TPN therapy (P5 0.516) did not show statistically significant differences in risk of mortality. However, there was a significantly higher incidence of mortality in patients who underwent change in TPN therapy in comparison with those who did not (16.3%, 83.7%, P=0.007). Additionally, those with change in TPN had significantly shorter duration of time from peak Liver enzyme value to death (P5 0.028). Conclusion: This study observed a link between TPN modification and higher mortality rates despite not having a correlation between duration on TPN therapy and mortality. In considering the simultaneous findings of significantly reduced time from peak Liver enzymes to death, this suggests that alterations in TPN therapy may be critically delayed till severe progression of liver disease. Our study highlights the need for early consideration of TPN adjustment and further clinical studies to promote better outcomes in patients with TPN associated liver disease.

Gastroenterology

Alluri S, **Todd S**, **Lloyd J**, and **Jafri SM**. Lynch Syndrome and Liver Disease - Connecting the Dots. *Am J Gastroenterol* 2024; 119(10):S2885. Full Text

S. Alluri, Henry Ford Health, West Bloomfield, MI, United States

Introduction: Lynch syndrome (LS) is an autosomal-dominant disorder that increases risk of carcinogenesis via defects in DNA mismatch repair genes. Typically, it has been associated with colorectal and gynecological cancers, but has been more rarely been connected to biliary cancers as well. The intricate relationship between LS and liver disease is highlighted by the increased incidence of hepatobiliary manifestations, making vigilant screening and management imperative. Case Description/Methods: We report the case of an elderly White woman with hypothyroidism, who presented with a long history of persistently elevated Alkaline phosphatase, with presenting values of ALT 24, AST 30, ALP 305, and total bilirubin 0.50. She was asymptomatic without toxometabolic risk factors. The patient has an interesting family history of 2 sisters with PMS2 positive LS, one of whom also had autoimmune hepatitis (AIH) and intrahepatic cholangiocarcinoma, and a brother who underwent liver transplantation for cirrhosis of unknown etiology. Serologies positive for antimitochondrial antibody (AMA) of 17 U/mL, antinuclear antibody (ANA) ratio >1:55, SSA/SSB antibodies >240 and 167 U/mL, and positive smooth muscle antibody (SMA). Liver biopsy showed chronic cholestasis and patchy portal inflammation without bile duct inflammation or granulomas. She was initiated on Ursodiol and MRCP was ordered, with repeat bloodwork after 2 months showing near normalization of ALP to 144. Discussion: This case observes an elderly women with newly diagnosed PBC without cirrhosis, who prompted extensive hepatobiliary workup due to personal and family history of LS and liver disease. Mutations in PMS2 genes carry a lower risk for malignancy compared to other mismatch repair genes, which has led some experts to suggest less rigorous screening approach. However, as this case highlights, assessing for hepatobiliary manifestations of LS is extremely important. This case also demonstrates the importance of both laboratory and pathologic screening for various pathologies in liver disease. While family history, serologies and clinical presentation suggested LS and PBC, biopsy introduced new suspicion for PSC. Family history of idiopathic cirrhosis and cholangiocarcinoma further complicates the clinical picture, raising questions about the interplay between autoimmune liver disease and LS. This case advocates for a comprehensive and thorough evaluation for liver disease in patients with history of Lynch Syndrome.

Gastroenterology

Alomari A, **Abusuliman M**, **Saleem A**, **Malick AN**, **Jomaa D**, Althunibat I, and **Gueorguieva I**. Paradoxical Psoriasis and Alopecia Areata After the Use of Anti-TNF in a Patient With Crohn's Cisease. *Am J Gastroenterol* 2024; 119(10):S2546-S2547. Full Text

A. Alomari, Henry Ford Hospital, Detroit, MI, United States

Introduction: Autoimmune reactions to anti-tumor necrosis factor (TNF) therapy present a clinical challenge while managing inflammatory bowel disease (IBD). Among these reactions, psoriasis and alopecia can occur as extraintestinal manifestation and due to immunosuppressive medication. We aim to highlight the complexity of autoimmune responses triggered by anti-TNF therapy in a patient with Crohn's disease who developed alopecia and psoriasis of the scalp. Case Description/Methods: A 20-year-old man patient was diagnosed with Crohn's disease after experiencing abdominal cramps, rectal pain, and bleeding. Colonoscopy showed aphthous ulcerations and severe inflammation in the terminal ileum. He was started on infliximab, which improved his symptoms. A year and a half later, his symptoms started to recur, requiring increased dosages. Four months later, the patient reported hair loss. Dermatologists saw the patient and noticed psoriasiform changes on the scalp and ears, and a biopsy showed psoriatic alopecia and alopecia areata features suggestive of anti-TNF alpha related alopecia. Treatments including Triamcinolone injections, clobetasol, and calcipotriene failed to alleviate symptoms. Ultimately, medication was changed to Ustekinumab, which improved his hair loss and Crohn's symptoms, further supporting the diagnosis of anti-TNF alpha-related alopecia. Discussion: The association between anti-TNF-α agents and onset of psoriasiform skin eruptions, and the paradoxical nature of these reactions are well described in the literature. The proposed mechanism relies on the role of IFNγ in the pathogenesis of psoriasis, as blocking TNFa leads to uncontrolled production of IFNγ contributing to the skin eruption. One Meta-Analysis described 134 patients who developed alopecia with IBD therapy. Of those, 78 were on anti-TNF-α therapy. Psoriatic Alopecia was the most reported (n = 41), followed by Alopecia Areata (n = 19), and psoriatic alopecia with alopecia areata features. (n = 3). Diagnosis criteria include absence of psoriasis history, alopecia plaque(s) on the scalp, and psoriasiform rash elsewhere after starting treatment. Our patient met the criteria, with hair regrowth after stopping infliximab. Differentiating these reactions from primary psoriatic alopecia/alopecia areata is important as it affects our management. Lastly, it is important to collaborate in a multidisciplinary approach involving gastroenterology and dermatology when caring for our IBD patient community.

Gastroenterology

Alomari A, **Nimri F**, **Shamaa O**, **Abusuliman M**, **Saleem A**, Nimri R, **Omeish H**, **Malick AN**, and **Zuchelli T**. Factors Associated With Worsening Ascites Following ERCP in Cirrhotic Patients: A Retrospective Analysis. *Am J Gastroenterol* 2024; 119(10):S1147. Full Text

A. Alomari, Henry Ford Hospital, Detroit, MI, United States

Introduction: Even in patients with liver cirrhosis, ERCP remains the gold standard treatment for pancreatic and biliary diseases. These patients are more likely to have adverse outcomes. We investigated the worsening of ascites as a complication of ERCP in cirrhosis patients. Methods: A retrospective chart review was carried out on all cirrhosis patients aged 18 years and above who had an ERCP at our center between January 2015, and November 2023. Our analysis did not include any patients with liver transplants. Basic patient demographics, ERCP indications, liver function markers, ERCP indications, and morbidity were among the collected data. Results: In patients with cirrhosis who underwent ERCP (n=277), 181 (65.3%) were males, 183 (66.1%) were white. The most common etiology of cirrhosis was alcohol in 108 (38.9%) patients. Jaundice was the most common indication for ERCP in 99 (35.7%) patients. The course of 22 (8%) patients was complicated by worsening ascites post procedural. Comparing those whose ERCP course was complicated by worse ascites to those who did not, patients with worsening ascites were more likely to have a higher MELD score at the time of ERCP (25.6 ± 8.0 vs. 18.6 ± 8.2, P< 0.001), higher INR (1.6 ± 0.5 vs. 1.4 ± 0.4, P = 0.049), and performed inpatient vs. outpatient (81.8% vs. 58.0%, P=0.029). Additionally, they had a higher incidence of ascites (90.9% vs. 59.1%, P=0.003) HRS (38.1% vs. 17.3%, P=0.019), and hyponatremia (63.6% vs. 36.4%, P=0.012) at presentation. Conclusion: While ERCP continues to be an invaluable procedure for

therapeutic and diagnostic interventions in pancreatic and biliary disorders, patients with liver cirrhosis have more risks for post-ERCP complications including ascites. Patients who have ascites at presentation have a higher risk for worsening ascites after ERCP. Patients with higher MELD score, higher INR, HRS, hyponatremia at the time of ERCP and those who are getting the procedure as inpatient have a higher risk of developing worsening ascites post ERCP. Understanding the specific risk factors associated with post-ERCP complications in patients with liver cirrhosis is crucial for optimal patient care and to lower rates of complications.

Gastroenterology
Alomari A, **Nimri F**, **Shamaa O**, **Saleem A**, **Abusuliman M**, Nimri R, Althunibat I, and **Zuchelli T**. Risk Factors and Predictors of Hepatic Encephalopathy Following ERCP in Cirrhotic Patients: A Retrospective Analysis. *Am J Gastroenterol* 2024; 119(10):S1355. Full Text

A. Alomari, Henry Ford Hospital, Detroit, MI, United States

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) poses unique challenges in patients with liver cirrhosis, a population prone to heightened post-procedural complications. We investigated hepatic encephalopathy (HE) as a complication of ERCP in patients with liver cirrhosis. Methods: A retrospective chart review was carried out on all cirrhosis patients aged 18 years and above who had an ERCP at our center between January 2015, and November 2023. Our analysis did not include any patients with liver transplants. Basic patient demographics, ERCP indications, liver function markers, ERCP indications, and morbidity were among the collected data. Results: In patients with cirrhosis who underwent ERCP (n=277), 181 (65.3%) were males, 183 (66.1%) were White. The most common etiology of cirrhosis was alcohol in 108 (38.9%) patients. Jaundice was the most common indication for ERCP in 99 (35.7%) patients. The course of 24 (8.6%) patients were complicated by HE. Comparing those whose ERCP course was complicated by HE to those who did not, patients with HE were likely to have a higher MELD score at the time of ERCP (26.7±9.4 versus 18.4±7.9, P<0.001), higher INR (1.9±0.6 versus 1.4±0.6, P<0.001), ascites (95.8% versus 58.3%, P<0.001), undergone balloon dilatation (75% versus 54%, P=0.047) , and had higher incidence of HE at presentation (62.5% versus 37.7%, P=0.018). Interestingly, cirrhotic patients with hypertension were less likely to develop HE post-ERCP (37.5% versus 59.3%, P=0.039). Conclusion: Our study highlighted the risk of hepatic encephalopathy (HE) in liver cirrhosis patients undergoing ERCP. Those who developed HE had higher MELD scores, INR levels, and were more likely to have ascites. Surprisingly, hypertension seemed to lower the risk of post-ERCP HE. Patients undergoing balloon dilatation during ERCP had a higher risk of HE. This emphasizes the importance of careful patient selection and procedural considerations to minimize HE risk in cirrhotic patients undergoing ERCP, especially if performed as an outpatient.

Gastroenterology
Alomari A, **Saleem A**, **Abusuliman M**, **Omeish H**, **Dababneh YJN**, Althunibat I, and **Ginnebaugh B**. Gastric Lap Band as a Cause of Pseudoachalasia. *Am J Gastroenterol* 2024; 119(10):S2259. Full Text

A. Alomari, Henry Ford Hospital, Detroit, MI, United States

Introduction: Achalasia is a rare esophageal motility disorder characterized by impaired relaxation of the lower esophageal sphincter and loss of esophageal peristalsis. Pseudoachalasia, often caused by malignancy or mechanical obstruction, mimics the clinical presentation of achalasia. [1] This case report highlights an unusual presentation of pseudoachalasia caused by a gastric lap band. Case Description/Methods: We present the case of an 80-year-old woman with a surgical history of laparoscopic gastric banding for obesity who was diagnosed with achalasia in 2013. Management was initially conservative following a comprehensive diagnostic workup including EGD, VFSS, esophageal manometry, and a barium study. The patient did not wish to undergo myotomy. She was lost to follow up for over 10 years and re-presented due to progressive solid and liquid dysphagia with accompanied regurgitation. After further chart review, it was found that her laparoscopic gastric band had not been assessed for 2 decades. Taking into account her surgical history, pseudoachalasia due to lap band migration or hyperinflation was considered. A repeat barium swallow study demonstrated delayed passage of contrast through a narrow lumen at the level of the gastric band suggestive of obstruction.

The patient was then referred to bariatric surgery for deflation of the gastric lap band. Discussion: Pseudoachalasia is a condition that mimics the clinical features of primary achalasia. It can be caused by a variety of etiologies including malignancy, particularly those involving the gastroesophageal junction, as well as anatomical abnormalities or previous surgical interventions. Identifying pseudoachalasia is imperative for effective treatment initiation. While primary achalasia may be managed with interventions such as Heller myotomy or POEM, pseudoachalasia requires addressing the underlying cause. For our patient, this meant deflation of the gastric lap band. Routine achalasia work-up sometimes fails to distinguish between pseudo and primary achalasia, thus a high clinical suspicion and proper history is paramount in initiating diagnostic work-up. This case highlights the importance of considering pseudoachalasia in patients with a history of gastric surgeries due to their altered anatomy.

Gastroenterology

Arif TB, Davuluri H, Sainatham C, Ur Rahman A, and **Khan MZ**. Undercover Ulcers: The Misleading Presentation of Duodenal Bulb Perforation as Pancreatitis. *Am J Gastroenterol* 2024; 119(10):S3006. Full Text

T.B. Arif, Sinai Hospital, Baltimore, MD, United States

Introduction: Duodenal ulcers and acute pancreatitis (AP) are common gastrointestinal diseases. AP can result from various factors, including cholelithiasis and alcoholism, and, rarely, from duodenal ulcer perforation (DUP). We report an 83-year-old woman with AP due to a large duodenal ulcer perforation extending into the pancreas, requiring emergent surgery. Case Description/Methods: An 83-year-old woman with Alzheimer's disease, osteoarthritis, and hypertension presented with worsening abdominal pain over 2-3 weeks, with no associated symptoms. Her home medications included aspirin, lisinopril, meloxicam, and donepezil. On presentation, she displayed normal vital signs. Physical examination revealed signs of dehydration and asthenia, with right upper quadrant and epigastric tenderness. Laboratory results indicated hyponatremia, elevated BUN and creatinine, anion gap metabolic acidosis, elevated lipase (1263 U/L), and leukopenia. An electrocardiogram showed sinus tachycardia. Intravenous fluids, morphine, bowel rest, and pantoprazole were started considering it as a case of AP. A computed tomography abdomen with contrast could not be performed initially due to acute kidney injury. Abdominal ultrasound revealed cholelithiasis without cholecystitis. Eventually, the patient developed hypoxia and was put on 4L oxygen. A chest X-ray revealed air under the diaphragm, prompting urgent surgical consultation. The patient went into cardiac arrest shortly but was successfully resuscitated. Following intubation, a computed tomography scan revealed free intraperitoneal air, leading to an urgent exploratory laparotomy. A 4 cm perforation was seen in the duodenal bulb with erosion into the anterior pancreas. Antrectomy and Roux-en-Y gastrojejunostomy were performed. Postsurgery, she was administered antibiotics resulting in improved lactate and lipase levels. Discussion: In this case, our patient initially presented with vague AP symptoms like epigastric pain, lethargy, and anorexia. Her rapid respiratory decline led to a chest X-ray, revealing air under the diaphragm. This case shows that physical exams can be nonspecific for DUP causing AP, especially in older adults. DUP should be considered in acute epigastric pain, particularly in patients with a history or risk factors of peptic ulcer disease (e.g., nonsteroidal anti-inflammatory drug use for osteoarthritis). Her renal dysfunction delayed a computed tomography scan and the DUP diagnosis that led to her decompensation. Therefore, it is crucial to rule out peptic ulcer disease in adults with risk factors when no clear trigger for AP is found to prevent morbidity and mortality (see Figure 1).

Gastroenterology

Arif TB, Ihsan R, Rahman AU, and **Khan MZ**. Unveiling the Uncommon: A Rare Case of Infected Intraductal Papillary Mucinous Neoplasm of Pancreas. *Am J Gastroenterol* 2024; 119(10):S1714. Full Text

T.B. Arif, Sinai Hospital, Baltimore, MD, United States

Introduction: Intraductal papillary mucinous neoplasm (IPMN) of the pancreas involves papillary growths within its ductal system. Complications, though extremely rare, include infections due to rupture, fistulization, or malignant transformation. We report a case of infected IPMN in a 76-year-old man with

recurrent abdominal pain, treated successfully with cyst drainage and antibiotics. Case Description/Methods: A 76-year-old man with a history of chronic obstructive pulmonary disease, prediabetes, and pancreatic cyst (on pancrelipase) presented with diffuse abdominal pain for 3 hours. He had a previous presentation 5 days ago with worsening abdominal pain, fever, chills, and nausea. Magnetic resonance cholangiopancreatography (MRCP) at that time showed a cystic mass affecting the left renal vein and pancreas, prompting a referral for endoscopic ultrasound (EUS). On examination, he had minor wheezes and mild diffuse abdominal tenderness. Labs showed elevated liver biochemistry panel, leukocytosis, and anemia. Computed tomography scan revealed a possible abscess connected to the known pancreatic cyst. Abdominal ultrasound suggested acute cholecystitis possibly related to the pancreatic mass. EUS showed pancreatic duct dilation and a heterogeneous lesion posterior to the left lobe of the liver. Fine needle aspiration (FNA) revealed inflammatory debris and pseudomonas aeruginosa growth in the drainage culture. Pancreatic cyst CEA was elevated with low amylase, indicating an infected IPMN. Antibiotics were continued, and the patient was discharged with oral therapy (ciprofloxacin and metronidazole) for follow-up imaging with gastroenterology. Discussion: This is the fourth known case of spontaneous IPMN infection. Previous cases involved patients with sepsis and multilocular cystic tumors, with one case being asymptomatic. All cases were treated with cyst drainage and antibiotics. Our case showed infection with pseudomonas aeruginosa. The pathogenesis is unclear, potentially involving retrograde bacterial translocation due to papillary orifice dilation or other factors like alcohol-induced pancreatitis or immunosuppression associated with diabetes. Imaging may show unusual fluid layering, with EUS revealing clumped mucin. Management typically involves drainage and antibiotics, with considerations for resection in cases of dysplastic transformation. Our case did not require resection as no malignancy was observed. Spontaneous IPMN infection is rare, varying from asymptomatic to severe sepsis. EUS-guided FNA can aid in diagnosis and management (Figure 1).

Gastroenterology

Bin Arif T, Ali SH, Sadiq M, Bhojwani KD, Hasan F, Ur Rahman A, and **Khan MZ**. Meta-Analysis of Global Prevalence and Gender Distribution of Irritable Bowel Syndrome (IBS) Using Rome III and IV Criteria. *Am J Gastroenterol* 2024; 119(10):S517. Full Text

T. Bin Arif, Sinai Hospital, Baltimore, MD, United States

Introduction: Estimating the prevalence of irritable bowel syndrome (IBS) is essential to understand its impact. Variations in data arise from different studies, regions, methods, and diagnostic criteria. This systematic review and meta-analysis used the latest Rome III and IV criteria to determine the global prevalence and gender distribution of IBS. Methods: We searched PubMed, Cochrane Library, and Google Scholar till June 1, 2024. Original studies reporting prevalence data on individuals ≥18 years either by Rome III or IV criteria were considered with the exclusion of academic surveys. Prevalence was the main outcome of interest, stratified by subtype, gender, country, and evaluation criteria. To assess the overall prevalence in each category, the Rome IV criterion was preferred. Open Meta-analyst and Review Manager were used for analysis. Prevalence was analyzed by DerSimonian-Laird random-effects model and gender distribution was analyzed by 2-arm analysis. Results: A total of 1435 full-text articles were retrieved and 96 remained after exclusion. The overall prevalence was 14% (12.1-16%) when accounted for study weight. When subtyped, mixed type (IBS-M) had the highest prevalence rate of 33.1% [25.7-40.5%] followed by diarrhea type (IBS-D) (28% [24.2-31.9%]), constipation type (IBS-C) (27.9% [15.6-40.1%]), and unsubtyped (IBS-U) (8.3% [6.3-10.6%]). In a nation-wise breakdown, the UK (36459 events) followed by Japan (13439 events) had the highest prevalence. Women were found to have a higher rate of IBS compared to men (OR 1.49, 95% CI [1.24-1.79]), $P < 0.00001$). Conclusion: We analyzed the highest prevalence data reported to date for IBS in =1 different countries from 96 studies. The overall prevalence was 14%, higher than previous reports (11.2%). Prevalence was higher with Rome IV criterion despite its restrictiveness, contrary to previous findings. IBS-M had a higher prevalence than IBS-D and IBS-C, but with Rome IV criterion, IBS-C was more prevalent than IBS-D. The UK had the highest IBS rate at 67.5% of global cases, attributed to data from the UK Biobank. IBS was modestly more common in women. Study heterogeneity was due to varying influences like education, culture, environment, ethnicity, and diet. More studies are needed on IBS-U prevalence and using validated questionnaires for Rome III/IV criteria. IBS management costs about ≥1 billion/year, highlighting the need for more trials on curative drugs and their cost-effectiveness, especially for the IBS-M subtype (see Figure 1, Table 1).

Gastroenterology
Brown K, Fricker ZP, Merwat SN, Izzy MJ, and Cardoza S. Retreatment Following Initial Treatment With Terlipressin Improved Clinical Outcomes Among Patients With Hepatorenal Syndrome-Acute Kidney Injury: A Pooled Post Hoc Analysis. *Am J Gastroenterol* 2024; 119(10):S1459. Full Text

K. Brown, Henry Ford Health, Detroit, MI, United States

Introduction: Terlipressin is used to treat hepatorenal syndrome-acute kidney injury (HRS-AKI), a potentially lethal form of AKI. In 3 Phase III clinical studies of terlipressin treatment of patients with HRSAKI, retreatment with the same blinded study drug was allowed for patients who initially responded to treatment with a ≥30% reduction in serum creatinine (SCr), but then met the HRS diagnosis criteria again (≤90 days from the first dose of study drug). This study assessed retreatment with terlipressin and its associated clinical outcomes using pooled data from the 3 Phase III clinical studies. Methods: The intent-to-treat (ITT) population of 3 Phase III studies (ie, OT-0401, REVERSE, and CONFIRM), in which patients with HRS-AKI were treated with terlipressin at 1-2 mg every 6 hours via intravenous bolus or matched placebo, were pooled for the analysis. Retreatment was allowed if patients responded initially with a ≥30% reduction in SCr but then subsequently developed a recurrence of HRSAKI. HRS reversal was defined as ≥1 SCr value of ≤1.5 mg/dL on treatment (≤24 h after the last dose of study drug), for both the initial treatment and subsequent retreatment period. Assessments also included: durable HRS reversal, defined as HRS reversal without renal replacement therapy up to Day 30; and the proportion of patients alive at Day 90 (from start of initial treatment). Results: There was a significant improvement in HRS reversal and durable HRS reversal with initial terlipressin treatment versus placebo (HRS reversal: 33.2% [117/352] vs 16.4% [42/256], P< .01001; durable HRS reversal, 30.1% [106/352] vs 15.2% [39/256], P< .01001). Moreover, HRS reversal was durable among most patients with initial reversal (terlipressin, 90.6% [106/117]; placebo, 92.9% [39/42]). Ten patients eligible for retreatment with terlipressin were retreated, with a median time to retreatment of 21 days (range: 12-75 days). Among those retreated with terlipressin, 60% (6/10) achieved HRS reversal. Most patients (70.1% [82/117]) with initial HRS reversal in response to terlipressin treatment were alive at Day 90. Similarly, most patients (90% [9/10]) who initially responded but later required retreatment with terlipressin were also alive at Day 90. Conclusion: Terlipressin retreatment significantly improved HRS reversal, which was durable. Among patients eligible for retreatment with terlipressin due to recurrent HRS-AKI, 6/10 achieved HRS reversal and 9/10 were alive at Day 90. .

Gastroenterology
Chaudhary A, Shahzil M, Hasan F, Muhammad A, **Jomaa D**, Ejaz A, **Faisal MS**, **Dababneh Y**, **Rodrigues PP**, Khaqan MA, and **Jafri SM**. IMPACT OF CLOSTRIDIOIDES DIFFICILE INFECTION ON OUTCOMES IN LIVER TRANSPLANT RECIPIENTS: A COMPREHENSIVE META-ANALYSIS. *Hepatology* 2024; 80:S1072-S1073. Full Text

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Background: Clostridioides difficile (C. difficile) is a Gram-positive, anaerobic, spore-producing bacillus common in the human gastrointestinal tract. Gastrointestinal dysbiosis, often due to antibiotic use, can lead to severe CDI, a frequent healthcare-associated complication, especially in liver transplant (LT) recipients. LT recipients are at higher risk due to compromised immune defenses and other factors. This meta-analysis aims to understand CDI mortality rates, hospital length of stay, MELD scores, PPI use, and CDI recurrence in LT recipients. Methods: This meta-analysis adhered to Cochrane guidelines and PRISMA standards. A comprehensive search was conducted across PubMed, MEDLINE, Embase, Scopus, and CENTRAL databases until October 2023. Inclusion criteria targeted RCTs and observational studies with LT patients. Data extraction followed PICOS criteria using Excel. Statistical analyses utilized RevMan with a random-effects model, considering results significant at $p < 0.05$. Risk of bias was assessed with the Newcastle- Ottawa Scale, and GRADE considerations determined evidence certainty. Results: Of 2144 screened studies, 10 studies with 1,216,500 LT patients were included: 39,309 with CDI and 1,177,191 without CDI. Primary outcomes assessed were mortality and hospital length of stay (LOS). Mortality showed no significant difference (RR: 1.34; 95% CI: 0.38, 4.72). LOS was significantly longer in

CDI patients (mean difference: 6.00 days; 95% CI: 2.83, 9.17). Secondary outcomes included PPI use and MELD scores. PPI use showed no significant association with CDI risk (RR: 2.18; 95% CI: 0.29, 16.27). MELD scores were significantly higher in CDI patients (mean difference: 2.77; 95% CI: 1.34, 4.20). CDI recurrence rate was 14.7%. Risk of bias was assessed with the Newcastle-Ottawa Scale, and evidence quality was evaluated using GRADE, showing moderate quality for most outcomes due to confounding bias and non-randomization. Conclusion: This meta-analysis shows that CDI significantly impacts morbidity and length of hospital stay in liver transplant recipients but does not affect mortality. Patients with CDI had longer hospital stays and higher preoperative MELD scores, highlighting the importance of vigilant postoperative monitoring. Further research is needed to identify specific risk factors and optimize patient outcomes through targeted interventions and preventive measures.

Gastroenterology
Chaudhary AJ, Al-Nabolsi A, Naveed M, Ali A, Iqbal R, Azeem B, Rehan MO, Asim R, Shafique N, **Jafri SM**, and Ashfaque F. Trends in Mortality Due to Pancreatitis Among Patients Aged 55 and Older in the United States: Insights from the CDC WONDER Database. *Am J Gastroenterol* 2024; 119(10):S60-S61. Full Text

A. Al-Nabolsi, Corewell Health Farmington Hills, Dearborn, MI, United States

Introduction: Pancreatitis remains one of the leading causes of death in the elderly in the United States. This study intents to analyze trends and demographic differences in mortality due to pancreatitis among patients aged 55 and older from 1999 to 2020. Methods: We employed a retrospective analysis to calculate age-adjusted mortality rates (AAMRs) per 100,000 persons using data from the CDC WONDER database. Average Annual Percentage Change (AAPC) and Annual Percentage Change (APC) were used to estimate the trends by calendar year, sex, race/ethnicity and geographic region. Results: Between 1999 and 2020, pancreatitis caused 129,208 deaths among older U.S. adults (55+). Most fatalities occurred in medical facilities (68.1%). The overall AAMR for pancreatitis-related deaths decreased from 9.1 in 1999 to 8.2 in 2020, with an AAPC of -0.92 (95% CI: -1.41 to -0.61, P< 0.000001). A moderate decline was seen from 1999 to 2016 (APC: -1.93, P = 0.003199), followed by a sharper increase from 2016 to 2020 (APC: 3.52, P = 0.047590). Stratified by sex, older men had higher AAMRs compared to older women (men: 9.5; women: 6.7). Both genders saw decreased AAMRs, with a slightly more pronounced decrease in women (men: AAPC: -0.91, P< 0.000001; women: AAPC: -1.01, P< 0.000001). Racial disparities were evident, with the highest number of deaths among Whites (78.90%). AAMRs were highest among Black or African Americans, followed by American Indians or Alaska Natives, Whites, Hispanics, and Asians. All racial groups saw variable decreases in AAMRs from 1999 to 2020, with the most pronounced decline in Asians (AAPC: -3.36, P< 0.000001). Geographically, AAMRs varied, highest in West Virginia (12) and lowest in New York (5.9). The Southern region had the highest average mortality (8.5). Nonmetropolitan areas had higher AAMRs than metropolitan areas (9.4 vs 7.6). Both areas saw decreases in AAMRs from 1999 to 2020. Conclusion: This study identifies trends and disparities in pancreatitis mortality among older adults in the US. Despite declining overall rates, differences persist across sex, race/ethnicity, and regions. Targeted interventions and equitable healthcare access are crucial to reduce mortality and enhance outcomes. Further research is needed to understand and address these disparities effectively. (Figure Presented).

Gastroenterology
Chaudhary AJ, **Khan MZ**, Jaan A, Sohail A, **Jomaa D**, Shahzil M, **Manivannan A**, Asif H, **Saleem A**, **Faisal MS**, **Jamali T**, **Faisal MS**, and **Schairer J**. Outcomes of Needle Knife Stricturotomy (NKSt) and NKSt With Balloon Dilation (NKSt-BD) in Patients With IBD Strictures: A Single Center Experience. *Am J Gastroenterol* 2024; 119(10):S1056. Full Text

A.J. Chaudhary, Henry Ford Health, Detroit, MI, United States

Introduction: In recent years, endoscopic balloon dilatation (BD), and needle knife stricturotomy have emerged as safe and effective options for managing strictures associated with inflammatory bowel disease (IBD). These bowel sparing techniques, individually, have gained popularity and served as an alternative to surgical interventions. In this study, we delve into our tertiary care center's experience with

using these techniques simultaneously, to treat IBD related strictures. Methods: A retrospective chart review was performed on patients with Crohn's disease that underwent NKSt alone and NSKt with BD at our tertiary care center between 2018 to 2023. Retrospective demographic, clinical, and procedure-specific information was extracted from the electronic medical record. Patients with strictures related to a disease other than IBD were excluded from the study. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC). Results: In this study involving 50 patients with IBD related fibrotic strictures, 39 (78%) patients underwent NKSt intervention, while 11 (22%) underwent simultaneous NKSt with balloon dilation (NKSt-BD). Patients who underwent NKSt-BD were younger (43.0 ± 10.9 vs 51.2 ± 15.8) and predominantly male (72.7%). (Table 1) NKSt alone was the most common intervention in IBD patients with anastomotic strictures (61.5%) while NKSt-BD was used in 6 patients with anastomotic strictures and 5 patients with non-anastomotic strictures. NKSt-BD was usedmostly for longer strictures (2.76 1.3 cm) and NKSt without BD was used for relatively shorter strictures (1.2 6 1 cm). Bleeding was the most common peri-procedural complication (7.7%) followed by abdominal pain (2.5%) in NKSt group. No complications were observed in the NKSt-BD group. Only 4 patients in the NKSt group developed complications within 10 days of procedure. (Table 1) Symptoms recurred in 9 (23%) patients in NKSt group and 2 (18.1%) patients who underwent NKSt-BD. 15 (38.4%) patients in NKSt group and 7 (63.6%) patients in NKSt-BD had to undergo repeat endoscopy; 1 patient in the NKSt group underwent surgery. Conclusion: Our study demonstrates the clinical and technical success of using NSKt in conjunction with BD compared to NSKt alone. The NSKt-BD group was effective and safer in longer fibrotic strictures, however statistical significance was not achieved likely due to the sample size. More multi-centre studies with larger population size need to be conducted to improve generalizability (see Figure 1).

Gastroenterology

Chaudhary AJ, **Khan MZ**, Naveed M, Jaan A, Iqbal R, Rehan MO, Azeem B, Ali A, Ansari H, Ahmed F, Ullah H, and **Jafri SM**. Trends in Mortality Due to Non-Alcoholic Fatty Liver Disease Among Patients Aged 25 and Older in the United States: Insights from the CDC WONDER Database. *Am J Gastroenterol* 2024; 119(10):S1450-S1451. Full Text

A.J. Chaudhary, Henry Ford Health, Detroit, MI, United States

Introduction: Non-Alcoholic Fatty Liver Disease (NAFLD) is an emerging health concern with increasing mortality rates. This study examines trends and demographic disparities in mortality due to NAFLD among adults aged 25 and older in the United States from 1999 to 2020. Methods: A retrospective analysis was conducted using death data from the CDC WONDER database spanning 1999-2020. Age-adjusted mortality rates (AAMRs) per 100,000 persons were calculated, and trends assessed using Average Annual Percentage Change (AAPC) and Annual Percent Change (APC). Data were stratified by year, sex, race/ethnicity, and geographical regions. Results: Between 1999 and 2020, NAFLD accounted for 71,623 deaths among adults aged 251 in the US Deaths primarily occurred in medical facilities (37.8%) and at decedents' homes (40.9%). The overall AAMR for NAFLD-related deaths increased from 1.1 in 1999 to 3.1 in 2020, with an AAPC of 5.29 (95% CI: 4.80 to 6.04, P < 0.000001). AAMR showed a minor increase from 1999 to 2012 (APC: 1.32, P = 0.150), followed by a striking rise from 2012 to 2020 (APC: 12.07, P < 0.000001). Men exhibited slightly higher AAMRs compared to women (men: 1.6; women: 1.4). The AAMR of women showed a significant increase than men. Racial disparities were evident, with Americans having the highest AAMR (3.7), followed by Hispanics (1.7), Whites (1.6), Blacks (0.9), and Asians (0.6). All racial groups experienced increased AAMRs except Black individuals, who saw a decrease. The increase was most pronounced in Americans (AAPC: 6.08, P < 0.000001).Geographically, AAMRs ranged from 0.8 in Alabama to 2.5 in Oklahoma. The Western region had the highest average AAMR (2.1). Nonmetropolitan areas exhibited higher AAMRs than metropolitan areas (nonmetropolitan: 1.6; metropolitan: 1.5). Conclusion: This study reveals the notable increase in mortality rates due to NAFLD in past 2 decades. Our target population was adult liver disease patients aged 25 and above in the United States. Interestingly, the AAMR has nearly tripled from 1999 to 2020. The results highlights the disparities in race trends and geographic regions. Thus, there is an urgent need for focused interventions which would improve overall health outcomes (Figure 1). .

Gastroenterology

Chaudhary AJ, **Samad M**, **Khan MZ**, Naveed M, Azeem B, Iqbal R, Ali A, Rehan MO, Mohammad T, Ansari H, and Muhibullah F. Trends in Mortality Due to Disorders of Peptic Ulcer Among Patients Aged 55 and Older in the United States: Insights from the CDC WONDER Database. *Am J Gastroenterol* 2024; 119(10):S1660-S1661. Full Text

M. Samad, Henry Ford Hospital, Rochester Hills, MI, United States

Introduction: Peptic ulcer disease remains a significant cause of morbidity and mortality among older adults. This study aims to analyze trends and demographic disparities in mortality due to peptic ulcers among patients aged 55 and older in the United States from 1999 to 2020. Methods: Utilizing data from the Centers for Disease Control and Prevention (CDC) WONDER database, a retrospective analysis was conducted to determine age-adjusted mortality rates (AAMRs) per 100,000 persons. Trends were assessed using average annual percentage change (AAPC) and annual percent change (APC), stratified by year, sex, race/ethnicity, and geographical regions. Results: Between 1999 and 2020, peptic ulcers caused 150,717 deaths among adults aged 55 and older in the US, mostly in medical facilities (66.3%). The overall AAMR decreased significantly from 18.4 in 1999 to 7.7 in 2020, with an AAPC of -4.60 (95% confidence interval [CI]: -5.0 to -4.23, P< 0.000001). Notably, a sharp decline was seen from 1999 to 2009 (APC: -8.53, P< 0.000001), followed by a slower decrease from 2009 to 2020 (APC: -0.86, P5 0.129). Men had slightly higher AAMRs than women (men: 11.3; women: 8.1), with both experiencing decreased rates (men: AAPC: -4.76, P< 0.000001; women: AAPC: -4.16, P< 0.000001). Racially, Whites had the highest AAMR (9.6), followed by Black or African Americans (9.4), Asian or Pacific Islanders (8.9), American Indian or Alaska Natives (8.8), and Hispanic or Latino populations (7.1). All racial groups saw significant declines in AAMRs from 1999 to 2020, with the most substantial decrease in Asian individuals (AAPC: -5.51, P< 0.000001).Geographically, AAMRs varied by state, highest in Vermont (AAMR: 13.6) and lowest in Massachusetts (AAMR: 6.7). The Western region had the highest average AAMR (11.7). Nonmetropolitan areas had slightly higher AAMRs than metropolitan areas throughout, both seeing significant decreases from 1999 to 2020 (Figure 1). Conclusion: This study reveals significant declines in mortality rates due to peptic ulcers among older adults in the United States from 1999 to 2020. However, demographic disparities persist, underscoring the need for targeted interventions and equitable healthcare access to further reduce mortality and improve health outcomes in affected populations. Further research is warranted to explore underlying factors contributing to these disparities and to inform effective public health strategies.

Gastroenterology

Chaudhary AJ, Tepe G, Hafeez N, **Jamali T**, **Khan MZ**, **Adil SA**, and **Ginnebaugh B**. A Rare Case of Colorectal Cancer With Delayed Duodenal Metastasis: A Case Report. *Am J Gastroenterol* 2024; 119(10):S2146-S2147. Full Text

A.J. Chaudhary, Henry Ford Health, Detroit, MI, United States

Introduction: The liver is the most common site of colorectal cancer (CRC) metastasis, followed by the lung, regional lymph nodes, and peritoneum. We present an exceptionally rare case of CRC metastasizing to the duodenum in a patient with a history of resolved stage IV-A ileocecal adenocarcinoma and previous liver metastasis, who had been adherent to post-surgical surveillance. Case Description/Methods: A 42-year-old woman presented with a 2-week history of persistent fatigue, shortness of breath, presyncope, and hematochezia. Her medical history was notable for stage IV-A ileocecal adenocarcinoma with liver metastasis, for which she had undergone a right hemicolectomy and partial hepatectomy, both with negative margins for dysplasia and adenocarcinoma. Subsequent surveillance, including annual carcinoembryonic antigen (CEA) levels and computed tomography (CT) scans, consistently showed no evidence of disease recurrence. However, during the current presentation, the patient exhibited a hemoglobin level of 5.9 g/dL, necessitating a transfusion of 2 units of blood. A CT scan of the abdomen and pelvis with intravenous contrast revealed a central mesenteric mass, measuring up to 3 cm in long axis dimension. This mass invaded the duodenum, encased the superior mesenteric artery, abutted the superior mesenteric vein, and displayed a new 8 mm lesion in the peripheral hepatic segment 5/8. Notably, CEA levels were elevated at 11.1 ng/mL, down from 13.1 ng/mL a year prior. An

esophagogastroduodenoscopy revealed a 3 cm fungating mass in the second part of the duodenum, raising concerns for carcinoma. Biopsies confirmed the presence of invasive adenocarcinoma originating from the colon and metastasizing to the duodenum. Subsequent colonoscopy identified diverticulosis, non bleeding hemorrhoids, and ulcers in the colon. The case was presented to the tumor board, which collectively determined that the patient was not a candidate for surgical resection due to vascular involvement, and palliative care was consulted given the poor prognosis. Discussion: Among CRC patients, the most common cause of death is disease recurrence and metastasis. Despite adhering to current guidelines, our patient developed recurrent metastatic disease in both the colon and duodenum. Further evaluation and possible modification in the guidelines for perioperative surveillance of high-risk patients can help to anticipate disease recurrence and improve health outcomes, particularly as it relates to less common CRC metastatic sites.

Gastroenterology
Chaudhary AJ, Tepe G, **Jamali T**, **Zarrar Khan M**, Shahzil M, **Saleem A**, **Faisal MS**, and **Russell S**. Unique Endoscopic Variations of Asymptomatic Segmental Colitis Associated with Diverticulosis (SCAD): A Case Report. *Am J Gastroenterol* 2024; 119(10):S2388-S2389. Full Text

A.J. Chaudhary, Henry Ford Health, Detroit, MI, United States

Introduction: Segmental colitis associated with diverticulosis (SCAD) is a rare condition characterized by segmental circumferential thickening of the colonic wall, particularly in the sigmoid region, alongside colonic diverticulosis. We present a unique case of asymptomatic SCAD in a 69-year-old man with a significant history of peripheral artery disease (PAD), who exhibited distinctive SCAD findings on colonoscopy. Case Description/Methods: A 69-year-old man patient with an extensive history of PAD requiring multiple vascular stents and right femoral endarterectomy presented with acute right-sided leg pain. Computed tomography angiography was obtained which revealed bilateral superficial femoral artery occlusion and an incidental diffuse sigmoid wall thickening. On review of systems the patient denied any diarrhea, constipation, nausea, vomiting, or hematochezia. Physical exam findings were unremarkable, with no abdominal pain, tenderness, or distension. Despite the patient's benign presentation, given his significant vascular history and concurrent Computed tomography findings colonoscopy was performed to explore potential etiologies such as ischemia or malignancy. Colonoscopy identified multiple diverticula and polypoid lesions, without significant ulceration or inflammation in the sigmoid colon, located between 25 and 30 cm proximal to the anus. This unique endoscopic variation of SCAD has not been reported in existing literature (Figure 1A, B, C, D). Notably, the patient was asymptomatic, differing from typical SCAD presentations. Histopathology was further obtained 30 cm proximal to the anus which revealed colonic mucosa with reactive changes and no evidence of active inflammation, dysplasia, or carcinoma. Ultimately, given the patient's asymptomatic nature, active treatment was deferred and follow-up colonoscopy was scheduled in 3 years. Discussion: The presentation of SCAD is diverse; in this case, our patient was asymptomatic and exhibited atypical findings on endoscopy. Most SCAD cases follow 1 of 4 patterns-A, B, C, or D-but our patient presented outside these typical endoscopic patterns. In addition, our patient denied any history of typical SCAD symptoms including chronic intermittent abdominal pain, non-bloody diarrhea, and hematochezia. By sharing this case, we contribute to the collective knowledge base, enhancing our understanding of atypical presentations in gastrointestinal pathology, particularly SCAD.

Gastroenterology
Chen KY, and **Jafri SM**. An Unusual Case of Peutz-Jeghers Syndrome With ASC. *Am J Gastroenterol* 2024; 119(10):S1761. Full Text

K.Y. Chen, Wayne State School of Medicine, Detroit, MI, United States

Introduction: Peutz-Jaghers Syndrome (PJS) is a rare genetic disorder that clinically presents as mucocutaneous hyperpigmented macules caused by increased melanin in basal cells and hamartomatous gastrointestinal polyps. We present an unusual case of elevated liver enzymes and hematochezia with diagnosis of PJS and ASC. Case Description/Methods: A 19-year-old man with recurrent Clostrioides difficile (C. diff) presents with hematochezia and elevated liver enzymes. The patient has recurrent C. diff infections with diarrhea and alanine transaminase of 199, aspartate

aminotransferase of 68, alkaline phosphatase of 49, and total bilirubin of 1.0. Esophagogastroduodenoscopy (EGD) and endoscopic ultrasound (EUS) of the abdomen reveal enlarged hydropic gallbladder and dilated common bile duct. Colonoscopy for hematochezia detects multiple hamartomatous colon polyps, showing polypoid colorectal mucosa with branching smooth muscle, suggesting PJS. Initial genetic testing is negative for PJS, but the genetics team presumes PJS diagnosis based on the clinical presentation. Endoscopic retrograde cholangiopancreatography (ERCP) shows a moderate biliary stricture in the terminal bile duct requiring stent placement and diffuse intrahepatic rarefaction and beading. Immunoglobulins are elevated with IgG 1 at 1218 and IgG 4 at 149. Anti-nuclear antibody is 1:320 and smooth muscle antibody is 88. Liver biopsy shows portal inflammation and cholangiopathy reflective of autoimmune disease. Prednisone and ursodiol treatment is started for ASC with rapid improvement of liver enzymes and biliary stricture on treatment allowing stent removal. Steroid dosing is tapered due to side effects of steroid-induced obesity and prediabetes. Patient's biliary duct stricture improves over multiple subsequent ERCPs. The patient remains stable with plans for close laboratory and annual endoscopic monitoring. Discussion: ASC is a form of primary sclerosing cholangitis overlapped with autoimmune hepatitis characterized by bile duct sclerosis and liver inflammation. Diagnosis is determined based on histology, imaging, and autoantibody testing. Current treatment of combined immunosuppression and ursodiol are suggested as soon as ASC is diagnosed. PJS is an autosomal dominant disorder caused by a mutation in STK11 (LKB1) on chromosome 19p13.3, a possible tumor suppressor gene. Due to the increased risk of cancer, general cancer screenings and close monitoring of polyps is suggested.

Gastroenterology
Chen KY, and **Jafri SM**. Hyperammonemia-Induced Cerebral Edema Following Transjugular Intrahepatic Portosystemic Shunt (TIPS). *Am J Gastroenterol* 2024; 119(10):S2789. Full Text

K.Y. Chen, Wayne State School of Medicine, Detroit, MI, United States

Introduction: Severe hepatic encephalopathy with elevated ammonia may occur following TIPS. Cerebral edema is a rare and potentially deadly complication. We present a rare case of severe hyperammonemia, cerebral edema, and seizure following TIPS procedure. Case Description/Methods: A 53-year-old man with alcoholic liver cirrhosis presents with gastrointestinal bleeding on apixaban. Evaluation reveals large gastric varices not amenable to endoscopic management for which he undergoes a TIPS procedure. Two months later, the patient presents with confusion, recurrent hematemesis and respiratory failure. The patient receives blood, ceftriaxone, and pantoprazole and undergoes an esophagogastroduodenoscopy (EGD) that shows acute gastritis and multiple small ulcers in the gastric antrum. Bleeding resolves, however the patient experiences severe agitation. Laboratory evaluation reveals significant hyperammonemia (highest > 1000 mcmol/L) and status epilepticus with tonic-clonic movements. The patient receives lactulose and rifaximin without improvement. Continuous renal replacement therapy (CRRT) is started and levetiracetam is administered. Electroencephalogram (EEG) shows generalized encephalopathy and left hemispheric focal disturbances. CT (computed tomography) head indicates cerebral edema with complete effacement to the cerebral sulci and ventricles. TIPS reversal is considered but not performed due to active seizures. Ammonia levels are brought down to normal limits but the patient continues to display acute episodes of jerking movements and posturing. Following discussion with family, care is withdrawn. Discussion: TIPS procedures create a connection between the portal vein and a hepatic vein via a bypass stent-graft that shunts blood away from the portal vein. The procedure is performed as a response to portal hypertension with refractory varices or ascites. Hepatic encephalopathy is a relatively common side effect from the procedure, developing in approximately 10%-44% of patients. Hyperammonemiainduced cerebral edema complicates this particular case. Hyperammonemia may rarely lead to astrocyte swelling due to glutamine accumulation. Cerebral edema is a rare, but serious complication that should be taken into consideration and monitored for following the TIPS procedure and TIPS reversal is suggested as soon as edema complications are discovered.

Gastroenterology
Cox TW, **Ashraf T**, and **Jafri SM**. A Rare Lymphoma Associated With a Ubiquitous Disease: A Case of Gastrointestinal Extra-Nodal Natural Killer/T-Cell Lymphoma. *Am J Gastroenterol* 2024; 119(10):S2924. Full Text

T.W. Cox, Henry Ford Health, Detroit, MI, United States

Introduction: Extra-nodal Natural Killer/T-cell Lymphoma (ENKTL) is a rare extra-nodal lymphoma commonly associated with Epstein-Barr Virus (EBV) infection. This malignancy usually presents in the facial and nasopharyngeal areas. We present an unusual case of ENKTL with a primary locus in the liver. Case Description/Methods: A 38-year-old woman with a medical history of type 1 diabetes mellitus, congestive heart failure, and necrotizing pneumonia is admitted for abnormal liver function tests (LFTs) and accompanying severe abdominal pain. The patient's LFTs show alanine aminotransferase (ALT) 99, aspartate aminotransferase (AST) 179, alkaline phosphatase (ALP) 541, and total bilirubin 0.4. Abdominal computed tomography (CT) shows an ill-defined hyperintensity in the left hepatic lobe of the liver and moderate ascites. Paracentesis is significant for 45% abnormal lymphoid cells possessing NK phenotype. No clonal T-cell receptor gene rearrangement is seen in the sample. Lab evaluation by in-situ hybridization reveals EBV viremia with an elevated viral load of 1,070,006 international units/milliliter. The patient's coagulopathy and liver function continue to worsen. Liver biopsy specimens are obtained and confirm extra-nodal NK-cell lymphoma causing acute liver failure and shock. Chemotherapy is initiated with methotrexate, ifosfamide, and etoposide (mSMILE). The patient soon develops disseminated intravascular coagulation. Tachypnea and hypoxia develop with bilateral pleural effusions and diffuse volume overload requiring thoracentesis. While undergoing chemotherapy, the patient develops a neutropenic fever thought likely due to GI translocation, and requires frequent transfusions due to hematochezia. Due to her precipitous decline, she is transitioned to hospice care less than one month after her initial presentation. Discussion: ENKTL is a malignancy most frequently associated with EBV infection. Though a few potential genetic predispositions have been identified, a direct causal link between ENKTL development and associated EBV infection has yet to be defined. Gastrointestinal presentation of ENKTL is uncommon, and its comparatively worse prognosis is not well understood.

Gastroenterology
Cox TW, **Gordon S**, and **Jafri SM**. An Unusual Case of Cured Hepatitis C But Persistent Liver Enzyme Elevations Leading to Diagnosis of Paget's Disease. *Am J Gastroenterol* 2024; 119(10):S2924. Full Text

T.W. Cox, Henry Ford Health, Detroit, MI, United States

Introduction: Raised serum alkaline phosphatase in the setting of pre-existing liver disease may delay appropriate diagnosis of underlying bone disease. Case Description/Methods: A 73-year-old man patient with polycystic liver presented to the hepatology clinic because of a positive anti-HCV test and confirmed HCV viremia. His past medical history also included right shoulder and bilateral knee osteoarthritis. Laboratory studies showed elevation of aspartate aminotransferase/alanine aminotransferase (AST/ALT) at 41/40 U/L and a raised serum alkaline phosphatase (ALP) of 272 IU/L. Liver stiffness as assessed by transient elastography showed F0-F1 fibrosis and moderate hepatic steatosis. Computed tomography imaging demonstrates smooth liver contour and hepatic cysts measuring a maximum of 2.5 cm in diameter without biliary dilation. The patient was treated with oral glecaprevir-pibrentasvir for 8 weeks and achieved a sustained viral response (SVR). At follow-up after achieving SVR, the alkaline phosphatase remained elevated at 328 IU/L. Additional testing revealed a positive antinuclear antibody titer of 1:160, negative liver kidney microsomal (LKM) antibodies, negative mitochondrial M2 antibodies, negative smooth muscle antibodies, elevated immunoglobulin A, and a normal gamma-glutamyl transferase value. Alkaline phosphatase isozymes showed a high percentage of bone isozyme at 74%, and a low percentage of liver isozyme at 15%. A technetium bone scan shows increased radiotracer uptake in the left hemipelvis, left femoral head, L1 and L4, confirming Paget's disease of those areas. The patient was referred to his primary team for further management and consideration of bisphosphonate therapy. Discussion: Paget's disease of the skeletal system involves a faulty bone remodeling process that can cause fragile and oddly shaped bones to develop. Patients with Paget's disease often have no symptoms, with the disease being discovered incidentally on imaging. When patients do have symptoms, these may include fractures, bone and joint pain, or musculoskeletal deformities. Because pain secondary to Paget's disease can be misdiagnosed as arthritis, it should be ruled out in cases of unexplained elevated ALP, especially in older patients at risk of falls and fractures. In this case, underlying chronic viral hepatitis and polycystic liver delayed the investigation for non-hepatic etiologies of raised serum ALP.

Gastroenterology
Dababneh YJN, and **Salgia RJ**. Atypical Late Presentations of Metastatic Hepatocellular Carcinoma After Liver Transplant. *Am J Gastroenterol* 2024; 119(10):S2809-S2810. Full Text.

Y.J.N. Dababneh, Henry Ford Health, Detroit, MI, United States

Introduction: Liver transplantation (LT) is the primary curative option for hepatocellular carcinoma (HCC). Two cases here exemplify late and atypical metastatic HCC post-LT Case Description/Methods: Case 1: A 67-year-old woman with a history of hepatitis C (HCV) cirrhosis complicated by HCC underwent liver transplantation in 2011. She received pre-transplant treatment Pathology results of the explanted liver revealed 4.5 cm well-differentiated HCC without evidence of any invasion. Post-LT, the patient underwent routine surveillance every 6 months for 5 years. Elevated AFP was noted incidentally 12 years post-LT which led to the discovery of metastatic HCC in the right mesorectal fascia. During surgery an ovoid peritoneal metastasis was found and excised. Pathology revealed moderately differentiated HCC. Despite initiation of tyrosine kinase inhibitor (TKI) therapy, AFP levels exhibited resurgence. Continued surveillance revealed the presence of a new adnexal mass prompting bilateral salpingo-oophorectomy, which confirmed metastatic HCC. Following surgery, AFP levels demonstrated a decline. Case 2:71-year-old man with a history of HCV cirrhosis complicated by HCC underwent LT in 2006. Patient underwent pre-LT treatment. Pathology report of the explanted liver revealed a 3.5 cm moderately differentiated HCC without any invasion. Post-LT surveillance for recurrent HCC was conducted. However,15 years post-LT, AFP was noted incidentally to be elevated at 644 ng/ml. Despite negative initial imaging studies, subsequent surveillance identified 2 masses abutting the sigmoid colon. Biopsy confirmed metastatic HCC. The patient was initiated on TKI-based therapy, with plans for surgery, which revealed extensive peritoneal carcinomatosis. Biopsy confirmed metastatic HCC. Despite therapeutic interventions, AFP levels continued to rise, prompting a shift to second and subsequently third-line systemic therapy. Notably, due to disease progression, patient opted for immune checkpoint inhibitor therapy, which was discontinued due to graft rejection Discussion: These cases demonstrate the challenges with post-LT HCC recurrence. Post-LT surveillance entails imaging studies and AFP assessments up to 5 years. Elevated AFP beyond this period warrants pelvic imaging if standard scans are inconclusive. The feasibility of continued AFP monitoring beyond 5 years needs further research. In summary, late and atypical HCC recurrence post-LT calls for the need for innovative diagnostic approaches to enhance patient outcomes (see Figure 1 Table 1).

Gastroenterology
Darwiche L, **Ashraf T**, and **Jafri SM**. Management of Gastrointestinal Bleeding Due to Esophageal Varices Utilizing Metallic Esophageal Stent. *Am J Gastroenterol* 2024; 119(10):S2173-S2174. Full Text

L. Darwiche, Henry Ford Health, Detroit, MI, United States

Introduction: We present an unusual case of esophageal varices and refractory gastrointestinal bleeding managed with placement of esophageal stents. Case Description/Methods: A 34-year-old woman with a medical history of esophageal varices, alcoholic cirrhosis, portal hypertensive gastropathy, and sickle cell trait presents with hematemesis. Esophagogastroduodenoscopy (EGD) reveals grade II esophageal varices treated with one band. One week later, the patient develops recurrent hematemesis and hemorrhagic shock. Repeat EGD reveals extensive bleeding and low visibility. A Sengstaken-Blakemore tube is placed to temporize the bleeding. Another EGD is completed the following day which shows large .5 mm grade III varices bleeding actively in the lower one-third of the esophagus. The varices are stented with a metallic esophageal stent coated in silicone, placed 25 to 37 cm from the incisors, and 2 hemostatic clips are placed to keep the stent in place. Continued bleeding after stent placement results in a second esophageal stent placed 23 to 33 cm from the incisors. The patient is weaned off pressors without further bleeding. Three days later, a repeat EGD is performed. The esophageal stents are removed with rat-tooth forceps and reveal underlying non-bleeding varices. Slight mucosal irritation from the stents are observed and 4 esophageal bands are placed with complete eradication of the esophageal varices. No active bleeding nor varices are observed in the stomach and the patient stabilizes. The patient does continue to drink and has repeat bleeding episodes over the next year. Varices were

managed with serial banding with no varices on latest endoscopy. Discussion: Many cirrhotics do not respond to conventional band ligation and need alternative treatments such as stents to manage acute esophageal variceal bleeding. Stents can provide temporary management before definitive treatment with banding protocol or transjugular intrahepatic portosystemic shunts (TIPSs). Stents function by compressing varices after expansion in the lower esophagus. Current studies reveal limitations of stents, such as ulceration after stent removal, stent migration causing irritation, and the need for follow-up imaging to confirm stent position and rebleeding. This report summarizes a case in which stent placement successfully controlled bleeding without ulceration or stent migration, and ultimately prevented a fatal outcome.

Gastroenterology
Darwiche L, **Ashraf T**, and **Jafri SM**. Potential Complications With Robotic-Assisted Hepatectomy and Liver Transplant. *Am J Gastroenterol* 2024; 119(10):S2696. Full Text

L. Darwiche, Henry Ford Health, Detroit, MI, United States

Introduction: We present the first completed robotic assisted hepatectomy leading to living donor right lobe liver transplant with complex vascular construction at our institution. Case Description/Methods: An 18-year-old man with a medical history of ulcerative colitis, primary sclerosing cholangitis complicated by liver cirrhosis and refractory pruritus, presents for liver transplantation. The patient is listed for liver transplantation with an altruistic liver donor allowing for scheduled transplantation. A robotic hepatectomy is performed in a piggyback transplant manner. The patient's liver is immobilized and the bile duct is transected above the cystic duct. The hepatic arteries are transected distal to their anterior and posterior branch points. The right and left portal veins are isolated and only the left portal vein is ligated. Once the donor's right liver lobe becomes available, the operation is converted to an open surgery. Tissue is removed off of the inferior vena cava (IVC) and the right hepatic vein is transected. The middle and left hepatic veins and right portal vein are isolated and ligated. A right lateral drain is placed posterior to the right lobe and a right medial drain is placed posterior to the hilum. The donor bile duct is found to be smaller than the recipient bile duct, leading to a bifurcated duct to duct anastomosis. The patient's estimated blood loss is 1.5 liters total for the procedure. Postoperatively, liver enzymes are elevated and white blood cell count rises. A hepatobiliary iminodiacetic acid (HIDA) scan reveals a bile leak. Computed tomography shows a 3 cmfluid collection anterior to the IVC. An endoscopic retrograde cholangiopancreatography (ERCP) confirms a high-grade bile leak and 2 plastic biliary stents are placed. Eighteen days after discharge, the patient presents with drain site pain and green output. Imaging shows 6 cm fluid collection along the superior liver margin requiring additional drain placement with antibiotic and antifungal treatment. Repeat ERCP shows improvement of bile leak. Discussion: Robotic hepatectomy and liver transplant display promising surgical benefits, but the associated learning curve with the procedure can impact outcomes. Studies of robotic hepatectomy reveal shorter operative duration, lower blood loss, and lower complications with more experience. In this case, biliary duct injury with bile leak occurred with our first robotic hepatectomy and liver transplant.

Gastroenterology
Davis W, **Adil SA**, **Varma AK**, and **Bhan A**. Atypical Presentation of Rectal Bleeding: Unveiling Severe Proctosigmoiditis and Concurrent HIV, Syphilis, Gonorrhea, and Chlamydia Infections. *Am J Gastroenterol* 2024; 119(10):S1934. Full Text

W. Davis, Henry Ford Health, Madison Heights, MI, United States

Introduction: Proctitis is defined as inflammation involving the distal rectum. The presenting symptoms can be non-specific, thus takes a careful history and diagnostic work-up for diagnosis and management. We present a case of a 30-year-old man presenting for hematochezia and rectal pain initially attributed to hemorrhoids; however, diagnostic work-up led to diagnosis of infectious proctitis. Case Description/Methods: A 30-year-old previously healthy man presented to the emergency department with a 2-month history of painful rectal bleeding, initially attributed to hemorrhoids on outpatient work up. The severity of his pain led to fear of defecation, food aversion, and a 30-pound weight loss. Despite laxatives, topical creams, and Sitz baths, he found no relief. Upon assessment, he exhibited diaphoresis and

tachycardia. Initial hemoglobin levels revealed a significant drop from his baseline of 13 g/dL to 7.5 g/dL. A rectal examination elicited pain and identified a small external hemorrhoid. Colonoscopy was performed for further evaluation and revealed multiple ulcerated, violaceous, and erythematous plaques from the anal verge to 20 cm and multiple perianal condylomas. Rectal biopsies were taken, revealing severe active proctitis. Due to suspicion of sexually transmitted infections, infectious work up was completed showing positive for HIV (CD4 count: 553, viral load: 85,000), syphilis, along with positive gonorrhea and chlamydia lymphogranuloma venereum. On further history, he reported multiple sexual partners, including men and women that was previously denied. Infectious disease consultation led to initiation of antiretroviral therapy and treatment for syphilis, gonorrhea, and chlamydia. A month after admission, the viral load was undetectable, and hemoglobin levels had risen to 11 g/dL. Patients rectal bleeding had resolved, however continues to report significant rectal pain 1 month after diagnosis. Discussion: As seen in this case, the diagnosis of proctitis can often be delayed and can result in significant patient distress. Our patient's endoscopic findings were consistent with long standing LGV, characterized by diffuse granulomatous lesions. As with our patient, co-infection can often be seen in concomitant HIV. Thus, patients with suspicion of infectious proctitis should have a detailed infectious work up to ensure complete treatment. This emphasizes the importance of a thorough history to guide diagnostic work up for prompt diagnosis and treatment (see Figure 1).

Gastroenterology

Davis W, **Singh B**, **Kutait A**, and **Abbas O**. Malakoplakia Mimicking Metastatic Colon Cancer. *Am J Gastroenterol* 2024; 119(10):S1934. Full Text

W. Davis, Henry Ford Health, Madison Heights, MI, United States

Introduction: Malakoplakia is a rare, chronic granulomatous inflammatory disease that results from impaired histiocyte clearance of bacteria in immune compromised individuals. We present a case of a postlung transplant patient that was suspected to have diffuse colonic metastatic disease based on computed tomography (computed tomography)that was later deemed to be diffuse malakoplakia related to systemic infection. Case Description/Methods: A 62-year-old woman with history of lung transplant on tacrolimus presented with abdominal distension and diarrhea. Vital signs were stable on arrival. Laboratory results including a complete blood count, liver and chemistry panels were noncontributory. Blood cultures repetitively grew Achromobacter xylosoxidans despite escalation of antibiotic therapy. Abdominal and pelvic computed tomography demonstrated gastric distension, and a colonic filling defect at the hepatic flexure with extensive adenopathy evading the duodenal serosa. At this time there were concerns of metastatic colon cancer with concomitant systemic infection. Interventional radiology performed lymph node biopsy revealing malakoplakia and negative for malignancy. Multidisciplinary discussion between infectious disease and gastroenterology was performed with concerns for the colonic filling defect as the origin of patient's persistent bacteremia. Colonoscopy was performed showing diffuse nodularity with ulcerations encompassing the right colon without a targetable lesion for source control. Biopsies were obtained redemonstrating malakoplakia. The patient's hospital course was complicated by COVID-19 pneumonia and ultimately expiring due to respiratory failure. Discussion: Malakoplakia is a poorly understood and rare chronic granulomatous inflammatory disease that results from bactericidal defect of histiocytes. This manifests in an accumulation of phagolysosomes most commonly in immune compromised individuals. Symptoms are non-specific ranging from asymptomatic to altered bowel habits, abdominal pain, rectal bleeding, and intestinal obstruction. Endoscopic appearance can range from flat lesions to multiple ulcerated polypoid nodules. Thus, as in this case, the diagnosis can often be delayed and result in unnecessary interventions until a true diagnosis is achieved. Once diagnosed antibiotic therapy is tailored to the culprit organism resulting an accumulation within histiocytes and killing the bacteria. This case serves to educate the reader of this rare disease presentation to limit extensive work up and expedite treatment (see Figure 1).

Gastroenterology

Dawod S, **Ali SA**, **Khalil N**, **Betcher S**, **Xiong T**, and **Mullins K**. Unexpected Visitors: A Primary Esophageal Melanoma. *Am J Gastroenterol* 2024; 119(10):S2274-S2275. Full Text

S. Dawod, Henry Ford Health, Detroit, MI, United States

Introduction: Melanoma, a malignancy arising from melanocytes, is predominantly associated with the skin, yet its occurrence in extracutaneous sites such as the esophagus is rare, constituting less than 1% of esophageal malignancies. As of 2021, only 347 cases have been reported in the literature. Endoscopically, esophageal melanoma presents with varied appearances, from pigmented spots and patches to amelanotic masses, posing challenges in differentiation from other esophageal tumors. We present a case of primary esophageal melanoma in an 81-year old patient. Case Description/Methods: Our patient is an 81-year-old man with history of metabolic syndrome, esophagitis, and cryptogenic cirrhosis. He presented to the office for evaluation of difficulty swallowing of 3 weeks duration. He denied heartburn, regurgitation, or weight loss. He endorsed preceding cough and fatigue for months prior as well. He was not on any acid suppression therapy. His last esophagogastroduodenoscopy (EGD) was 2 years prior, and was only remarkable for grade I esophageal varices, as well LA grade A esophagitis. His physical exam was unremarkable. He underwent an esophagogastroduodenoscopy (EGD) which showed a large fungating mass that was partially obstructing and partially circumferential, at the level of the middle esophagus. (Figure 1) The mass was sampled, and was consistent with a malignant melanoma. He subsequently underwent full body imaging with PET-CT which was remarkable for paraesophageal lymphadenopathy. (Figure 1) Dermatologic exam was normal. Brain MRI ruled out intracranial metastasis. The patient was referred to oncology and was initiated on immunotherapy. Discussion: Our case highlights a rare instance of esophageal melanoma. Presenting symptoms, such as difficulty swallowing in our 81-year-old patient, often mimic more common esophageal conditions, emphasizing the diagnostic challenges. Esophageal melanomas tend to be aggressive, as evident by his normal EGD 2 years prior, with a high risk for metastasis. Therapeutic options for esophageal melanoma remain challenging due to its rarity, with surgery being a cornerstone, often complemented by immunotherapies. However, the absence of standardized treatment guidelines accentuates the need for ongoing research to establish optimal therapeutic strategies. Its rarity calls for a multidisciplinary approach involving gastroenterologists, oncologists, surgeons, dermatologists and pathologists in forming personalized treatment plans for optimal patient outcomes.

Gastroenterology

Dean R, Yazdanfar M, Zepeda JB, Patel I, Levy C, Lammert C, Bordia R, Cosar D, Specht K, Pratt D, **Gordon S**, Forman L, Barry F, Li M, Assis D, McGirr A, McLaughlin M, Mukherjee S, Gungabissoon U, and Bowlus C. INVESTIGATING THE CHOLESTATIC PRURITUS OF PRIMARY SCLEROSING CHOLANGITIS (ITCH-PSC): A CROSS SECTIONAL STUDY OF PATIENTS PARTICIPATING IN THE CONSORTIUM FOR AUTOIMMUNE LIVER DISEASE (CALID). *Hepatology* 2024; 80:S1801-S1802. Full Text

R. Dean, University of California Davis, Mississauga, Canada

Background: Primary Sclerosing Cholangitis (PSC) is a chronic cholestatic liver disease with no approved treatment and few effective off-label therapies to reduce the symptom burden. Pruritus is frequently reported by patients with PSC, but only limited data exist using patient-reported outcomes measures. ItCh-PSC aims to characterize the frequency and severity of pruritus and determine its impact on quality of life and relationship with biomarkers of pruritus in patients with PSC. Methods: Patients aged 18 and older, diagnosed with PSC and without a liver transplant were enrolled at 7 centers. Itch numeric rating scale (NRS), 5-D Itch, PSC-PRO, and SF-36 were completed and serum collected. For the NRS, patients reported their average and worst itch (WI) in the past 24 hours, 7 days, and 6 months. Colitis activity was assessed in patients with inflammatory bowel disease (IBD) by the Simple Clinical Colitis Activity Index (SCCAI). Total serum bile acids (TSBA) and liver biochemistries were measured. Results: A total of 200 patients were enrolled (51% male; mean (SD) age of 46.0 (15.4) years; 71% White, 11% Black/African American; 15% cirrhosis). Most patients (77%) had large duct PSC while 4% had small duct PSC and 2% had PSC-AIH. IBD was present in 79% (57% ulcerative colitis/19% Crohn's disease/3% indeterminate). WI in the past 24 hours, 7 days, and 6 months was reported as moderate-to-severe (WI-NRS > 4) by 42 (21%), 48 (24%), and 76 (38%) patients, respectively. WI-NRS in the past 7 days was greater in patients with cirrhosis ($P = 0.02$); and correlated with 5-D Itch ($r = 0.75$), PSC-PRO ($r = 0.69$), and SF-36 physical component ($r = -0.47$) and mental component ($r = -0.32$) scores ($P < 0.0001$ for all); but did not differ by age, sex, race, PSC type, or IBD status. Among patients with IBD, SCCAI was greater in those with worse

WI-NRS. Average and WI-NRS scores reported at all times correlated with alkaline phosphatase, AST, albumin, total and direct bilirubin, and TSBA. Among 48 patients with an WI-NRS > 4 in the past 7 days, antihistamines were used by 19 (40%), bile acid binding resins by 12 (25%), rifampin by 7 (15%), sertraline by 4 (9%), and fenofibrate by 4 (8%). Conclusion: Patient-reported moderate-to-severe pruritus in this large cohort of patients with PSC was common and correlated with advanced liver disease; worsening cholestasis; and impaired quality of life, but medical treatment of moderate-to-severe pruritus in this group was infrequent.

Gastroenterology
Dunn W, Alkhouri N, Yip TCF, Castera L, Takawy M, Adams L, Verma N, Arab JP, **Jafri SM**, Zhong B, Dubourg J, Chen V, Singal A, Díaz LA, Dunn N, Nadeem R, Wong V, Abdelmalek M, Wang Z, Duseja A, Almahanna Y, **Omeish H**, Ye J, Harrison S, Arrese M, Robert S, Wong GLH, Bajunayd B, and Shao C. ENHANCING PREDICTION OF MODERATE FIBROSIS OR HIGHER IN MASLD PATIENTS FOR RESMETIROM TREATMENT VIA MACHINE LEARNING. *Hepatology* 2024; 80:S553-S555. Full Text

W. Dunn, University of Kansas Medical Center, Rochester, United States

Background: The recent FDA approval of Resmetirom for treating Metabolic Dysfunction-Associated Steatohepatitis (MASLD) in patients with moderate to advanced fibrosis necessitates precise patient selection for liver biopsy. Currently, a Vibration-controlled Transient Elastography (VCTE) based algorithm FAST is utilized to diagnose at-risk MASH (≥ F2 + NAS 4). However, no existing VCTE-based algorithm effectively targets moderate fibrosis or higher (≥F2) alone. The mAchine Learning ADvanceD fibrosis and at-risk mash Novel predictor (ALADDIN) study addresses this gap by introducing a novel machine learning-based web calculator that estimates the likelihood of moderate fibrosis using routine laboratory parameters with and without VCTE measurements. Methods: A total of 3708 patients with biopsy-confirmed MASLD from six centers worldwide were divided into Training and Test Set on a 1:1 basis, supplemented by 1289 patients from nine centers for External Validation. ALADDIN models, employing Random Forest, Gradient Boosting Machines, and XGBoost enhanced by Bayesian updates, were developed to evaluate moderate fibrosis (stage ≥ F2). Results: In the Test Set, the ALADDINF2-VCTE model demonstrated an Area Under the Curve (AUC) of 0.789 (95% CI 0.767-0.810), significantly outperforming the FAST model (AUC: 0.663, 95% CI 0.637-0.689, p <0.0001). In the External Validation Set, this model maintained an AUC of 0.796 (95% CI 0.769-0.823), again outperforming FAST (AUC: 0.705, 95% CI 0.673-0.737, p < 0.0001). The ALADDIN-F2-Lab model, which employs routine laboratory parameters without VCTE, achieved an AUC of 0.762 (95% CI 0.741-0.784) in the Test Set and 0.735 (95% CI 0.708-0.762) in the External Validation Set. The 95% CI for the difference in AUCs was 0.075 to 0.129 in the Test Set and -0.014 to 0.061 in the External Validation Set. It did not exceed the preset noninferiority margin Δ of -0.1. Furthermore, the ALADDIN-F2-VCTE model demonstrated superior calibration, decision curve analysis, and classification accuracy using a dual cut-off approach compared to the FAST model. Conclusion: The VCTE-based ALADDIN-F2-VCTE model, accessible through ALADDIN1, has demonstrated superior performance compared to established VCTEbased indices, FAST, for diagnosing moderate fibrosis or higher. As the only model specifically developed to target moderate fibrosis or higher using VCTE, ALADDIN-F2-VCTE uniquely supports the refined selection of patients, potentially reducing the necessity for liver biopsies and allowing more patients to receive appropriate treatment with Resmetirom. Additionally, the ALADDIN-F2-Lab model, employing routine laboratory parameters without VCTE, accessible through https://aihepatology.shinyapps.io/ ALADDIN2/, offers an effective alternative when VCTE is unavailable, facilitating broader application in clinical practice. (Figure Presented).

Gastroenterology
Espiritu C, Ganchua S, Eley T, Gray K, Yuen MF, Heo J, Nahass R, Wong G, Burda T, Bhamidimarri KR, Hu TH, Nguyen TT, Lim YS, Chen CY, **Gordon S**, Holmes J, Chuang WL, Kohli A, Alkhouri N, Lam A, Sofia M, Sims K, and Thi E. SOLUBLE IMMUNE BIOMARKER PROFILING OF CHRONIC HEPATITIS B SUBJECTS TREATED WITH IMDUSIRAN IN COMBINATION WITH PEGYLATED INTERFERON ALFA REVEALS PHASES OF IMMUNE ACTIVATION. *Hepatology* 2024; 80:S307-S308. Full Text

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Background: Functional cure of chronic hepatitis B (CHB) requires suppression of viral replication, reduction of HBV antigens and induction of anti-HBV immune response. Pegylated interferon alfa-2a (IFN) is a standard of care immunomodulator with limited efficacy against HBV. Imdusiran (AB-729, IDR) is an N-Acetylgalactosamine- conjugated single trigger siRNA targeting all HBV RNA transcripts, resulting in suppression of all viral antigens including HBsAg. In an ongoing Phase 2a study assessing IDR as lead-in (24 weeks) followed by 12 or 24 weeks of IFN ± additional IDR doses in HBeAg-negative CHB subjects virally suppressed on nucleos(t)ide analog (NA) therapy (AB-729-201, IM-PROVE I), soluble immune biomarkers were profiled and association with HBsAg response assessed. Methods: Longitudinal plasma samples were collected from 43 subjects during the 24-week IDR lead-in, IFN treatment and follow-up periods. Soluble immune biomarkers were assessed using Luminex multiplex panels (58 analytes). Results: Transient increases ≥3 to 31-fold from baseline in immune biomarkers associated with immune activation (sCD40, sCD28, sCD80, sCD86), Th1 cell-mediated response (IL- 6, IL-12 p40, IL-12 p70, IL-7, IL-10), inflammation regulation (GROa, PDGF-AA, PDGF-AB, VEGF), and immune checkpoint proteins (PD-1, PD-L1, CTLA-4, LAG- 3, BTLA) were observed during IDR lead-in, with peaks occurring during the plateau of HBsAg reduction in assessed subjects to date. Elevations occurred again during IFN treatment, during which time increase in the Th2 cytokine IL-5 was also observed. At 24 weeks post IFN treatment, 6 subjects achieved HBsAg loss and HBsAg seroconversion. 5/6 subjects with HBsAg loss had greater Th1/inflammation-related responses during IDR lead-in or IFN treatment compared to those without HBsAg loss. Further increases in Th2 cytokines IL-4 and IL-13 after end of IFN treatment were associated with HBsAg seroconversion. Conclusion: IDR treatment in combination with IFN was associated with distinct phases of soluble immune biomarker signatures. Immune biomarkers associated with Th1 immune activation and regulation of inflammation were observed in subjects during IDR lead-in, coinciding with the establishment of a plateau in HBsAg reduction. Secondary transient elevations of these immune biomarkers were observed to occur during IFN treatment and were followed by appearance of Th2 immune biomarker signatures that were associated with HBsAg seroconversion.

Gastroenterology

Faisal MS, **Chaudhary AJ**, **Saleem A**, **Abusuliman M**, **Kostecki P**, **Ahmad Adil S**, **Faisal MS**, **Yudovich A**, and **Entz A**. Esophagitis and Melena: A Rare Presentation of Stevens-Johnson Syndrome. *Am J Gastroenterol* 2024; 119(10):S2463-S2464. Full Text

M.S. Faisal, Henry Ford Health, Detroit, MI, United States

Introduction: Esophageal involvement in Stevens-Johnson syndrome (SJS) is relatively rare but can occur. It may manifest as focal ulcerations or diffuse esophagitis, potentially leading to bleeding and melena in severe cases. We present a case of a patient who presented with severe esophagitis and gastrointestinal bleeding as the presenting symptom of SJS. Case Description/Methods: A 67-Year-old-man presented to the emergency department with confusion, agitation and productive cough. These symptoms had progressively worsened over a week. He had no relevant past medical history. On initial presentation, he was found to be febrile, tachypneic and tachycardic. Chest X-Ray was concerning for lobar pneumonia and the patient was started on Vancomycin and Cefepime for hospital-acquired-pneumonia. On day 7 of admission, the patient had 3 melenic stools with a Hemoglobin drop from 8.4 g/dl to 6.7 g/dl within 24 hours. The patient was transfused with 2 units of packed RBCs and underwent an Esophagogastroduodenoscopy (EGD) for evaluation. EGD findings included severe esophagitis with stigmata of recent bleeding, 1 gastric ulcer with mild oozing and 2 duodenal ulcers. Patient was started on Intravenous Pantoprazole and Carafate. Over the next 2 days, the patient had continued melena and drops in Hemoglobin requiring frequent blood transfusions, along with sloughing of skin in the groin and oral mucosa. SJS with oral and esophageal involvement was suspected and the patient was started on IV steroids. Antibiotics were discontinued considering they could be the offending agent. A cutaneous biopsy confirmed SJS. The patient passed away 3 days after the EGD due to complications of the disease Discussion: Esophagitis and Gastrointestinal bleeding have a wide range of differential diagnosis, including Gastroesophageal reflux disease, Peptic ulcer disease and esophageal varices. Although typically recognized for its cutaneous manifestations, SJS can also present with gastrointestinal complications which can precede cutaneous symptoms. Esophageal manifestations of SJS include ulceration, esophagitis, strictures and potentially melena. Management focuses on supportive care and

withdrawal of causative agents. Early recognition of SJS in such presentations is crucial for improved outcomes. This case highlights the need for heightened awareness among clinicians to consider SJS in differential diagnoses of unexplained melena, despite its rarity in causing gastrointestinal bleeding. (Figure Presented).

Gastroenterology
Faisal MS, Fatima M, **Saleem A**, **Chaudhary AJ**, Shahzil M, **Abusuliman M**, **Faisal MS**, and **Jafri SM**. Association of Glucagon-Like Peptide-1 Therapies and Risk of Cancer in Liver Transplant Patients. *Am J Gastroenterol* 2024; 119(10):S1368. Full Text

M.S. Faisal, Henry Ford Health, Detroit, MI, United States

Introduction: Patients who undergo liver transplantation are at higher risk of complications from diabetes and obesity. Glucagon-like peptide-1(GLP-1) analogues have revolutionized management of these conditions and are increasingly being used in post-transplant patients. However, the safety of these agents in this population, particularly their association with cancer risk, is controversial. We aimed to assess the association of semaglutide and tirzepatide with cancer in patients who undergo liver transplant. Methods: All patients who underwent liver transplant at our institution were included from 2018-2023. We did a retrospective cohort study to assess whether they received GLP-1 analogues, including semaglutide and tirzepatide, before and after liver transplant. Data including patient demographics, comorbidities and exposure was collected. Primary outcome was development of malignancy. Secondary outcomes were 1-and 3-year mortality. Results: Overall, 366 patients underwent liver transplant from 2018-2023. Of these, 42(13%) were exposed to semaglutide or tirzepatide while 324(88%) had no such exposure after transplant. No patients were exposed before transplant. The mean age was 58.12 +/- 7.6 in the exposed group and 58.44 +/- 11.5 in the control group. 14(33.6%) were female in the exposed group while (119) 36.7% were female in the control group. 37(88.1%) in the exposed group had diabetes while 111(34.2%) in the control group had diabetes(P<0.001). Similarly, 28(66.7%) patients in the exposed group had BMI >30 while 111(34.5%) patients in the control group had BMI >30(P<0.001). Follow up period was 3.74 +/-1.3 years 4.01 +/-1.5 years in the exposed and control groups respectively. In this period, 2(4.8%) patients in the exposed group were diagnosed with cancer versus 26(8.1%) in the control group (P=0.76). There was no cancer related mortality at 1 year while at 3 years, it was similar in both groups. For malignancies, 1(50%) patient in the exposed group had HCC, while 5(18%) patients in the control group had either HCC or CCA. No patient in the exposed group was diagnosed with skin malignancies, while 13(46%) patients in the control group were diagnosed with such malignancies. 11 in the control group were diagnosed with other malignancies including lymphoma, follicular thyroid cancer, and leukemia. Conclusion: The use of semaglutide and tirzepatide was not associated with cancer in patients who undergo liver transplantation. We were limited by single center and smaller number of patients (see Table 1).

Gastroenterology
Faisal MS, **Obri M**, **Faisal MS**, **Nimri F**, **Dawod S**, **Youssef RM**, **Chaudhary AJ**, **Alluri S**, **Dang D**, **Watson A**, **Elatrache M**, **Singla S**, **Piraka C**, **Pompa R**, and **Zuchelli T**. Utility of Imaging in Predicting Biliary Strictures Post Liver Transplant. *Am J Gastroenterol* 2024; 119(10):S107-S108. Full Text

M.S. Faisal, Henry Ford Health, Detroit, MI, United States

Introduction: Post liver transplant biliary strictures are a common complication following orthotropic liver transplantation. ERCP with stenting is the standard of care for management of these strictures. However, ERCP carries risks of infection, bleeding and pancreatitis. Therefore, confirming strictures on imaging can prevent unnecessary procedures. We aimed to assess the accuracy of MRI/MRCP and CT prior to ERCP in predicting biliary strictures. Methods: All patients who had ERCP post-transplant for biliary strictures were included in the study from 2015-2022. We then retrospectively assessed whether they had MRI/MRCP or CT prior to ERCP to look for a biliary stricture. If imaging was obtained, we assessed whether it was suspicious for biliary stricture as characterized by focal narrowing and upstream biliary dilation. We assessed the factors that were associated with either a positive or a negative image prior to ERCP. Results: Eighty-nine patients were confirmed to have a post-transplant anastomotic biliary stricture

on ERCP during this time. The mean age of the population was 59.74 +/- 10.8 years. Thirty-3 (37.1%) were female and 73% were White 73%. Median days post-transplant for initial ERCP was 68 (IQR 30-175). Stenting was done for 98.9% of the patients. Initial stenting was done by plastic stents in 91.0%. There was documented removal of stone and sludge in 64.0% of the cases. Main complications encountered were post ERCP pancreatitis in 5.6% and cholangitis 4.5%. MRCP was done prior to ERCP in 44 (49.4%) of cases and it was definitive for a stricture in 33 cases (75%). CT was done prior to ERCP in 27 (30.3%) of cases. It was definitive for a stricture in 9 patients (33.3%). 83 (93.3) had recurrent strictures after initial ERCP requiring further stenting. Median number of procedures following initial stenting was 1 (Range 1-7). Patients who had MRCP diagnostic for stricture had the test done further from transplant median 110 (IQR 47-221) days, compared median 64 (IQR 30-200) days post transplant in patients who had MRCP negative for a stricture (P=0.09) possibly indicating improved accuracy of MRCP further away from transplant. Conclusion: ERCP with stenting is the standard of care for post-transplant biliary strictures. While CT does not appear to be accurate in diagnosing post-transplant biliary strictures, MRCP prior to ERCP can be a safe and effective noninvasive test to define anatomy and confirm a stricture (Figure Presented).

Gastroenterology
Faisal MS, **Saleem A**, **Chaudhary A**, Fatima M, Shahzil M, **Abusuliman M**, **Faisal MS**, and **Jafri SM**.
NO INITIAL INCREASE IN CANCER RISK WITH GLUCAGON LIKE PEPTIDE-1 THERAPIES FOLLOWING LIVER TRANSPLANTATION. *Hepatology* 2024; 80:S1050-S1051. Full Text

M.S. Faisal, Henry Ford Hospital, Detroit, MI, United States

Background: Patients who undergo liver transplantation are at higher risk of complications from diabetes and obesity. Recently, Glucagon-like peptide-1(GLP-1) analogues have revolutionized management of these conditions and are increasingly being used in post-transplant patients. However, the safety of these agents in this population, particularly their association with cancer risk, is controversial. We aimed to assess the association of semaglutide and tirzepatide with cancer in patients who undergo liver transplant. Methods: All patients who underwent liver transplant at our institution were included from 1/2018-12/2023. We did a retrospective cohort study to assess whether they received GLP-1 analogues, including semaglutide and tirzepatide, after the liver transplant. Data including patient demographics, comorbidities and exposure to semaglutide or tirzepatide were collected. Primary outcome was development of malignancy. Secondary outcomes were 1-and 3-year mortality. Results: 366 patients were included who underwent liver transplant from 01/2018-12/2023. Of these, 42 (13%) were exposed to semaglutide or tirzepatide while 324 (88%) had no such exposure. The mean age of the population was 58.12 +/- 7.6 in the exposed group and 58.44 +/- 11.5 in the control group. 14(33.6%) were female in the exposed group while (119) 36.7% were female in the control group. Comorbidities, including HTN, stroke and ESRD were comparable in both groups. 37(88.1%) in the exposed group had diabetes while 111(34.2%) in the control group had diabetes($p<0.001$). Similarly, 28(66.7%) patients in the exposed group had BMI>30 while 111(34.5%) patients in the control group had BMI>30($p<0.001$). The follow up period was 3.74 +/-1.3 years for the exposed group and 4.01 +/-1.5 years in the control group. For outcomes, 2(4.8%) patients in the exposed group were diagnosed with cancer in the follow up period versus 26(8.1%) in the control group ($p=0.76$). There was no cancer related mortality at one year while at 3 years, it was similar in both groups. For malignancies, 1(50%) patient in the exposed group had HCC, while 5(18%) patients in the control group had either HCC or cholangiocarcinoma. No patients in the exposed group were diagnosed with skin related malignancies including BCC, SCC and Malignant Melanoma, while 13 (46%) patients in the control group were diagnosed with such malignancies. 1 patient in the exposed group was diagnosed with Post Transplant Lymphoproliferative Disorder. 11 patients in the control group were diagnosed with other malignancies including prostate cancer, lymphoma, follicular thyroid cancer, and leukemia. Conclusion: In our cohort, the use of semaglutide and tirzepatide was not associated with cancer in patients who undergo liver transplantation. We were limited by single center and smaller number of patients. Further large scale, multicenter studies are needed to confirm the safety of these medications.

Gastroenterology

Fatima M, Shahzil M, **Faisal MS**, Khalid A, Munir L, Qureshi AA, Rehmani M, **Javaid Chaudhary A**, Ali Khaqan M, and **Faisal MS**. Trends and Disparities in Chronic Hepatitis-Related Mortality in the United States, 1999-2020: An Epidemiological Analysis. *Am J Gastroenterol* 2024; 119(10):S1227. Full Text

M. Fatima, King Edward Medical University, Punjab, Lahore, Pakistan

Introduction: Chronic hepatitis caused 1.1 million deaths in 2019 and 1.3 million in 2022 according to World Health Organization. These results underline the impact of behavioral, environmental and cultural factors despite available testing and treatment. This study analyzes trends in chronic hepatitis-related mortality from 1999 to 2020, using age-adjusted mortality rates (AAMR) to identify patterns across demographic and regional populations. Methods: Data from Centers for Disease Control Wonder database, examining chronic hepatitis-related death trends from 01/1999 to 12/2020, using International Classification of Diseases-10 code K73.0., was collected. AAMRs per 100,000 population and average annual percentage change (AAPC) were calculated. Annual percentage change (APC) with 95% Confidence Interval (CI) was assessed to understand AAMR trends. Mortality rates were standardized to the 2000 United States Population and Joinpoint was used for regression analysis across various demographics. Age trends were studied in pediatric, young adults, middle adults, and older adults groups. The Monte Carlo Permutation Procedure (MCPP) analyzed mortality trends. Statistically significant results were determined with a P-value < 0.05. Results: From 1999 to 2020, there were 8,862 chronic hepatitis B related deaths. Mortality declined, with age-adjusted rates (AAR) showing a consistent decrease. The APC was -2.46 from 1999-2002, -31.0 from 2002-2005, and -2.86 from 2005-2020. A significant decrease was seen in Northeast and Midwest. Females experienced a steeper decline from 2002-2005 (APC: -41.39, P=0.003883, CI [-57.94, -18.32]), while males declined from 2001-2007 (APC: -13.23, P=0.000405, CI [-17.99, -8.20]). Black individuals had higher mortality with a significant decrease until 2007 (APC: -17.90, P=0.000019, CI [-23.53, -11.85]), while White individuals saw declines from 2002-2005 (APC: -31.16, P=0.006319, CI [-46.37, -11.64]). Urban areas showed significant drops from 2002-2005 (APC: -31.10, P=0.009090, CI [-47.09, -10.27]). High mortality was seen in the 65-74-year group before 2002 but evened out across age groups afterward (Figure 1). Conclusion: This study reveals a decline in chronic hepatitis-related mortality from 1999 to 2020 with disparities across gender, race, and regions. Females and Black individuals experienced higher but decreasing mortality rates and urban areas saw substantial drops, especially from 2002 to 2005. Even then, high mortality persisted in the 65-74 age group before 2002. Targeted public health interventions are essential to address these disparities and disease burden. (Table Presented).

Gastroenterology

Gholam P, **Gordon S**, Jesudian A, Nair S, Russo M, Black R, and Cardoza S. THE IMPACT OF TERLIPRESSIN TREATMENT ON LIVER TRANSPLANTATION RATES IN PATIENTS WITH HEPATORENAL SYNDROME-ACUTE KIDNEY INJURY (HRS-AKI) IN THE CONTEXT OF THE CHANGING MELD SCORE DEFINITIONS ? *Hepatology* 2024; 80:S1633-S1634. Full Text

P. Gholam, Cleveland Medical Center, United States

Background: HRS-AKI is a lethal complication of cirrhosis. Liver transplantation (LT) is the only curative option for patients (pts) with HRS-AKI. In the US, organ priority allocation is based on the Model for End-Stage Liver Disease (MELD) score. MELD-sodium (MELD-Na) score has been used since 2016; and in 2023, MELD 3.0 (which also includes albumin and sex) replaced MELD-Na. Terlipressin (terli) is the only US FDA-approved drug for the treatment of HRS-AKI. However, the reduction in MELD score, secondary to an improvement in serum creatinine (sCr) due to HRS reversal, may negatively affect pt prioritization for LT. To assess outcomes in pts who would be eligible for treatment per the terli FDA label (ie, MELD score <35 if transplant listed, sCr <5 mg/dL, and acute-on-chronic liver failure [ACLF] grade 0-2, henceforth referred to as the mitigated population), we evaluated the LT rate and changes in the 3 MELD score variants in this population. Methods: The rate of LT up to the end of the study observation period (ie, 90 days) and change from baseline to the end of treatment in MELD, MELD-Na, and MELD 3.0 scores were retrospectively assessed in the mitigated population from the Phase III pbo-controlled

CONFIRM study (NCT02770716). Results: LT rate by Day 90 was 22.7% (30/132) and 21.1% (15/71) in the terli and pbo arms, respectively (P =.793); 2.3% (3/132) and 1.4% (1/ 71) of pts, respectively, received a simultaneous liverkidney transplant (SLKT) (P = 1.0) (Figure). The median time to transplantation was 22 days (terli arm) vs 11.5 days (pbo arm; P= .147). Data to calculate changes in MELD scores were available for 107/132 pts in the terli arm and for 55/71 pts in the pbo arm. All 3 MELD scores decreased from baseline to the end of treatment in the terli arm (all P< .001), but not in the pbo arm. Median score changes were -3.0 in MELD, -4.0 in MELD-Na, and -6.0 in MELD 3.0 in the terli arm, while changes for all 3 MELD scores in the pbo arm were 0. The difference in changes between the terli and pbo arms was significant in all cases (all P < .01). Conclusion: Improvement in MELD due to terli treatment did not lead to a decrease in transplantation rate, despite a decrease in all 3 MELD score variants for terli vs pbo in the mitigated population. The rates of LT and SLKT in this population were similar in both treatment arms.

Gastroenterology
Gordon R, **Ashraf T**, and **Jafri SM**. Diagnostic and Therapeutic Challenges in Hypereosinophilic Syndrome. *Am J Gastroenterol* 2024; 119(10):S2331. Full Text

R. Gordon, Wayne State University, School of Medicine, Oak Park, MI, United States

Introduction: Hypereosinophilic syndrome (HES) is a heterogeneous group of disorders characterized by sustained overproduction of eosinophils. Normally involved in responses to parasites and allergens, excessive eosinophils can cause tissue infiltration and organ damage. We present a case of an adult woman with asthma, allergies, and reflux, presenting with abdominal pain and ascites. Case Description/Methods: A 42-year-old woman's symptoms began after an allergic reaction with generalized urticaria. Despite resolution with antihistamines, she developed severe pruritus, generalized abdominal pain, nausea, vomiting, and diarrhea. Her symptoms continued to persist 1 month later and she was ultimately hospitalized. Her white blood count was noted to be elevated at 22.0x10/L with predominant eosinophils at 8.80x109/L. Computed tomography scan shows moderate ascites, mild bowel wall thickening, and a mildly thickened appendix. Subsequent paracentesis reveals exudative fluid with 85% eosinophils. She tested positive for Clostridioides difficile and started oral vancomycin. Upper endoscopy and colonoscopy showed patchy eosinophils throughout the gastrointestinal tract. Her abdominal pain and diarrhea improves and she is discharged home. As an outpatient, her eosinophilia increases to 15.31x109/L, prompting referral to an allergist and immunologist. Normal serum IgE and tryptase levels ruled out common allergic and mast cell disorders. A prednisone taper is initiated, improving her pruritus and urticaria. Hematological assessment reveals hypereosinophilia in peripheral blood, normocellular marrow with maturing trilineage hematopoiesis, and no evidence of lymphoproliferative disorder or metastatic carcinoma. Genetic testing shows normal karyotype and no significant mutations or fusions. Fluorescence in situ hybridization analysis was normal for all tested regions. Family history is noncontributory. Her symptoms and eosinophilia improve on steroids, normalizing over the next 6 months. However, 4 months later, the patient develops recurrent abdominal pain and nausea refractory to medication. She is diagnosed with idiopathic HES and begins treatment with mepolizumab. Discussion: HES is marked by sustained eosinophil overproduction, leading to organ damage. Early identification and intervention are crucial to prevent irreversible damage and improve outcomes. Comprehensive diagnostics, including bone marrow biopsy and genetic testing, are essential to rule out hematologic malignancies and other causes of eosinophilia.

Gastroenterology
Gordon R, **Jamali T**, and **Jafri SM**. Complicated Course of Herpes Simplex Virus (HSV) Hepatitis in a Young Female With Systemic Lupus Erythematosus. *Am J Gastroenterol* 2024; 119(10):S2946-S2947. Full Text

R. Gordon, Wayne State University, School of Medicine, Oak Park, MI, United States

Introduction: Herpes Simplex Virus (HSV) hepatitis is a viral-induced hepatitis that can rapidly progress into acute liver failure (ALF) and death if rapid diagnosis and prompt intervention are not pursued.We present an interesting case of HSV-2 related hepatitis in a young female with recurrent genital infections, fevers, chills and body aches. Case Description/Methods: A 29-year-old woman with a past medical

history of hypertension, pulmonary cavitary lesions, and nephrotic range proteinuria presents with complaints of fevers, chills and body aches for over one month. Laboratory evaluation reveals pancytopenia, hematuria, nephrotic range proteinuria, antinuclear antibody positive to 1:1280 and positive SSA. The patient is diagnosed with systemic lupus erythematosus (SLE) and lupus nephritis and is started on hydroxychloroquine, mycophenolate, and steroids. She then develops acute encephalopathy and seizures, attributed to posterior reversible encephalopathy syndrome (PRES). PRES is confirmed by magnetic resonance imaging (MRI) and no cerebral edema is noted. The patient develops persistent fevers and transaminitis, originally believed to be related to medication. Doppler ultrasound of the liver is unremarkable. Physical examination reveals mucocutaneous herpetic lesions and HSV-2 DNA by polymerase chain reaction (PCR) is detected, suggesting HSV hepatitis. At this time, the patient exhibits elevated levels of aspartate transaminase (AST) at 233 IU/L, alanine transaminase (ALT) at 312 IU/L, alkaline phosphatase (ALP) at 168 IU/L, and creatine at 1.89 mg/dL. Bilirubin levels and prothrombin time/international normalized ratio are within normal limits. Patient was treated with 2.5 mg/kg IV acyclovir daily for 2 days and is then discharged on 1g valacyclovir twice daily for 3 weeks. Following completion of course, the patient still presented with extensive genital ulcers and continued to test positive for HSV-2 DNA in blood, so she is prescribed 400 mg valacyclovir twice daily. Two months later, her AST, ALT, ALP, and creatinine values decrease to within normal limits and mucocutaneous lesions are absent. Discussion: HSV hepatitis is a rare form of viral-induced hepatitis with nonspecific symptoms such as fever, encephalopathy, and elevated liver enzymes that particularly affects immunocompromised individuals. While the gold standard for HSV hepatitis is a liver biopsy, empiric antiviral treatment in cases of suspected HSV hepatitis based on serology may be warranted to minimize morbidity and mortality.

Gastroenterology

Hartgerink C, **Moonka D**, and **Jafri SM**. A Rare Case of Spontaneous Regression of Hepatocellular Carcinoma. *Am J Gastroenterol* 2024; 119(10):S2738-S2739. Full Text

C. Hartgerink, Wayne State University, School of Medicine, Detroit, MI, United States

Introduction: Spontaneous regression of hepatocellular carcinoma (HCC) is a rare, but not unprecedented, phenomenon. Here, we present a case of a large HCC tumor which regressed without treatment. Case Description/Methods: A 73-year-old man with a past medical history of hepatitis C (treated with confirmed sustained virologic response) and HIV infection well controlled on antiretroviral therapy presented to clinic with abdominal pain, nausea and 20-pound weight loss over 3 months. He was found to have a palpable abdominal mass in the right upper quadrant tender to palpation. Computed tomography (CT) demonstrated a large, complex mass measuring 7.7 x 9.0 x 10.7 cm occupying the medial segment of the left hepatic lobe with a combination of tumor and bland thrombus extending into the left portal vein (Figure 1A). Alpha fetoprotein (AFP) was elevated at 73,279 ng/mL. CT-guided core needle biopsy demonstrated poorly-differentiated HCC with extensive necrosis. Liver synthetic function was preserved with no evidence of cirrhosis on transient elastography. Patient was also found to have small left lower lobe pulmonary emboli and placed on apixaban. The patient was not a candidate for liver transplant or surgical resection. A repeat CT scan 6 weeks after diagnosis showed interval decrease in the mass to 7.6 x 5.8 x 8.6 cm but with continued extension into the left portal vein (Figure 1B). The patient was scheduled for systemic therapy with atezolizumab and bevacizumab, but he declined therapy for HCC. Eight months after initial diagnosis, AFP had decreased to 54.8 ng/dL. A third CT scan 10 months after the initial diagnosis showed remarkable regression of the mass (Figure 1C). Without treatment, the HCC regressed to 3.0 x 2.6 cm with an 11 mm nodule of faint enhancement and washout consistent with a small nidus of residual tumor. Left portal vein involvement was no longer seen. The patient declined further follow-up. Discussion: Although rare, cases of spontaneous HCC regression have been reported. Proposed mechanisms for spontaneous HCC regression include tumor hypoxia and systemic immunological reactions. In this case, necrosis was seen on the biopsy suggesting tumor regression may have already been occurring at the time of diagnosis potentially from ischemia. The primary blood supply for HCC is the hepatic artery, but the tumor may have outgrown its arterial supply or tumor invasion may have disrupted the artery. Thrombus involvement of the left portal vein may have further contributed to coagulative necrosis.

Gastroenterology
Hartgerink C, **Todd E**, **Nagai S**, **Muszkat Y**, **Beltran N**, and **Jafri SM**. Safety and Tolerability of Everolimus in Intestinal and Multivisceral Transplantation Patients. *Am J Gastroenterol* 2024; 119(10):S1590. Full Text

C. Hartgerink, Wayne State University, School of Medicine, Detroit, MI, United States

Introduction: Intestinal and multivisceral transplant patients are at high risk for renal dysfunction after transplant. In other solid organ transplants, everolimus has been shown to have renal-sparing benefits, and everolimus may be useful for preserving renal function in intestinal transplantation. However, data are limited regarding the use and tolerance of everolimus in intestinal and multivisceral transplantation patients. Methods: We performed a retrospective analysis of patients who had an intestinal or multivisceral transplant at a single tertiary care center between 2012 and 2022. Patients who were placed on everolimus at any time after transplant were included in the study. Data extracted included length of time on everolimus and reason for discontinuing everolimus. Results: A total of 15 patients, 9 isolated intestinal transplant patients and 6 multivisceral transplant patients, were included in the study. The mean age at time of transplant was (47.0 ± 9.8) years and 53% (8/ 15) patients were women. Everolimuswas started an average of (25.1 ± 25.9) months after transplant, with a range of 1 month to 102 months. Average duration of everolimus therapy was (557.2 ± 751.4) days with a range of 4 to 2437 days. Of the 15 patients placed on everolimus, 60% (9/15) of patients were on everolimus for at least 90 days. Ultimately, 87% (13/15) of the patients were removed from medication due to side effects or complications. 47% (7/15) of patients remained on medication 1 year following initiation and 20% (3/15) of patients remained on medication 3 years following initiation. The most common reason for stopping everolimus was developing diarrhea (5 patients). The other reasons for discontinuing everolimus were to improve wound healing in the setting of surgery (3 patients), severe systemic infection (3 patients), peripheral edema (1 patient), and oral ulcers (1 patient). No patients died while being treated with everolimus. Conclusion: In summary, this retrospective study of 15 patients indicates that tolerability of everolimus in intestinal and multivisceral transplant patients is highly variable. Diarrhea, concern for wound healing, and severe infection were the most common reasons for discontinuing everolimus. These are all labeled adverse reactions of everolimus, as well as common issues faced by intestinal and multivisceral transplant patients at baseline. Clinicians should be aware of the adverse reactions and the high rate of intolerance in these patients when considering everolimus. .

Gastroenterology
Jafri SB, and **Kutait A**. Assessment of General Public Attitudes Regarding Transplantation for Alcoholic Liver Disease. *Am J Gastroenterol* 2024; 119(10):S1366. Full Text

S.-B. Jafri, Henry Ford Health, Detroit, MI, United States

Introduction: Management of alcoholic hepatitis has changed across the field of liver transplant emphasizing history of recidivism, social support and commitment to sobriety.We evaluated attitudes among the general public regarding alcoholic hepatitis and alcoholic cirrhosis 5 years following the alcoholic liver disease consensus conference. Methods: Participants with no relation to the medical field completed a detailed survey regarding attitudes surrounding case examples with acute alcoholic hepatitis with recent alcohol use and no recidivism and alcoholic cirrhosis and recent alcohol use with clear history of recidivism. Responses were collected regarding time to transplant listing, psychosocial requirements, and post-transplant testing. Results: As regards alcoholic hepatitis with no recidivism, 90% of respondents felt patients should be listed, but only 53% embraced immediate listing; 32% felt patients should wait 6 months. Forty-seven percent felt zero support persons should be required for listing, 11% felt 1 person, 26% 2, and 16% 3. Eighty-four percent felt patients should be listed even with no relatives or friends. Seventy-nine percent felt patients must agree to relapse prevention at some point to be listed, 47% felt relapse prevention should completed prior to listing, and 58% felt patients should not be required to agree to ongoing lab draws to assess sobriety following transplant. As regards alcoholic cirrhosis with recent recidivism, 90% of respondents felt patients should be listed, 74% embraced immediate listing with 16% wanting 6 months wait time, 53% felt zero support persons should be required, 90% felt patient

should be listed if they can produce no social support, 63% felt they should not get transplant if refusing relapse prevention, 47% felt relapse prevention should be completed prior to listing, 68% felt they should not be listed if they feel unable to remain sober, 47% felt patient should not be required to agree to ongoing lab draws to assess sobriety following transplant. Conclusion: Evaluation of the general public attitudes regarding liver transplant for alcoholic hepatitis without recidivism and alcoholic cirrhosis with recidivism revealed strong desire to list and transplant these patients. The public did not embrace need for social support requirements but did embrace need for relapse prevention. This study emphasizes room for public education regarding management of alcoholic liver disease including the importance of social support following liver transplantation.

Gastroenterology
Jamali T, **Nimri F**, **Dababneh YJN**, **Patel-Rodriguez P**, **Adil SA**, **Tosch K**, **Faisal MS**, **Zuchelli T**, and **Pompa R**. A Rare Case of a Large Duodenal Lipoma Resulting In Intussusception and Gastric Outlet Obstruction. *Am J Gastroenterol* 2024; 119(10):S3027-S3028. Full Text

T. Jamali, Henry Ford Health, Farmington Hills, MI, United States

Introduction: Duodenal lipomas are uncommon benign lesions containing fat cells, and the vast majority of cases are asymptomatic. Larger lesions can result in abdominal pain, gastrointestinal bleeding, and obstruction1. Here, we report a rare case of a large duodenal lipoma that had resulted in intussusception and gastric outlet obstruction. Case Description/Methods: A 45-year-old man with progressive symptoms of poor oral intake, nausea, vomiting, and early satiety for a few months was referred to our center for further evaluation of a large submucosal lesion found on recent esophagogastroduodenoscopy (EGD). Repeat EGD revealed a large lesion protruding through the pylorus and extending into the duodenum to the level of the major papilla resulting in duodenal obstruction (Figure 1A). The length of this lesion was at least 6-7cm, and the stalk/base was wide (4-5cm). The major papilla was not involved. The patient was referred to surgical oncology outpatient, however he presented 1 month after initial endoscopy with gastrointestinal bleeding. Repeat EGD revealed the same gastroduodenal lesion with a small superficial ulcerated area and evidence of old blood. Bleeding resolved spontaneously, so no endoscopic treatment was performed. Given worsening symptoms of obstruction and bleeding, patient was evaluated for earlier surgery. He underwent distal gastrectomy with duodenal resection and Roux-en-Y gastrojejunostomy. He tolerated the procedure well and was discharged 6 days post-operatively with a full liquid diet. Surgical pathology (Figure 1B) revealed a submucosal lipoma with fat necrosis (9.4 cm in greatest dimension) and no evidence of dysplasia or malignancy. Discussion: We present this case to highlight an extremely rare presentation of a large duodenal lipoma resulting in bleeding, intussusception, and gastric outlet obstruction. Initial diagnosis can be made with cross-sectional imaging, endoscopy, and/or endoscopic ultrasound. Although there are no clear guidelines for management of these lesions, endoscopic excision is usually favorable. However, for larger lesions, surgical excision may be the more optimal approach. Endoscopists should be aware of the endoscopic/endosonographic features, locations, and unique clinical presentations of these rare lesions.

Gastroenterology
Jamali T, **Nimri F**, and **Jafri SM**. An Unusual Complication of Variceal Band Ligation: Complete Esophageal Obstruction. *Am J Gastroenterol* 2024; 119(10):S2215. Full Text

T. Jamali, Henry Ford Hospital, Detroit, MI, United States

Introduction: Here we present a rare case of esophageal obstruction as a sequela of variceal banding. Complications after variceal band ligation can include: perforation, variceal bleeding, stricture formation. Complete esophageal obstruction with symptoms of dysphagia as a result of variceal band ligation has very scarcely been reported in the literature. Case Description/Methods: A 73-year-old woman with a history of decompensated cirrhosis (with ascites and large varices) secondary to metabolic associated steatotic liver disease presented initially as an outpatient for variceal screening. On upper endoscopy, she was found to have large varices in the distal esophagus and 6 variceal bands were placed successfully. One day after this procedure, patient presented to the hospital with nausea, vomiting, and blood streaked emesis. Her hemoglobin was stable around her baseline at 11 g/dL. There was no significant bleeding

after initial presentation. Patient was managed with supportive care and intravenous fluids in the hospital. Due to lack of improvement in tolerance of oral intake, a water-soluble esophagram was performed which showed contrast accumulated in the distal esophagus that did not pass into the stomach (Figure 1). There was no evidence of perforation. These findings were suspected to be consistent with esophageal obstruction as a sequela of engorged varices from variceal banding and post-banding edema. The patient was started on parenteral nutrition and advised to avoid oral intake temporarily. One week later, patient was able to tolerate liquid diet, and she was then advanced slowly to regular diet. She tolerated a regular diet well and parenteral nutrition was discontinued. Repeat endoscopy was scheduled to be completed in another 4 weeks for variceal surveillance. Discussion: Complete esophageal obstruction following variceal band ligation is an extremely rare complication. Our case demonstrates that these patients can be managed conservatively to allow time for postprocedural edema to resolve and allow for the varices to decompress. Esophagram is usually favored over repeat endoscopy in this setting to reduce risk of dislodging bands and causing further bleeding. Endoscopists should be aware of this potential complication, so that patients can be triaged appropriately and appropriate testing and management can be pursued.

Gastroenterology
Khan MZ, **Chaudhary AJ**, Shahzil M, Jaan A, Sohail A, **Manivannan A**, Asif H, **Saleem A**, **Faisal MS**, **Adil SA**, **Alluri S**, **Faisal MS**, and **Schairer J**. Needle-Knife Stricturotomy (NKSt) for IBD-Related Strictures: A Single-Center Experience. *Am J Gastroenterol* 2024; 119(10):S971-S972. Full Text

M.Z. Khan, Henry Ford Health, Detroit, MI, United States

Introduction: In recent years, various endoscopic treatment options have emerged for managing strictures associated with inflammatory bowel disease (IBD) and non-IBD conditions. Among these, needle knife stricturotomy (NKSt) has gained attention as a novel approach. By avoiding or delaying surgery, NKSt offers a potential alternative for patients with fibrotic strictures. In this study, we delve into our tertiary care centre's experience with NKSt, exploring its efficacy and role in treating strictures. Methods: A retrospective chart review was performed on patients with Crohn's disease who underwent NKSt at our tertiary care center between 2018 to 2023. Retrospective demographic, clinical, and procedure-specific information was extracted from the electronic medical record. Patients with strictures related to a disease other than IBD were excluded from the study. Results: In this study involving 48 patients, 30 (62.5%) had anastomotic strictures (AS), while 18 (37.5%) exhibited non-anastomotic strictures (NAS). Demographically, both populations were comparable across all variables assessed. Treatment approaches varied; anti-TNF agents were predominantly used in the AS cohort. (Table 1) At the time of NKSt, steroids were being used by 4 (22.2%) NAS patients and 7 (23.3) AS patients. Abdominal pain was the chief symptom for both groups (NAS: 61%; AS 56.7%) The colon was identified as the most frequent stricture location in both subgroups (AS: 33.3%, NAS: 27.7%). Non-anastomotic strictures had a marginally greater mean length (1.58 ± 0.36 cm) compared to AS (0.9 ± 0.5 cm). In addition to the NSKt, balloon dilatation was performed concurrently on 5 NAS patients (28%) and 6 AS patients (20%). No peri-procedural complication was observed in either group. Symptom recurrence was observed in 22% of NAS cases and 23% of AS cases post-procedure. Subsequent endoscopic intervention was necessary for half of the participants; however, surgical intervention was not required for any patient within either group. Conclusion: In recent times endoscopic stricturotomy has emerged as a safe and effective way of treating AS, and non-AS. The rates of complications in our study were low and the patients had an uneventful procedural course. Previous case series have demonstrated the efficacy of this intervention in strictures , 3 cm such as in our study. With a small sample size being a limitation of this study, we aim to gather more data to increase generalizability and compare NKSt with other endoscopic methods (Figure 1).

Gastroenterology
Kostecki P, **Jomaa D**, and **Pompa R**. Rare Case of Thymoma Metastasizing to the Liver as an Incidental Finding. *Am J Gastroenterol* 2024; 119(10):S2847. Full Text

P. Kostecki, Henry Ford Hospital, Detroit, MI, United States

Introduction: Thymomas are the most common anterior mediastinal mass but make up less than 1.5% of adult malignancies. The occurrence is 0.13 cases per 100,000 person-years. The 2021 WHO classification includes 6 types: A, AB, B1-3 and thymic carcinoma. Staging is based on tumor capsule invasion, locoregional spread, lymph node involvement, and distant metastasis. They can present asymptomatically or with paraneoplastic syndromes, like Myasthenia Gravis. They carry malignant potential regardless of type or stage and can recur despite resection. The 5-year survival for nonresectable metastatic disease is 24%. We present a case of an asymptomatic thymoma with rare, isolated liver metastasis that was identified incidentally Case Description/Methods: An 89-year-old man presented with acute urinary retention, attributed to benign prostatic hyperplasia (BPH). CT imaging revealed a significantly enlarged prostate (.10 cm). He had previously declined treatment for BPH. Incidental imaging findings included a 1.9 cm lesion in the left hepatic lobe and a 6.8 x 5.2 cm mass in the aortopulmonary window. Subsequent CT chest showed a left anterior mediastinal mass, and biopsies confirmed malignant thymoma with Type B2 features. An MRI of the abdomen redemonstrated the hepatic mass, which grew 1.3 cm over 4 years. Endoscopic ultrasound (EUS) guided biopsy of the liver confirmed metastatic thymoma. PET-CT did not suggest other metastatic sites. Thoracic tumor board recommended radiation to the primary site and liver. Systemic chemotherapy and surgery were not advised due to his age, social support, and functional status. He completed 30 fractions of radiation to the mediastinum and 3 of 5 fractions to the liver. He continues to require a chronic foley catheter for BPH Discussion: We present a rare case of metastatic B2 thymoma isolated to the liver, identified only in 3 other reports. A 2023 review found only 39 cases of extra-thoracic thymoma metastasis, with 12 involving the liver; 5 were types B1 or B2 and liver was the only site in 3 cases. Thymomas often spread locally within the mediastinum, with rare distant metastasis. Extra-thoracic metastasis occurs in 3-6% of cases Despite surgical resection, recurrence rates vary, and prognosis can be poor. Given the unpredictable nature of thymomas, close surveillance with regular CT or MRI is recommended. Advanced endoscopy could also play a role in monitoring and diagnostic for indeterminate findings (see Figure 1).

Gastroenterology

Kowdley K, Ghali MP, Bonder A, **Gordon S**, Rahimi R, Kostrub C, Nunes T, Shelton J, Garner W, Vig P, and Alkhouri N. PILOT STUDY OF VOLIXIBAT CO-ADMINISTERED WITH OCA FOR PRIMARY BILIARY CHOLANGITIS (PBC) TREATMENT: THE VLX-602 TRIAL. *Hepatology* 2024; 80:S1829-S1830.
Full Text

K. Kowdley, Liver Institute Northwest, Seattle, WA, United States

Background: PBC is a progressive inflammatory cholestatic disease with liver bile flow impairment and destruction of intrahepatic bile ducts. Bile acid (BA) levels are commonly elevated with disease severity and progression with cholestatic pruritus being a debilitating complication. Volixibat (VLX) is an ileal bile acid transporter (IBAT) inhibitor that interrupts BA uptake in the small intestine, leading to greater BA fecal elimination with subsequent reductions in the systemic BA pool. IBAT inhibitors have shown efficacy to treat cholestatic pruritus, including in PBC, but concurrent use of an IBAT inhibitor and obeticholic acid (OCA) is not well studied. VLX-602 is a pilot study to evaluate the safety of VLX (80 mg BID) in participants with PBC who were on active treatment with OCA (5 or 10 mg). Methods: VLX-602 was a multicenter, open-label study that enrolled patients with PBC with ongoing treatment with OCA for ≥ 3 months with a stable ALP level. The study consisted of screening (14 days), study treatment (OCA + VLX, 6 weeks), and follow-up (1 week) periods. Safety was assessed by TEAE collection and laboratory measurements, including liver chemistry. Other assessments included: 7aC4, sBA, PK and autotaxin levels, along with the itch PROs (PIS-Itch, WI-NRS, and PGICItch). Results: Six participants were enrolled, all female, with mean age of 56.5 years. The most common TRAE was diarrhea (83.3%). Other TRAEs that affected 1 participant each (16.7% each) were nausea, fatigue, and vomiting. Other TEAEs (not related to study drug) that affected 1 participant each (16.7% each) were toothache, nasopharyngitis, and upper respiratory tract infection. No severe, serious, or events that led to study discontinuation or death were reported. Mean levels of AST, ALT, total bilirubin, and ALP were stable between baseline and end of the treatment period. Overall, 3 participants showed improvement in their itch scores for both WI-NRS and PIS-Itch while on VLX. At the follow-up visit, after VLX was discontinued, 3 and 4 participants had worsening in their WI-NRS scores and PIS-Itch scores, respectively. Conclusion: These safety pilot study data were consistent with the known safety profile of IBAT inhibitors. The addition of VLX to OCA

treatment in PBC led to improvement in itch in some patients, with reversal of the effect upon VLX cessation. The results of this study justify additional investigation of the safety and efficacy of VLX for the treatment of PBC, with or without a background regimen of OCA.

Gastroenterology
Manas F, **Davydov E**, **Caines A**, **Estrada K**, and **Shill JE**. A Case Report Of Drug-Induced Liver Injury Secondary To Sublingual Estradiol In A Transgender Woman. *J Endocr Soc* 2024; 8:A532-A533. Full Text

F. Manas, Henry Ford Health System, Detroit, MI, United States

Drug-induced liver injury (DILI), the leading cause of acute liver failure in the United States, occurs in response to a medication or natural compound. Estrogens can lead to idiosyncratic DILI. According to LiverTox [livertox.nih. gov], estrogen has a likelihood score of A (highly likely) to cause DILI, whereas spironolactone has a likelihood score of D (rare). The current formulations of estrogens usually produce a mixed or cholestatic pattern of liver enzyme elevations, however very early, the ALT levels can be markedly elevated (5- to 20-fold). One can be asymptomatic. Often the liver injury resolves after removing the offending agent. We present a case of DILI with elevations of both alanine transferase (ALT) and aspartate transferase (AST), secondary to sublingual estradiol (E2). A 23-year-old transgender female presented for feminizing gender-affirming care. She was started on sublingual E2 2 mg once daily and spironolactone 100 mg orally twice daily. Approximately 14 weeks later, sublingual E2 was increased to 2 mg twice daily for a below-target E2 level, and spironolactone was decreased to 50 mg twice daily due to gas and nausea. Routine blood work three weeks later showed elevated liver function tests (LFTs) in a hepatocellular pattern with ALT of 216 IU/L (normal:<52IU/L), AST of 223 IU/L (normal:<35 IU/L), with normal total bilirubin and alkaline phosphatase. LFTs were normal six months prior. At the time of liver injury, she had consumed six alcoholic beverages in the previous fourteen days, and two doses of acetaminophen. She had no personal history of autoimmunity and no family history of liver disease. Acute hepatitis screen was normal. Abdominal US with liver Doppler was unremarkable. E2 and spironolactone were discontinued. Evaluation by hepatology lead to a diagnosis of DILI from sublingual E2, based on the temporal relationship between initiation of E2 and LFT elevation. Other potential causes of elevated LFTs were excluded. Although she reported alcohol use, the AST/ALT elevation was not in a classic 2:1 pattern. Three weeks after cessation of E2 and spironolactone, her LFTs normalized. Spironolactone was resumed along with E2 by patch, but due to skin-adherence issues she was transitioned to injectable E2 valerate. Her LFTs have remained normal since. This case illustrates a rare but potentially dangerous adverse event of DILI secondary to sublingual E2. Due to the low incidence of liver injury in various studies of individuals with gender incongruence on hormone therapy, current evidence does not support routine liver enzyme monitoring. Clinicians should be aware of the potential risk of liver injury and counsel patients accordingly. As in this case, patients may be successfully rechallenged with the offending DILI medication. Further studies on different formulations of hormone therapy and their effects on the liver would be beneficial in this unique population.

Gastroenterology
Mandiga P, **Salin N**, and Turk I. A Rare Case of Endometriosis of the Sigmoid Colon. *Am J Gastroenterol* 2024; 119(10):S1988. Full Text

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Introduction: Endometriosis is a condition characterized by ectopic implantation of endometrial tissue (endometrial glands and stroma) beyond the confines of the uterine cavity. The exact frequency is hindered by the fact that many women with endometriosis remain asymptomatic and undiagnosed. Current estimates suggest 10-15% of women of reproductive age will have endometriosis (1). The ectopic presence of endometrial tissue can lead to a range of symptoms, including pelvic pain, painful menstrual periods and infertility. Severity can vary and in some cases could be asymptomatic.While endometrial tissue typically confines itself to the pelvic region, it is rare to encounter its infiltration into the colon. This becomes more exceptional when the growth manages to penetrate the entire mucosa of the sigmoid colon. In light of the rarity of such occurrences, we present a case of a young woman with endometriosis

of the sigmoid colon. Case Description/Methods: A 30-year-old woman with morbid obesity, endometriosis presents with progressive worsening of sharp, lower abdominal pain, constipation with bright red blood per rectum. Initial labs indicated microcytic anemia with Hgb of 10.7 computed tomography abdomen pelvis revealed GE junction thickening and extensive endometriosis with adhesions inseparable from the sigmoid colon and a suspected hydrosalpinx (Figure 1A). A sigmoidoscopy showed extrinsic compression and intraluminal narrowing in the sigmoid colon, attributed to the bulky endometriosis. There was one specific area within the rectosigmoid junction that showed abnormal tissue with erosion and stigmata of recent bleeding likely consistent with endometriosis with intramural penetration (Figure 1B, C). Biopsy confirmed the diagnosis of endometriosis. A multidisciplinary team recommended surgical excision, but concerns about sparing the uterus led to a challenging decision. Ultimately, the patient opted for outpatient follow-up with potential future consideration of surgery. Discussion: This extraordinary case underscores the complexity and varied presentation of endometriosis, urging a deeper exploration into its pathogenesis and the implications for both diagnosis and treatment. Several theories proposed about the pathogenesis of endometriosis, but none of them were conclusive and able to explain the range of the clinical pictures of the disease. We are hoping with this case to shed light on the intricate puzzle of endometriosis so we get closer to unraveling its mystery and advancing more targeted and effective treatment.

Gastroenterology

Nabaty RM, **Agha YH**, and **Suresh S**. Unmasking Intestinal Plasmablastic Lymphoma in an Immunocompetent Crohn's Disease Patient. *Am J Gastroenterol* 2024; 119(10):S2567. Full Text

R.M. Nabaty, Henry Ford Health, Detroit, MI, United States

Introduction: Plasmablastic lymphoma (PBL) is a rare and aggressive subtype of diffuse large B-cell lymphoma. Originally reported in the oral cavity of immunocompromised Human immunodeficiency virus (HIV) patients, it has also been associated with immunosuppression and Epstein-Barr virus (EBV) infection. It commonly manifests in extranodal sites like the GI tract, especially in patients with inflammatory bowel disease (IBD). Diagnosis is challenging due to histological similarities with plasmablastic myeloma, but factors like EBV status and myeloma-defining signs aid in differentiation. We present a rare case of an HIV-negative, immunocompetent, patient with Crohn's disease post proctocolectomy and end-ileostomy who presented with acute blood loss anemia and was found to have small bowel PBL. Case Description/Methods: A 75-year-old man with a history of Crohn's disease and adenocarcinoma of the colon, status post total proctocolectomy with abdominoperineal resection and end-ileostomy, presented with ileostomy bleeding and a significant hemoglobin decrease. He underwent bi-directional endoscopy. Upper endoscopy was unremarkable. Ileoscopy was notable for an obstructing and circumferential ulcerated mass in the distal ileum and severe luminal stenosis. Biopsies of the mass revealed high-grade neoplasm with plasmocytic phenotype, consistent with PBL. CT enterography revealed a long segment of small bowel wall thickening in the right abdomen and numerous distant abdominal lymph nodes, and no evidence of metastasis. Upon follow-up with oncology, he began chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone. Discussion: PBL, while primarily associated with HIV patients, has been reported in HIV-negative patients with IBD, and more frequently in Crohn's disease. This has been hypothesized to be attributed to immunosuppressive therapy or an immunocompromised state. While rare in presentation, reported cases of primary GI-PBL have presented with progressive odynophagia, melena, obstruction, hematochezia, and B symptoms commonly seen in malignancy. There is a paucity of literature on GI-PBL, limited to case series and reports. Our case highlights a primary GI-PBL associated with Crohn's disease in an immunocompetent patient with no history of HIV or EBV. To date, a treatment regimen has not been well defined. Despite treatment advancements, PBL patients have an average survival of 19 months. Thus, it is vital to consider GI-PBL on the differential and continue research on this rare and diagnostically challenging malignancy.

Gastroenterology

Nimri F, **Jamali T**, Nimri R, **Hammad T**, **Zuchelli T**, and **Singla S**. Simultaneous Occurrence of Adenocarcinomas in the Stomach and Biliary Tree: A Rare Case Report. *Am J Gastroenterol* 2024; 119(10):S1822. Full Text

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Introduction: Synchronous adenocarcinomas in stomach and biliary tree are extremely rare phenomenon, with very scarce literature. The factors leading to the development of synchronous primary cancers within the gastrointestinal (GI) tract remain poorly understood, but genetic predisposition, environment and molecular alterations may play a role. Case Description/Methods: A 66 year old man with history of hypertension, dyslipidemia, and prostate cancer was evaluated by hepatology clinic for new and persistent elevation of liver enzymes (LFTs) on routine check-up with alanine aminotransferase of 137 IU/L, aspartate aminotransferase of 60 IU/L, and alkaline phosphatase of 415 IU/L, while he had normal total bilirubin of 0.8 mg/dL, and INR 0.99. All LFTs were normal a year ago. He denied any associated symptoms. Further testing including viral hepatitis panel, autoimmune liver diseases, and hemochromatosis testing were negative. Liver US was normal. Magnetic resonance imaging with magnetic resonance cholangiopancreatography revealed a 2cm central lesion with left intrahepatic biliary ductal dilatation and questionable delayed enhancement. Advanced GI performed esophagogastroduodenoscopy which showed an ulcerated and friable tumor on the gastric antrum greater curvature concerning for malignancy and was biopsied. Endoscopic ultrasound to characterize the mass showed invasion into at least the muscularis propria. Endoscopic retrograde cholangiopancreatography revealed a single moderate biliary stricture found in the left main hepatic duct. Exploration with cholangioscopy demonstrated focally abnormal epithelium concerning formalignancy, and was biopsied and brushing performed for fluorescence in situ hybridization (FISH) and cytology. The right hepatic duct was not involved though could be secondarily compressed. Common bile duct and CHD were normal. A biliary sphincterotomy was performed.The stricture was dilated to 4 mm (with persistent waist) then stented with a 7 Fr by 12 cm straight plastic biliary stent. Pathological analysis of both gastric and left main hepatic duct stricture revealed moderately differentiated adenocarcinoma. FISH Bile Duct Malignancy panel showed evidence of trisomy 7 which has only a little evidence to suggest that trisomy 7 meets the criteria for a diagnosis of cholangiocarcinoma. Discussion: This case report highlights a rare occurrence of simultaneous diagnosis of 2 adenocarcinomas, one in the stomach and the other in the biliary tree. It is challenging to determine whether these are 2 primary adenocarcinomas in 2 anatomically separate sites versus one primary lesion while the other is a metastatic lesion of that primary. Such a presentation is extremely rare and proposes challenging clinical diagnostic and therapeutic scenarios. (Figure Presented).

Gastroenterology

Nimri R, **Nimri F**, **Jamali T**, **Varma AK**, and **Jafri SM**. Herb Hazard: Ashwagandha Induced Liver Injury. *Am J Gastroenterol* 2024; 119(10):S2785. Full Text

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Introduction: We present a case of medication related liver injury secondary to ashwagandha. Ashwagandha is an Ayurvedic herb, found as an over-the-counter herbal preparation, used mainly for its proposed anti-inflammatory effects. Ashwagandha is thought to be safe from a liver perspective, but recently there have been case reports of possible liver injury with its use. Case Description/Methods: A 62-year-old woman with a past medical history of migraine headaches, and hyperlipidemia, presented to the ED with acute onset of sharp right upper quadrant pain with nausea and vomiting for one day. Diagnostic work-up revealed elevated ALT 229, AST 333, total bilirubin (TB) 1.4 with direct (DB) 0.6, and alkaline phosphatase (ALP) 101. Liver enzymes (LFT) were normal a month prior on routine check. Otherwise, INR, CBC, BMP, troponin, and lipase are normal. Further work-up revealed normal Acetaminophen levels, autoimmune liver panel including (Anti-mitochondrial, antismooth muscle, and anti-liver-kidney microsomal antibodies), alpha-1 antitrypsin protein, ceruloplasmin, iron, ferritin, and creatine phosphokinase, as well as negative acute hepatitis screen (hepatitis A, B, C), hepatitis E, EBV, CMV, VZV, HSV, COVID-19, and influenza testing. CT of abdomen and pelvis showed mild gallbladder wall thickening without gallstones, pericholecystic fluid or biliary ductal dilatation. Abdominal US showed partially contracted gallbladder with no evidence of acute cholecystitis. No stones visualized. No intrahepatic or extrahepatic biliary dilatation. HIDA scan was also negative. She denied any alcohol intake, family history of liver disease or any Tylenol use. Full review of systems was negative. A careful review of her medications revealed that she was taking Pravastatin for years, but started taking

Ashwagandha 5 days prior to presentation for 2 days then stopped it because it made her feel ill. LFTs the next day showed ALT 477, AST 248, TB 2.0, DB 0.5, ALP 87. Ashwagandha-induced liver injury was suspected and N-Acetylcysteine (NAC) was started on day 2 and her LFT improved on day 3 with ALT 328, AST 100, TB 0.7, DB 0.2, ALP 101 and NAC continued for 72 hours with significantly improved LFT with ALT 176, AST 46, TB 0.9, DB 0.2, ALP 132 and she was discharged. Repeat liver enzymes in a week were normal with ALT 39, AST 18, TB 1.0, DB 0.2, ALP 99. Discussion: This case reveals a potential liver injury with elevated liver enzymes in the setting of ashwagandha use that improved with cessation of ashwagandha and NAC therapy (see Table 1).

Gastroenterology

Noronha K, **Betcher S**, **Varma AK**, and **Jafri SM**. A Rare Case of Symptomatic Esophageal Squamous Papilloma. *Am J Gastroenterol* 2024; 119(10):S2317. Full Text

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Introduction: Esophageal squamous papillomas (ESPs) are rare lesions of the esophagus, prevalent in only 0.01% of patients. ESPs are commonly associated with the lower esophagus due to chronic mucosal irritations such as gastroesophageal reflux disease (GERD). We report a rare case of an upper ESP with associated symptoms of dysphagia in the setting of GERD. Case Description/Methods: A 58-year-old woman patient with a history of GERD presented to the clinic with 2 episodes of dysphagia over the course of a few months. She stated a history of dysphagia several years ago prior to the most recent attacks. She also experienced chest pain earlier in the year, attributed to acid reflux for which she was previously prescribed omeprazole daily. The initial differential included a peptic stricture versus eosinophilic esophagitis, and she was recommended to undergo an esophagogastroduodenoscopy (EGD) with biopsies of the esophagus as well as the body and antrum of the stomach. The duodenal bulb and first 2 portions of the duodenum were also to be examined. While performing the EGD, a small pedunculated lesion measuring 1-cm was noted in the proximal esophagus which was removed in a piecemeal fashion. The rest of the esophagus was unremarkable with no signs of eosinophilic esophagitis. Biopsies of the stomach were normal, showing only mild signs of chronic gastritis. A test for the presence of H. pylori was ordered, and it returned negative. The duodenum also did not present with any abnormalities. The removed lesion within the proximal esophagus was determined to be an esophageal squamous papilloma (ESP). The papilloma was said to not be malignant, and a repeat EGD in 8-weeks was recommended to assess the resolution of the papilloma. She has not experienced any episodes of dysphagia since removal of the ESP. Discussion: ESPs are rare, often benign lesions of the epithelia of the esophagus. The pathogenesis of ESPs remains uncertain, but there are many noted risk factors to their development, one being mucosal irritations such as GERD. If GERD is the cause of the ESP, the ESP will typically develop in the distal third of the esophagus due to its close proximity to the stomach. ESPs are commonly found incidentally when performing an EGD due to their asymptomatic nature. Larger ESPs can produce bothersome symptoms such as dysphagia. In most cases, the appropriate choice of treatment is surgical excision of the lesion followed by endoscopic surveillance to ensure the development of a malignant tumor does not occur.

Gastroenterology

Noronha K, and **Jafri SM**. Refractory Abdominal Pain Following Gastric Bypass Due to Persistent Gastric Ulcer. *Am J Gastroenterol* 2024; 119(10):S3255. Full Text

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Introduction: Ulceration is an uncommon complication of gastric bypass and is generally managed with proton pump inhibitor therapy with resolution. We present a case of refractory abdominal pain and poor oral intake associated with the development of a severe marginal ulcer following Roux-en-Y gastric bypass surgery with failed medication therapy. Case Description/Methods: A 29-year-old woman with a history of gastroesophageal reflux and obesity presents with burning abdominal pain in the epigastric region, occurring primarily after meals. She was initially prescribed several proton pump inhibitors and H2 blockers without effect. She undergoes an esophagogastroduodenoscopy (EGD) and 24hr pH impedance, revealing reflux, mild erythema of the lower esophagus, and chronic gastritis. She has an

unremarkable barium swallow and esophageal manometry. She has a successful Roux-en-Y gastric bypass and is symptom free for a few months while also losing thirty pounds. However, she again begins experiencing oral intolerance and progressive abdominal pain, resulting in malnutrition and dehydration. An EGD is performed, and a large cratered marginal ulcer is found at the surgical site of her gastrojejunostomy. She is prescribed omeprazole and sucralfate to remedy the ulcer. Eight weeks later, a repeat EGD is performed, and the marginal ulcer is identified on the jejunal side of her gastrojejunostomy, meaning the medication treatment failed to heal the gastric ulcer. She is admitted for total parenteral nutrition to address her poor nutritional status, and upon improvement, she undergoes resection of the marginal ulcer and revision of her gastrojejunostomy. Apart from a right lower-quadrant abdominal wall port site abscess, which was fixed through an incision and drainage, she did not experience any complications with the procedure. Two months after surgery, she is able to tolerate diet without the use of supplemental nutrition, and she has not experienced any symptoms of nausea, vomiting, or abdominal pain. Discussion: Nissen Fundoplication remains the gold standard procedure for patients with severe acid reflux. For obese subset of patients, Roux-en-Y gastric bypass is preferred. Marginal ulcers are an uncommon complication for Roux-en-Y gastric bypass surgeries with an incidence rate of 1-5%. The majority of these cases are remedied with medication therapy. If medical management is unsuccessful, resection of the ulcer and revision of the gastrojejunostomy may be appropriate.

Gastroenterology
Omeish H, **Chaudhary AJ**, **Jamali T**, **Saleem A**, and **Khan MZ**. A Rare Case of Pancreatic Cancer Causing Secondary Achalasia. *Am J Gastroenterol* 2024; 119(10):S2272. Full Text

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Introduction: Secondary achalasia or pseudoachalasia is a rare esophageal motility disorder resembling idiopathic achalasia. Most pseudoachalasia cases involve neoplasia at or near the esophagogastric (EG) junction. Pancreatic cancer rarely causes pseudoachalasia. This disorder may result from circumferential obstruction of the distal esophagus or malignant infiltration destroying inhibitory neurons. We present a rare case of pseudoachalasia caused by pancreatic cancer highlights the need to consider malignancies beyond the EG junction in diagnosis. Case Description/Methods: A 77-year-old woman with a history of pancreatic adenocarcinoma presented with a 6-month history of dysphagia, abdominal pain, and a 30 lb weight loss over 3 months. Laboratory findings revealed leukocytosis, high anion gap metabolic acidosis due to starvation ketosis, and elevated liver enzymes (AST 299 U/L, ALT 384 U/L, alkaline phosphatase 942 IU/L). A CT scan of the abdomen showed progression of the pancreatic head mass, encasing vascular structures, worsening biliary duct dilation, centrally necrotic mesenteric lymph nodes, and new small ascites. An esophagogram revealed significant narrowing of the distal esophagus, gastroesophageal junction, and proximal stomach. An EGD with ERCP demonstrated type 3 achalasia and a single moderate localized malignant biliary stricture treated with biliary sphincterotomy and stent placement. The patient received 5 cycles of radiation therapy followed by resumption of chemotherapy. Due to declining health and comorbidities, further pancreatic cancer treatment was considered inappropriate. After discussion with the patient and family, they opted for hospice care, and the patient passed away 5 months later. Discussion: This case underscores the critical need to broaden the differential diagnosis when evaluating patients with unexplained dysphagia. While rare, pseudoachalasia, which has been associated with pancreatic cancer in only 4 reported cases, should be considered in such patients. When standard treatments fail to alleviate symptoms in typical achalasia cases, secondary achalasia may be suspected (see Figure 1).

Gastroenterology
Omeish H, **Khan MZ**, **Chaudhary AJ**, **Salgia R**, and **Jafri SM**. A Case of Acute Budd Chiari Syndrome Treated With Portosystemic Shunting. *Am J Gastroenterol* 2024; 119(10):S2882. Full Text

H. Omeish, Henry Ford Health, Detroit, MI, United States

Introduction: Budd-Chiari syndrome (BCS) is a rare condition involving hepatic venous outflow obstruction. While it typically progresses slowly, it can cause acute decompensation of liver disease creating significant management challenges. Here we present a case of acute BCS leading to severe

decompensation of liver disease managed by Transjugular intrahepatic portosystemic shunt (TIPS). Case Description/Methods: A32-year-oldwomanwith a history of iron deficiency anemia, presented with sudden right upper quadrant abdominal pain. Labs showed ALT of 255 U/L and AST 196 U/L, bilirubin 1.7 mg/dL, hemoglobin 6.8 mg/dL, platelets 140 x 10∧9/L, and INR 1.35. CT abdomen revealed thrombi in the hepatic and portal veins, suggestive of BCS, and signs of portal hypertension. Serological workup including autoimmune, Wilson's disease, viral hepatitis, etc, were negative. Liver biopsy showed centrilobular hepatocellular necrosis, sinusoidal dilatation, and mild portal fibrosis consistent with hepatic venous outflow obstruction. Hypercoagulable workup revealed Paraoxysmal nocturnal hemoglobinuria. Multi-disciplinary discussion with hematology and hepatobiliary surgeons was ensued and the patient was started on continuous heparin. Despite anticoagulation therapy, the patient's condition did not improve, leading to consideration for liver transplant. Due to extent of the clot, limited experience with management of PNH, and the patient's hesitance, dTIPS was performed. Her proceeding hospital course was complicated by gastrointestinal bleeding from hepatic artery aneurysms, managed with coil embolization. Otherwise she did well and was discharged in stable condition. Discussion: BCS, a rare hepatic venous outflow obstruction disorder, predominantly affects women in their third or fourth decade, presenting with abdominal pain, ascites, and hepatomegaly. Most cases of BCS entail an underlying thrombophilia disorder, with PNH contributing to 19% of cases. In PNH patients, management is often complicated as morbidity and mortality with thrombosis is high. In recent times Eculizumab has proven to mitigate thromboembolism risk. Symptoms onset can range from acute presentation, such as our case, to chronic TIPS typically has been used to manage chronic decompensation of liver disease caused by BCS but has seldom been used as a rescue therapy for sequealae of portal hypertension, such as in our case. Therefore, multidisciplinary decision-making is important when encountering rare causes and presentation of BCS.

Gastroenterology

Omeish H, **Mueller A**, **Jafri SM**, and **Moonka D**. NOVEL INSIGHTS INTO THE ACCURACY OF FIB-4 AND FIBROSCAN SCORES COMPARED TO LIVER BIOPSY IN THE ASSESSMENT OF LIVER FIBROSIS IN PATIENTS WITH MASLD. *Hepatology* 2024; 80:S452. Full Text

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is prevalent, with fibrosis stage being a critical predicting prognosis. Liver biopsy is the gold standard for staging but is invasive and costly. Non-invasive tests like FibroScan and FIB4 aid in pre-selecting patients for biopsy. This study compares FibroScan and FIB4 accuracy in predicting fibrosis staging in patients with MASLD. Methods: A cross-sectional study on 116 MASLD patients undergoing both FibroScan and liver biopsy within one year was conducted. Demographic, biochemical data, and FIB4 levels were collected. Patients were categorized by fibrosis levels: minimal/no (F0-F1), moderate (F2- F3), and severe (F4), using FibroScan kPa scores, FIB4 levels, and biopsy results. Results: Of 116 patients (55 males, 61 females; 82 < 65 years, 34 older; 89 white, 25 non-white; 26 BMI < 30, 89 BMI > 30), 37.07% were F0-1 by FIB4, with 64.71% agreement by FibroScan. For F2-3, 58.62% were identified by FIB4, with 60% agreement by FibroScan. In F4, 4.31% were classified by FIB4, with 60% agreement by FibroScan. Kappa statistic (0.1253) indicates slight agreement beyond chance, emphasizing caution when using these methods interchangeably. Table-1 compares FIB4 values and biopsy stages, showing moderate agreement, particularly for F4. Among 43 F0-1 cases by FIB4, 52.17% matched F0-1 biopsy, 38.24% were F2-3, and 11.63% were F4. For 68 F2-3 cases by FIB4, 16.18% were F0-1, 58.82% were F2-3, and 25.00% were F4. Among 5 F4 cases by FIB4, none were F0-1, 40.00% were F2-3, and 60.00% confirmed F4 by biopsy. Table-1 also correlates FibroScan and biopsy stages. Of 17 F0-1 cases by FibroScan, 64.71% matched biopsy, 35.29% were F2-3, none F4. Among 55 F2-3 cases by FibroScan, 16.36% were F0-1, 74.55% F2-3, 9.09% F4. Of 44 F4 cases by FibroScan, 6.82% were F0-1, 47.73% F2-3, and 45.45% confirmed F4 by biopsy. Significant F2-3 agreement, some F0-1 and F4 discrepancies were observed. Conclusion: Both FIB-4 and FibroScan showed a correlation with liver fibrosis, particularly in moderate fibrosis. However, discrepancies exist across different stages, with better performance in moderate fibrosis. Caution is advised when using non-invasive tests interchangeably with biopsy for fibrosis assessment in MASLD patients.

Gastroenterology
Omeish H, **Mueller A**, **Jafri SM**, and **Moonka D**. How Accurate Is FIB-4 vs Fibroscan in Clinical Practice: Comparing Methodology of Liver Fibrosis Assessment. *Am J Gastroenterol* 2024; 119(10):S1385. Full Text

H. Omeish, Henry Ford Health, Detroit, MI, United States

Introduction: The associated risks of liver biopsy for assessing fibrosis in patients with Metabolic dysfunction-associated steatotic liver disease (MASLD) have heightened the need to validate non-invasive fibrosis scores for accuracy and efficacy. This study aims to compare the accuracy of the FIB-4 (Fibrosis-4) and Fibroscan scores in diagnosing fibrosis in MASLD patients. Methods: A total of 116 patients were categorized into 3 groups based on their Fibroscan kPa (kilopascal) scores: Group I with mild fibrosis (MF), comprising F0 to F1, and Group II with moderate fibrosis (AF), comprising F2-F3, with group 3 with advanced fibrosis classified as F4. Results: The study evaluated the correlations between Fibroscan, FIB-4 values and liver biopsy stage in various subgroups of patients. In the overall cohort (N=116), significant positive correlations were found between Fibroscan and liver biopsy stage (R=0.246, P=0.008), and liver biopsy stage and FIB-4 value (R=0.537, P<0.001). Among males (N=55), a strong significant correlation was observed between liver biopsy stage and FIB-4 value (R=0.727, P<0.001), though correlations involving Fibroscan were not significant. In females (N=61), significant positive correlations existed between all pairs of measures, with the strongest being between liver biopsy stage and FIB-4 value (R=0.349, P=0.006). Age-related analysis showed that in patients younger than 65 (N=82), significant correlations were found between Fibroscan and liver biopsy stage (R=0.332, P=0.002), and liver biopsy stage and FIB-4 value (R=0.602, P<0.001). For those aged 65 or older (N=34), only the correlation between liver biopsy stage and FIB-4 value was significant (R=0.390, P=0.023). Racial analysis revealed that in the White race group (N=89), significant correlations were found across all measures, while in the non-White group (N=25), only the correlation between liver biopsy stage and FIB-4 value was significant (R=0.706, P<0.001; Table 1). Conclusion: Both FIB-4 and Fibroscan can be used to rule out advanced fibrosis in MASLD patients. However, a stronger relationship between liver biopsy stage and FIB-4 value was noted compared to their individual associations with Fibroscan.

Gastroenterology
Omeish H, **Nimri F**, **Alomari A**, **Saleem A**, and **Tang J**. A Mysterious Case of Abdominal Pain and Distention Revealing Eosinophilic Enteritis. *Am J Gastroenterol* 2024; 119(10):S2054-S2055. Full Text

H. Omeish, Henry Ford Health, Detroit, MI, United States

Introduction: Eosinophilic Gastroenteritis (EGE) is a rare disorder marked by eosinophilic infiltration and peripheral eosinophilia. It can occur anywhere in the gastrointestinal tract without specific causes of eosinophilia. While its exact cause is unknown, hypersensitivity is significant. Symptoms include nausea, vomiting, abdominal pain, and weight loss. Diagnosis involves endoscopic biopsies, and prevalence is increasing with more endoscopic procedures. First-line treatment is steroids. We describe a case of diffuse abdominal pain leading to EGE diagnosis. Case Description/Methods: A 25-year-old woman presented with a month-long history of diffuse abdominal pain, fatigue, bloating, nausea, vomiting, poor appetite, and decreased oral intake. She denied fever, weight loss, rash, or allergic disease history and reported recent travel to the Bahamas and Jamaica. Physical exam was unremarkable except for mild tachycardia. Labs showed leukocytosis with hypereosinophilia. Extensive workup ruled out secondary causes (Table 1). Computed tomography revealed small bowel thickening, ascites, and pleural effusions. Paracentesis removed 900 cc, showing a Total Nucleated Cell Count of 1,637 and 87% eosinophils. Esophagogastroduodenoscopy showed gastropathy (Figure 1), and duodenal biopsies revealed extensive eosinophilic infiltration, suggesting eosinophilic enteritis. Treatment included IV ceftriaxone, Flagyl, and Ivermectin, later switching to pantoprazole and high-dose prednisone. Follow-up showed complete resolution of symptoms after 3 weeks. Discussion: EGE is a rare condition with peripheral eosinophilia and gastrointestinal eosinophilic infiltration. Early suspicion is crucial, and secondary causes must be ruled out. EGE often affects men over 30 with allergy history and high serum IgE. It can impact any part of the digestive system, especially the stomach's antrum. Diagnosis involves gastrointestinal

symptoms and eosinophilic infiltration. The incidence is rising, but true prevalence is unknown. Treatment, primarily steroids, shows up to 90% improvement. Alternatives include antihistamines, mast cell stabilizers, leukotriene antagonists, and PPIs. Early diagnosis is key. (Figure Presented).

Gastroenterology
Patel-Rodrigues P, **Harris K**, **Piraka C**, **Alsheik E**, **Ahsan B**, **Nalamati S**, and **Yudovich A**. A Case of Multiple NSAID-Induced Strictures of the Ascending Colon. *Am J Gastroenterol* 2024; 119(10):S2044. Full Text

P. Patel-Rodrigues, Henry Ford Health, Detroit, MI, United States

Introduction: Nonsteroid anti-inflammatory drugs (NSAID) are one of the most widely used medications in the world. Chronic NSAID use can cause several complications including inflammatory changes to the bowel mucosa that can result in diaphragm-like strictures resulting in abdominal pain, anemia, and small bowel obstructions. NSAID-induced small bowel strictures, although rare, have been well-described in the literature. NSAID-induced colonic strictures are a rarer presentation and are delayed in diagnosis. We describe a case of multiple colonic strictures in the setting of chronic NSAID use. Case Description/Methods: A 72-year-old woman with iron deficiency anemia presented with abdominal pain, weight loss, and fatigue for 3 months and was found to have a hemoglobin of 5.6. She had never undergone an upper endoscopy or colonoscopy. Her daily medications included diclofenac 50 mg twice a day. Computed tomography of her abdomen showed circumferential wall thickening of the terminal ileum and ileocecal valve. Colonoscopy showed a severe stricture with erythema in the ascending colon that could not be traversed. Repeat colonoscopy with interventional gastroenterology 2 weeks later showed 2 strictures. The distal stricture was dilated to 10 mm under fluoroscopic guidance. The upstream colon was examined endoscopically using a direct visualization system, like a cholangioscope, through the colonoscope. A second stricture was seen in the proximal ascending colon which was traversed in a similar fashion. The strictures and surrounding areas were biopsied. Biopsies showed focal erosion, fibrin, architectural disarray, and granulation tissue. Due to ongoing symptoms, she underwent a right hemicolectomy with colorectal surgery 2 months later. The final pathology of the stricture showed submucosal fibrosis and haphazard arrangement of smooth muscle, nerves, and vessels. This constellation of features is associated with NSAID use. She was seen 1 month post-operatively with improved symptoms. Discussion: Colonic diaphragmatic strictures are a rare side effect of chronic NSAID use. This case highlights how important it is for physicians to be mindful of this condition, inquire about NSAID use, and make a prompt and accurate diagnosis. Without awareness of this entity, diclofenac may not have been stopped and a possible incorrect diagnosis of Crohn's disease may have been made. Many cases improve with use of endoscopic therapies and withdrawal of NSAIDs. In more severe cases, such as this, surgical intervention may be required. (Figure Prresented).

Gastroenterology
Raina S, Cooper C, Feld J, Johnson L, Brown A, Martinez A, Conway B, **Gordon S**, Asselah T, Uribe L, Li M, Iacob A, Marcinak J, Kaur J, Semizarov D, and Pol S. GLECAPREVIR/ PIBRENTASVIR IN CHRONIC HCV: AN INTEGRATED ANALYSIS OF PATIENTS ON MULTIPLE CONCOMITANT MEDICATIONS. *Hepatology* 2024; 80:S372. Full Text

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Background: The safety of direct acting antivirals (DAAs) can be impacted by drug-drug interactions (DDIs). This integrated analysis of phase 2 and phase 3 studies uses the pangenotypic DAA regimen of glecaprevir and pibrentasvir (G/P) to analyze the efficacy and safety of glecaprevir/pibrentasvir (G/P) in the presence of multiple co-morbidities and concomitant medications. Methods: An integrated pooled analysis was carried out across twenty-one (21) randomized controlled clinical trials in patients with chronic HCV genotype 1-6 infection with or without compensated cirrhosis receiving G/P for 8, 12 or 16 weeks that were on concomitant medications. Primary analyses assessed safety and efficacy (sustained virologic response at post-treatment week 12; SVR12). Patients were stratified for analysis by number of concomitant medications, age > 65yrs, having a co-morbidity and use of injectable and other drugs (PWUD). Results: Among 6569 patients in this analysis, 1170 (17.8%) were age > 65yrs, 2049 (31.2%)

had a psychiatric disorder, 300 (4.6%) had a cardiovascular disorder, 1786 (27.2%) had HIV-HCV co-infection, and 2049 (31.2%) were PWUD. 2705 patients were on > 3, 1638 patients were on > 5, 439 patients were on > 10, 138 patients were on > 15 and 59 patients were on > 20 concomitant medications. High efficacy of G/P (mITT SVR12) was observed overall (98.6%) including in patients on > 20 (98.2%) concomitant medications. Treatment emergent serious adverse events (TESAEs) occurred at low rates (overall 2.5%, range (2.4-5.1%) across all patient populations, with the most frequently reported SAE being infections, injuries/procedural complications and neoplasms. The majority of the TESAEs were considered unrelated to G/P with only 0.1% possibly related to G/P. Treatment related TESAEs in patients on > 1 concomitant medication were rare (0.1%, range0- 0.2%). Grade 3 elevations in alanine aminotransferase (ALT) or bilirubin were uncommon (0.5%, 0.1%) in the overall population as well as in patients > 65yrs of age (0.2, 0.4%), those with psychiatric comorbidities (0.5, 0.2%), cardiovascular comorbidities (0.7. 0.4%), HIVHCV co-infection (0.4, 0.1%), and PWUD (0.6, 0.1%). There were no patients with both Grade 3 ALT and Grade 3 bilirubin elevations. Conclusion: This integrated pooled analysis confirms the safety, tolerability and high efficacy of G/P in chronic HCV patients on as many as > 20 multiple concomitant medications, > 65 years of age, those with comorbidities and PWUD.

Gastroenterology
Rehman S, **Abusuliman M**, **Chaudhary AJ**, **Alluri S**, **Nabaty R**, **Saleem A**, and **Kutait A**. Risk Factors for Esophageal Variceal Ligation Ulcer Bleeding. *Am J Gastroenterol* 2024; 119(10):S437. Full Text

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Introduction: Esophageal Variceal Ligation (EVL) ulcer bleeding is defined as endoscopically confirmed bleeding from a post banding ulcer with no alternative bleeding source. EVL ulcer bleeding is a rare complication, difficult to manage and has a high rate of mortality. The data on the risk factors and treatment of EVL ulcer bleeding is limited. This study aims to identify risk factors for the development of EVL ulcer bleeding to better understand patients who may be at higher risk. Methods: Through a retrospective case control study, ICD 10 codes were used to identify patients who were 18 years or older with a history of cirrhosis who underwent EVL between 1/2016-12/2023 within our tertiary health system. We excluded patients who did not undergo EVL in our health system and those who had GI bleeding for any other reason besides EVL ulcer. We compared patients who had at least 1 episode of EVL ulcer bleeding as defined above to those with no episode of EVL ulcer bleeding by collecting demographic data, lab values at time of initial EVL and initial EVL endoscopy findings. We ran independent T test for continuous variables with equal variance and normal distribution, Mann-Whitney U Test for continuous variables with non-normal or non-parametric distribution and Chi square test for categorial variables. Results: In this time, 407 patients underwent at least 1 session of EVL in our health system and of these patients, 375 had no episodes of EVL ulcer bleeding and 32 had EVL ulcer bleeding. Those who developed EVL ulcer bleeding at baseline were on average younger (mean age 55 +/- 11.3 years, P=0.036), had higher MELD scores at initial scope (19.8 +/- 9, P=0.015), had more banding sessions (mean 3.5 +/- 2.6 bands, P=0.000) with more number of bands (4.7, P=0.000) placed per session, had a history of variceal bleeding (59%, P=0.005) and hepatic encephalopathy (81%, P=0.000). On labs, EVL ulcer bleeding patients had lower albumin (2.7, P=0.009). Endoscopy findings of stigmata of recent bleeding (P=0.006), management post initial scope (P=0.000) and mortality within 6 months (P=0.010) were statistically significant between the 2 groups. Conclusion: Our results demonstrate both the presence of patient specific demographic risk factors and endoscopic findings that increase risk of EVL ulcer bleeding. Whether this was due to predominately our patient population or sample size is unknown. Further studies assessing the treatment of EVL ulcer bleeding itself based on these risk factors is warranted (see Table 1).

Gastroenterology
Rehman S, **Abusuliman M**, **Chaudhary AJ**, **Alluri S**, **Saleem A**, **Nabaty R**, and **Kutait A**. Esophageal Variceal Ligation Ulcer Bleeding: Outcomes of Different Modalities Used for Treatment. *Am J Gastroenterol* 2024; 119(10):S438. Full Text

S. Rehman, Henry Ford Health, Detroit, MI, United States

Introduction: Esophageal Variceal Ligation (EVL) ulcer bleeding, defined as endoscopically confirmed bleeding from an ulcer due to slippage of a band with no alternative bleeding source, poses a challenge as there exists no standardized guidelines for treatment. Hemospray is a nonabsorbable hemostatic powder used for various gastrointestinal bleeding, however limited data exists for its use in EVL bleeding. This study aims to assess the treatment outcomes of different modalities used in EVL ulcer bleeding including the use of hemospray to shed insight into management strategies. Methods: We used ICD 10 codes to identify patients over the age of 18 with a history of cirrhosis who underwent EVL within our tertiary health system between 1/2016-12/2023. We excluded patients who did not have any EVL and those who had GI bleeding for any other reason besides EVL ulcer as defined above. Primary outcome was management of EVL ulcer and secondary outcomes were rebleeding, readmission within 3 months and mortality within 6 months. Results: 407 patients underwent at least 1 session of EVL in this time and of these, 32 (7.9%) developed EVL ulcer bleeding. Of the EVL ulcer bleeding patients, the mean age was 55 ±11.3 years and alcoholic cirrhosis was the most common cause of cirrhosis (59%, n=19). Mean MELD at initial EVL scope was (19.8± 9.25) compared to MELD at EVL ulcer bleeding scope (21.5± 9.98). On average, 10.76 ±5.01 days was time to repeat scope and hematemesis was most common indication for second scope (n= 21,54%). EVL ulcer bleeding was most frequently managed with rebanding (n=16, 50%), followed by endoscopic injection sclerosis (n=9, 28%) and hemospray (n=7, 22%). 17 patients (53%) had rebleeding post intervention, 12 were (38%) readmitted within 3 months and of these 6 (50%) had rebleeding as the most common reason for readmission.14 (44%) of EVL ulcer bleeding patients died within 6 months. When comparing management of EVL ulcer bleeding scope to rate of rebleed, no statistical significance across the different modalities (P=0.283) including hemospray and rebleeding risk (P=0.112). Conclusion: Our data suggests there is no standard treatment of EVL ulcer bleeding that prevents rebleeding including hemospray. Whether this is due to the small sample size or time frame remains unknown. Further studies should assess known risk factors for EVL ulcer bleeding with treatment outcomes to establish other underlying factors that impact EVL treatment bleeding outcomes in addition to modality used (see Table 1).

Gastroenterology

Rehman S, Garg N, **Rahman T**, **Jamil M**, **Abusuliman M**, **Alluri S**, Almasri W, **Nabaty R**, and **Jafri SM**. Effect of Mammalian Target of Rapamycin (mTOR) Inhibitor Everolimus Upon Skin and Other Malignancy Following Liver Transplantation. *Am J Gastroenterol* 2024; 119(10):S1323. Full Text

S. Rehman, Henry Ford Health, Detroit, MI, United States

Introduction: Malignancy after solid organ transplant especially skin cancers is common phenomenon. Some case reports and small single center studies highlight various antioncogenic effects of mammalian target of rapamycin (mTOR) inhibitor class of immunosuppressants especially everolimus. This study aims to assess the incidence of post transplant skin malignancy and outcomes among liver transplant recipients on everolimus. Methods: A retrospective chart review of liver transplant recipients transplanted at a large tertiary center between 1/2015-12/2019 was conducted. Patients were split into 3 groups: not on everolimus post transplant (group 1), started on everolimus within 1 year of transplant and discontinued before 3 years (group 2) and on everolimus for at least 3 consecutive years (group 3). Demographic data including age and gender were collected with primary outcome assessing the incidence of skin cancer post transplant. Secondary outcomes assessed other post transplant malignancies including non-hepatic gastrointestinal malignancy, transplant rejection and death. Results: Among 381 liver transplant recipients, 67% were in group 1 (n=257), 15% in group 2 (n=59), 17% in group 3 (n=65). 25 patients in group 1 (9.7%), 4 in group 2 (6.8%) and 6 (9.2%) in group 3 developed some skin malignancy with squamous cell carcinoma the most common among all 3 groups (group 1 vs 3, P 50.835; group 2 vs 3, P 50.513). 26 patients in group 1 (10.1%), 6 in group 2 (6.8%) and 5 (7.7%) developed some other type of malignancy, and among other malignancies, hematologic was most common in group 1 (n=6, 23%) and non-hepatic gastrointestinal was most common in group 2 (n=4, 67%) and 3 (n=4, 80%). There was no significant difference in incidence of skin malignancy (group 1 vs 3, P = 0.835; group 2 vs 3, P 50.513), death (group 1 vs 3, P = 0.502; group 2 vs 3, P 50.611) or transplant rejection among the 3 groups (group 1 vs 3, P = 0.305; group 2 vs 3, P 50.066). Conclusion: Our data demonstrates everolimus did not have a protective effect against skin malignancy, other post transplant malignancies, transplant rejection or mortality in liver transplant patients. The data demonstrated that the

duration of evrolimus therapy also had no effect on these variables. Whether these study findings were related to short duration of therapy or to a small sample size is unclear. Further investigations are warranted over a longer period of time and with other mTOR agents (see Table 1).

Gastroenterology
Rizwan A, **Siddiqui Y**, and **Jafri SM**. Role of Azathioprine as an Effective Alternative Therapy for Patients With Refractory Microscopic Colitis. *Am J Gastroenterol* 2024; 119(10):S1938. Full Text

A. Rizwan, Henry Ford Health, Northville, MI, United States

Introduction: Microscopic colitis (MC), a common cause of chronic diarrhea encompasses 2 histological subtypes: Collagenous and Lymphocytic colitis. Collagenous colitis, is chronic inflammation of the colon, causing an excess buildup of collagen, a fibrous protein in the lining of colon that can cause persistent diarrhea. The exact etiology of MC is unclear and is common in older female adults. With rising cases of refractory microscopic colitis; failing first line therapies including anti-diarrheal, budesonide (BDS), anti-tumor necrosis factors (anti-TNFs) and methotrexate. We present a case on effective therapeutic response of azathioprine (AZA) in a patient with refractory MC. Case Description/Methods: An 86-year-old woman with history of MC, Irritable bowel syndrome and sarcoidosis presented with persistent diarrhea despite being on BDS and dietary modifications. Pt underwent colonoscopy with biopsies of distal small bowel, terminal ileum; random colon to rule out inflammation. Biopsy showed irregular thickening of the collagen table, patchy areas of epithelial denudation and increase in mixed chronic inflammatory infiltrate within the lamina propria with prominent eosinophils consistent with collagenous colitis. No evidence of cryptitis, crypt abscess or granulomas were seen. Patient was treated with variety of agents for MC including Bismuth subsalicylate, mesalamine, cholestyramine, prednisone, BDS, infliximab (INX), adalimumab (ADA) without resolution of symptoms. Patient had not responded to INX and had a rash with ADA. Patient was started on AZA with good response and symptomatic improvement. Pt remained stable on AZA, without any major issues. Discussion: An abnormal immune system response in the colon is mainly believed to be the underlying mechanism for MC etiology. Risk factor includes autoimmune disorders, infections, genetic predisposition and certain medications like Non-steroidal anti-inflammatory drugs. AZA an immunosuppressive medication can be prescribed in refractory cases of MC, which help reduce inflammation and alleviate symptoms associated with MC. As with any medication, AZA also have side effects particularly with long-term use. Side effects of AZA includes nausea, vomiting, liver toxicity, increased risk of infection, certain types of cancer and bone marrow suppression. It is important to weigh the potential benefits against the risks and side effects. AZA can definitely be an option for treating MC with close monitoring especially given rise in cases of refractory MC.

Gastroenterology
Saad N, and **Jafri SM**. Liver Transplantation for Colorectal Cancer With Hepatic Metastases. *Am J Gastroenterol* 2024; 119(10):S2798-S2799. Full Text

S.-M. Jafri, Henry Ford Health, Detroit, MI, United States

Introduction: Colorectal cancer is the third most common cancer worldwide, and 25-30% of colorectal cancer patients develop liver metastases. The 5-year survival rate of patients with colorectal cancer with liver metastases (CRLM) who undergo surgical resection is 40%-50%. Liver transplantation is being investigated as a potentially curative treatment for CRLM. We present a 60-year-old man who underwent a liver transplant for CRLM Case Description/Methods: A 60-year-old man with a history of moderately differentiated adenocarcinoma of the sigmoid colon with liver metastasis undergoes a colon resection to remove the primary tumor chemotherapy, and a liver resection to remove initial hepatic metastases. Recurrence of the hepatic metastases occurs twice following liver resection despite liver ablative therapy. Following the second microwave ablation, the patient is listed for liver transplant. He undergoes liver transplantation 9 months after initial treatments for CRLM. Explant pathology reveals 3 foci of residual metastatic adenocarcinoma with partial treatment response. His course is complicated by cardiac arrest requiring transvenous pacemaker (TVP) placement, right-sided pleural effusion, and ischemic injury with portal vein thrombosis. The patient's liver allograft failed due to septic shock requiring high dose pressors. One month following the initial liver transplant surgery, the patient has a repeat liver transplant. Following

re-transplant, the patient has an episode of cardiac arrest and candidemia with retinitis treated with amphotericin. Patient developed kidney failure and prolonged respiratory failure requiring dialysis and tracheostomy. Six weeks after the liver re-transplant, the patient's symptoms and liver function tests improved Discussion: The organ procurement and transplantation network has developed guidelines for liver transplantation in patients with unresectable CRLM. Liver transplantation for unresectable CRLM can be considered for patients who had a complete RO resection of the primary tumor, excluded local recurrence within 3 months of transplantation based on colonoscopy, excluded extrahepatic disease using crosssectional imaging, and responded to first-line chemotherapy for at least 6 months. Despite initial allograft failure, the patient had a successful re-transplantation which indicates that liver transplant continues to be a potential cure for unresectable CRLM.

Gastroenterology

Sagubadi N, **Ashraf T**, **Fain C**, and **Jafri SM**. An Unusual Case of Rectal Mass Investigation Leading to Diagnosis of Syphilitic Proctitis. *Am J Gastroenterol* 2024; 119(10):S1903. Full Text

N. Sagubadi, Wayne State University, School of Medicine, Detroit, MI, United States

Introduction: We present an unusual case of a patient with syphilitic proctitis presenting as severe constipation and hematochezia. Case Description/Methods: A wonderful 42-year-old man with a history of well controlled human immunodeficiency virus (HIV), prior small bowel resection and right hemicolectomy due to a gunshot wound, presents to the emergency department for evaluation of severe constipation and rectal bleeding over the past 8 days. Computed tomography of the abdomen and pelvis notes marked circumferential wall thickening in the rectum suspicious for rectal adenocarcinoma. Additionally, multiple enlarged mesorectal, superior rectal, and inferior mesenteric artery lymph nodes are suspicious for metastatic disease. The patient undergoes colonoscopy, which reveals a 9 cm partially obstructing fungating mass in the distal rectum suspicious for malignancy. The lesion is biopsied and evaluation scheduled with colorectal surgery and oncology. Final pathology reveals rectal mucosa with ulceration and acute and chronic inflammation with dense plasmocytic infiltrates. Treponema pallidum immunostaining highlights numerous organisms. The findings are diagnostic for active syphilis infection, and there is no evidence of cancer cells. Plans are made for outpatient infectious disease evaluation, but the patient does not follow up. The patient returns with recurrent dyschezia and 2.8 cm perirectal abscess for which he is treated with penicillin G for 3 weeks. Discussion: Syphilitic proctitis is a rare manifestation of syphilis that usually presents as proctitis, ulcer, and neoplasm, but lacks defining characteristics. This poses a diagnostic challenge as it mimics rectal cancer clinically, radiologically, and endoscopically. Patients with syphilitic proctitis typically present with obstructive bowel symptoms. Histologic sections are often required for diagnosis, and reveal prominent plasma cells and abundant Treponema pallidum. Several cases of syphilitic proctitis have been described in patients who are positive for HIV, indicating that this population may be at risk for this condition, even when well controlled.

Gastroenterology

Sagubadi N, **Nimri F**, **Jamali T**, **Piraka C**, and **Jafri SM**. Full Thickness Resection of a Rare Cecal Granular Cell Tumor. *Am J Gastroenterol* 2024; 119(10):S1903. Full Text

N. Sagubadi, Wayne State University, School of Medicine, Detroit, MI, United States

Introduction: We present an interesting case of a 40-year-old patient who underwent colonoscopy and was found to have a granular cell tumor in the cecum. Case Description/Methods: Our patient is a wonderful 40-year-old woman with a history of alternating diarrhea and constipation for several years. She had 2 weeks of dark blood in her stool, bloating, and weight gain. She undergoes a colonoscopy which notes a submucosal nodule in the cecum. Biopsy reveals submucosal proliferation of large bland polygonal cells with granular cytoplasm and small oval nuclei. S100 and CD68 immunohistochemical stains are positive within the polygonal granular cells, confirming the diagnosis of a granular cell tumor. Surgical resection is considered. However, it is felt that the tumor can be completely removed endoscopically. She undergoes colonoscopy which notes a 5 mm submucosal nodule in the cecum. Standard endoscopic resection is not attempted since the nodule is in the submucosa. A FTRD (Full Thickness Resection device) is loaded onto the scope. The lesion is pulled into the FTRD cap via the

FTRD forceps. Full thickness resection is then performed using the FTRD device by deploying the clip and closing the snare, cutting the lesion in full thickness with hot snare on auto-cut. The patient tolerates the procedure well. Pathology reveals a granular cell tumor with clear margins. The patient denies any problems following the procedure. The patient is recommended to continue routine colon cancer screening. Discussion: Granular cell tumors are usually benign neoplasms that are most likely derived from Schwann cells. They are mostly seen in the oral cavity, skin, and subcutaneous tissues. When the gastrointestinal tract is involved, the most common sites are the esophagus, duodenum, anus, and stomach. Granular cell tumors of the cecum can usually be resected endoscopically. However, in some cases, laparoscopic resection has been performed, and may be preferred when the endoscopic procedure has a substantial risk of perforation. Resection is generally curative, however, in rare cases local recurrence has been reported. In extremely uncommon cases, malignant granular cell tumors have been described which require additional follow up.

Gastroenterology
Saleem A, **Al-Juburi S**, **Alomari A**, **Chaudhary AJ**, **Abusuliman M**, **Faisal MS**, **Omeish H**, **Samad M**, Nayeem M, **Rehman S**, Abbasi AF, and **Jafri SM**. Exploring the Limits: Minimizing Immunosuppression and Its Adverse Effects. *Am J Gastroenterol* 2024; 119(10):S1254. Full Text

A. Saleem, Henry Ford Health, Detroit, MI, United States

Introduction: Post liver transplantation survival has substantially improved over the last few decades. Post-transplant management remains particularly challenging due to the intricate balance between immunosuppression and its adverse effects. Excess immunosuppression can be associated with metabolic disease, infection, and malignancy. Our study aims to delineate this balance to guide clinicians in their ability to safely minimize immunosuppression without predisposing to rejection. Methods: Our study included patients who have had a 10-year liver transplant course starting in 2013 and were on tacrolimus immunosuppression. Patients who expired between 2018 - 2023 and those without adequate clinical data were excluded. Mean 5-year tacrolimus troughs 5 years after transplant (2018 - 2023) were calculated. A mean trough level of 4 was used as a cutoff to subcategorize our patients into those with a 5 year mean trough of ≤4 or >4. We compared the incidence of rejection, infection, malignancies, hyperkalemia, and nephrotoxicity between these 2 groups during this time period. Results: In 2013, 79 patients underwent liver transplants at our center; 33 expired or had inadequate data and were excluded. Forty-four patients met inclusion criteria, 17 Females (38%), 27 Males (61%). The mean age for our patients was 54.6 with a standard deviation of 8.9. Etiologies of cirrhosis were hepatitis C (45.45%), alcohol (18.18%), nonalcoholic steatohepatitis (18.8%), cryptogenic (9.09%), primary biliary cirrhosis (4.55%), primary sclerosing cholangitis (2.27%), and cystic fibrosis (2.27%). Twenty-three (52%) patients had a mean 5-year tacrolimus trough greater than 4 and 21 (48%) less than 4. Three patients experienced rejection in the .4 group and 1 in the , 4 group; 2 patients in each group were hospitalized for infection; 2 patients developed a malignancy in the >4 group and 3 in the ,<4 group. Two patients developed nephrotoxicity in the , 4 group and 1 patient in the >4 group. No significant relationship between the mean 5-year trough and incidence of rejection, hyperkalemia, infection, cancer, and nephrotoxicity was found in our analysis (Figure 1). Conclusion: Our findings underscore clinicians' abilities to down titrate tacrolimus levels without an associated increased risk of rejection. Higher tacrolimus levels were also not associated with an increased incidence of cancer, infections, nephrotoxicity, or hyperkalemia. This discussion may benefit from larger sample sizes for increased generalizability.

Gastroenterology
Saleem A, **Al-Juburi S**, **Saad Faisal M**, **Chaudhary A**, **Alomari A**, **Abusuliman M**, **Toiv A**, **Samad M**, **Haque M**, and **Jafri SM**. MINIMIZATION OF IMMUNOSUPPRESSION BEYOND FIVE YEARS FOLLOWING LIVER TRANSPLANT: LONG TERM OUTCOMES ON REJECTION, MALIGNANCY, AND MORBIDITY. *Hepatology* 2024; 80:S1073-S1074. Full Text

A. Saleem, Henry Ford Medical Center, United States

Background: Post liver transplantation survival and graft preservation has substantially improved over the last few decades. Post-transplant management remains particularly challenging due to the intricate balance between immunosuppression and its adverse effects. Excess immunosuppression can be associated with metabolic disease, infection, and malignancy. Our study aims to delineate this balance to guide clinicians in their ability to safely minimize immunosuppression without predisposing to rejection. Methods: Our study included patients who have had a 10-year liver transplant course. Patients who underwent transplantation in 2013 and initiated tacrolimus were included. Patients who expired between 2018 - 2023 and those without adequate clinical data were excluded. Mean 5-year tacrolimus troughs 5 years after transplant (2018 - 2023) were calculated. A mean trough level of 4 was used as a cutoff to subcategorize our patients into those with a 5 year mean trough of ≤4 or >4. We compared the incidence of rejection, infection, malignancies, and hyperkalemia between the groups during this period. Results: 79 patients underwent liver transplants at our center in 2013. 33 expired or had inadequate data and were excluded. 44 patients met inclusion criteria, 17 Females (38%), 27 Males (61%). The mean age for our patients was 54.6 with a standard deviation of 8.9. Etiologies of cirrhosis were Hepatitis C (45.45%), Alcohol (18.18%), Nonalcoholic Steatohepatitis (18.8%), Cryptogenic (9.09%), Primary Biliary Cirrhosis (4.55%), Primary Sclerosing Cholangitis (2.27%), and Cystic Fibrosis (2.27%). 23 (52%) patients had a mean 5-year tacrolimus trough greater than 4 and 21 (48%) less than 4. 3 patients experienced rejection in the >4 group and 1 in the <4 group during this period. 2 patients in each group were hospitalized for infection. 2 patients developed a malignancy in the > 4 group and 3 in the < 4 group. No statistically significant relationship between the mean 5-year trough and incidence of rejection, hyperkalemia, and infection was found in our analysis (Table 1). Conclusion: Our findings underscore clinicians' abilities to down titrate tacrolimus levels without an associated increased risk of rejection. Conversely, higher tacrolimus levels were also not associated with an increased incidence of cancer, infections, or hyperkalemia. Our study's results may reassure providers regarding the safety of minimizing immunosuppression. This topic can benefit from larger sample sizes for increased generalizability in the future.

Gastroenterology

Saleem A, **Chaudhary AJ**, **Jamali T**, **Samad M**, and **Tosch K**. Ileal Neuroendocrine Tumor: A Rare Incidental Finding. *Am J Gastroenterol* 2024; 119(10):S3012. Full Text

A. Saleem, Henry Ford Health, Detroit, MI, United States

Introduction: Ileal neuroendocrine tumors (NET) are rare, slow growing tumors that originate from enterochromaffin cells in the GI tract. The incidence of these tumors has been on the rise over the last few decades. Patients with small bowel NETs may initially be asymptomatic or may experience vague symptoms. Despite their indolent nature, these tumors may metastasize to the liver necessitating prompt diagnosis and treatment. We present the case of a rare, ileal neuroendocrine tumor discovered as an incidental finding. Case Description/Methods: We present the case of an asymptomatic 68-year-old African American man with a history of chronic kidney disease and tobacco use who underwent magnetic resonance imaging of the abdomen for evaluation of renal cysts. Imaging demonstrated complex renal cysts in addition to an incidental finding of a non-fatty enhancement of the ileocecal valve measuring 36 mm. Positron emission tomography scan demonstrated increased uptake in the cecum corresponding to the lesion along with non-specific uptake in adjacent ileocecal lymph nodes with no distant metastatic disease noted. Subsequent colonoscopy identified a partially obstructing tumor spanning more than half the intestinal lumen in the terminal ileum (Figure 1A). The mass was biopsied, and pathology revealed a grade 1, well differentiated neuroendocrine tumor with tumor cells positive for Cam 5.2, synaptophysin, and Ki67 < 3% (Figure 1B). A laparoscopic right hemicolectomy with small bowel resection was performed. Four out of thirteen excised adjacent lymph nodes were positive for metastatic neuroendocrine tumor. Our patient's postoperative course was complicated by ileus with eventual resolution. The case was discussed in a multidisciplinary tumor board and the decision for surveillance alone was made with a repeat computed tomography scan in 3 months. Discussion: Small bowel tumors represent less than 0.6% of all cancers with neuroendocrine tumors being the most common in this subset. More than half of these patients present with liver metastasis at the time of diagnosis. Liver metastasis may increase 5-year mortality by 10% - 20%, however, patients with liver metastasis are more likely to be symptomatic expediting diagnosis. Clinicians should be wary of certain risk factors

predisposing patients to this pathology such as smoking and the presence of Crohn's disease or genetic syndromes such as MEN1. Given its indolent nature and the mortality associated with liver metastasis, prompt diagnosis and treatment is necessary in these patients.

Gastroenterology
Saleem A, **Malick AN**, **Alomari A**, **Faisal MS**, **Abusuliman M**, **Rehman S**, **Chaudhary AJ**, Ibrahim AM, **Jamali T**, and **Suresh S**. Investigating Fecal Calprotectin: Unmasking the Sneaky Subtypes of Non-IBD Colitis. *Am J Gastroenterol* 2024; 119(10):S178. Full Text

A. Saleem, Henry Ford Health, Detroit, MI, United States

Introduction: The current gold standard for diagnosing non-inflammatory bowel disease (IBD) colitis is colonoscopy with biopsy. Imaging and stool-based tests are also often utilized during initial evaluation to screen for intestinal inflammation. Fecal calprotectin (FC) is a sensitive marker in assessing IBD disease activity, but its utility in non-IBD colitis has not been extensively evaluated. In this study, we aim to assess the utility of fecal calprotectin as a screening test for various subtypes of non-IBD colitis. Methods: This was a retrospective study of clinic patients at a tertiary care medical system who presented with subacute or chronic diarrhea between 2013-2023. Patients who had an abnormal FC during their clinic visit and underwent a colonoscopy within 3 months of this test result were included. Patients with a new or prior diagnosis of IBD or infectious colitis were excluded. Baseline patient characteristics, FC levels, histologic, and endoscopic findings on colonoscopy were collected from medical records. FC levels in patients with non-IBD colitis were compared to those without colitis. Results: 282 patients met our inclusion criteria, of which 36 had specific types of non-IBD colitis diagnosed based on histology. These clinical subtypes included microscopic colitis (66%), immune checkpoint inhibitor (ICI) colitis (14%), nonsteroidal anti-inflammatory drug induced colitis (6%), ischemic colitis (8%), radiation colitis (3%), and segmental colitis associated with diverticulosis (SCAD) (3%) (Figure 1). 233 patients had no gross or histologic features of colitis. The mean FC level of patients with a specific clinical subtype of non-IBD colitis was 246 (SD 265) compared to 90 (SD 284) in patients without colitis. Figure 1 shows the mean FC levels of patients diagnosed with each clinical sub-type of non-IBD colitis. A Mann-Whitney test was performed demonstrating a significant difference in these 2 groups ($P < 0.001$). Conclusion: Our study demonstrates a significant quantitative difference in FC level between patients with non-IBD colitis and those without colitis. However, this difference was primarily seen in patients with microscopic colitis and ICI colitis whereas patients with NSAID induced, ischemic, radiation colitis, and SCAD had FC levels similar to patients without colitis. These preliminary findings suggest that although FC shows promise as a screening marker for non-IBD colitis, clinicians should not rely too heavily on this test, especially when a patient has risk factors for a specific type of colitis. (Table Presented).

Gastroenterology
Saleem A, **Malick AN**, **Alomari A**, **Haque M**, **Faisal MS**, **Abusuliman M**, **Chaudhary AJ**, **Jamali T**, **Brennan B**, and **Suresh S**. Unraveling the Role of Fecal Calprotectin and CT Imaging in Non-IBD Colitis. *Am J Gastroenterol* 2024; 119(10):S178-S179. Full Text

A. Saleem, Henry Ford Health, Detroit, MI, United States

Introduction: Current literature details the utility of computed tomography (CT) imaging and its correlation with pathologic inflammation in inflammatory bowel disease (IBD). Higher fecal calprotectin levels in IBD patients have been associated with a greater likelihood of abnormalities noted on CT imaging. This relationship has not been explored in non-IBD colitis. We seek to elucidate the correlation between abnormalities on imaging and histologic colitis in the context fecal calprotectin (FC) with the hopes of commenting on the utility of CT imaging in assessing disease activity in non-IBD colitis. Methods: This was a retrospective study of clinic patients at a tertiary care medical system who presented with subacute or chronic diarrhea between 2013 - 2023. Patients who had an abnormal FC test during their clinic visit followed by a colonoscopy within 3 months of this test result were included. Patients with a new or prior diagnosis of IBD or infectious colitis were excluded. Baseline patient characteristics, CT imaging findings within a 4-month window, FC levels, histologic, and endoscopic findings on colonoscopy were collected from medical records. Imaging findings were compared between patients with high (>50 mg/g) and

normal (< 50 mg/g) FC levels in patients with histologically proven non-IBD colitis. Results: 282 patients met the inclusion criteria, of which 43 patients were diagnosed with non-IBD colitis based on histology. These 43 patients were stratified into 2 cohorts based on FC levels and the presence or absence of colitis on imaging. 28 patients had an elevated FC while 14 patients had normal FC. Of these 43 patients, 28 underwent CT imaging between their clinic visit and colonoscopy. 11 of these patients had abnormal CT imaging demonstrating colitis while 17 patients had normal imaging. A logistic regression analysis was performed to explore the relationship between FC and abnormal CT imaging which revealed no statistically significant correlation (P = 0.6). Figure 1 shows the distribution of normal and abnormal imaging findings in each cohort. Conclusion: Our study demonstrates no significant relationship between FC levels and CT imaging findings in patients with non-IBD colitis. This finding contrasts with studies showing an association between FC and abnormal imaging in patients with IBD. Clinicians should maintain high suspicion for non-IBD colitis in patients with high FC levels regardless of normal CT imaging and pursue appropriate diagnostic workup when otherwise indicated. (Table Presented).

Gastroenterology
Samad M, **Desai S**, **Marougail V**, **Sherbin E**, **Saleem A**, **Dababneh YJN**, and **Suresh S**. Smoking Can Reduce Treatment Response in Microscopic Colitis. *Am J Gastroenterol* 2024; 119(10):S219. Full Text

M. Samad, Henry Ford Hospital, Rochester Hills, MI, United States

Introduction: While existing research has focused on the association of specific risk factors with the development of microscopic colitis (MC), investigation of determinants affecting treatment response for MC patients is limited. The study aims to analyze whether certain risk factors affect treatment response in patients receiving initial therapy for MC. Methods: A retrospective cohort study was conducted at a single urban quaternary care center and consisted of 176 patients that received a new diagnosis of MC in the ambulatory setting. Demographic data, chronic medication use, comorbidities, and smoking status were collected for each patient. Patients received initial treatment and their daily number of bowel movements were recorded before and after therapy. Their response to treatment was the primary outcome. Treatment response was recorded as remission (complete resolution), partial response (>50% response), non-response (< 50% response), or intolerance due to medication side effect. Results: In total, 58 patients (33% of total cohort) achieved clinical remission while 90 (51%) had a partial response and 25 (14%) patients had no response to treatment. An additional 3 (2%) patients had intolerance to initial treatment. A univariate analysis assessing individual risk factors revealed that patients who were actively smoking had a significantly higher frequency of non-response to initial therapy (22%) compared to non-smokers (10%) (P = 0.007). No other risk factors studied had a significant effect on response to initial treatment in MC. Conclusion: This study demonstrates an association between active smoking and poor response to initial treatment in patients with MC. While active smoking is a known risk factor for the development of MC, this study reveals that smoking cessation is also a key component in achieving successful remission of this disease process. Further prospective multicenter studies are needed to explore the relationship between smoking and decreased treatment response and to minimize confounding variables. (Table Presented).

Gastroenterology
Samad M, **Desai S**, **Marougail V**, **Sherbin E**, **Saleem A**, **Dababneh YJN**, and **Suresh S**. Pill Poppers and Poop Problems: How Drug Exposure Affects Microscopic Colitis Recurrence Rates. *Am J Gastroenterol* 2024; 119(10):S220. Full Text

M. Samad, Henry Ford Hospital, Rochester Hills, MI, United States

Introduction: There is growing evidence that certain medications are associated with the development of microscopic colitis (MC), especially in the elderly population. However, there is limited data on how patients who are on these medications respond to treatment for MC and if they are at higher risk for disease recurrence. The study aims to analyze whether specific chronic medications are associated with higher disease recurrence rates following initial treatment in patients with MC. Methods: A retrospective cohort study was conducted at a single, urban quaternary care center in the midwestern United States and consisted of 176 patients who received a new diagnosis of MC. Data points that were collected included chronic medication usage of beta blockers, proton pump inhibitors, H2 receptor antagonists,

aspirin or non-steroidal anti-inflammatory, angiotensin receptor inhibitors, mineralocorticoid receptor antagonist, serotonin reuptake inhibitors, or oral hypoglycemic medications. Chronic medication usage was defined as taking the medication 3 times weekly for at least 2 weeks prior to presentation. The primary outcome measured was recurrence of symptoms, defined as lack of treatment response following initial therapy and re-presentation to the gastroenterology clinic within 1 year following initial treatment. Results: A univariate analysis of chronic medications and recurrence revealed a significant association between use of oral hypoglycemic medications and increased MC recurrence rates (Table 1). 15 patients from the cohort used oral hypoglycemic medications. A subgroup analysis revealed the most common drug used in this class was metformin. However, metformin was not independently associated with recurrence in patients treated for MC. Conclusion: Although oral hypoglycemic drugs have been previously shown to be a risk factor in development of MC, our study demonstrates that this class of medications is also associated with higher rates of symptom recurrence following an initial treatment course. While this does not necessarily establish a cause-effect relationship, future studies should focus on the proposed potential pharmacologic risk factors of oral hypoglycemic drugs on MC recurrence. (Table Presented).

Gastroenterology
Samad M, **Suresh S**, **Sherbin E**, **Desai S**, **Marougail V**, and **Dababneh YJN**. Prescriber Practices and Their Impact on Recurrence Rates in Microscopic Colitis. *Am J Gastroenterol* 2024; 119(10):S219-S220. Full Text

M. Samad, Henry Ford Hospital, Rochester Hills, MI, United States

Introduction: Microscopic colitis (MC) is a challenging disease to manage due to the high likelihood of disease recurrence following initial treatment. Some studies have shown that up to 80% of patients initially treated with budesonide experience symptoms within 3 months of stopping the medication. This study aimed to examine how various initial treatments prescribed for patients with newly diagnosed MC impact rates of short-term disease recurrence. Methods: A retrospective cohort study was conducted at a single, urban quaternary care center in the midwestern United States and consisted of 176 patients who presented in the ambulatory setting and received a new histologic diagnosis of MC. Data points that were collected including various patient demographics and initial treatment prescribed. Primary outcome measured was recurrence of symptoms, defined as lack of sustained treatment response following initial therapy and re-presentation to the gastroenterology clinic within 1 year following initial treatment. Results: 59 (34%) patients were treated initially with a budesonide 2-month taper and 53 (30%) patients were treated with a fixed daily dose of budesonide defined as a 2-month course. Additional treatments included 22 (12%) patients who received loperamide, 2 (5%) patients who received bismuth subsalicylate and 3 (8%) patients who received bile acid sequestrants. Other treatments included prednisone, sulfasalazine, and diphenoxylate/atropine which were prescribed in 7 (19%) of patients. A total of 40 (23%) patients who were treated with these medications experienced short-term recurrence of symptoms. A univariate analysis revealed no significant association between initial therapy attempted and frequency of recurrence (Table 1). Conclusion: This study found that the choice of initial treatment does not seem to impact symptom recurrence rates in patients with MC. This suggests that clinicians may tailor their initial choice of therapy to each patient while considering factors such as potential drug interactions and financial constraints without being concerned about decreased efficacy. These findings would benefit from validation on a larger scale since most patients in our cohort received initial treatment with budesonide while other treatments were prescribed far more infrequently. (Table Presented).

Gastroenterology
Samad M, **White C**, **Rehman S**, **Brahmbhatt N**, **Memon M**, **Youssef RM**, **Saleem A**, **Ali H**, and **Jafri SM**. Safety and Tolerability of Orthopedic Surgery Following Liver Transplants. *Am J Gastroenterol* 2024; 119(10):S1359. Full Text

M. Samad, Henry Ford Hospital, Rochester Hills, MI, United States

Introduction: Immunosuppression poses a potential risk for infectious complications following surgery. While most elective and some non-elective orthopedic procedures are generally safe, their post operative

infectious complications in liver transplant patients are understudied. Our purpose of this study is to evaluate risk factors for development of short-term infectious complications following elective and nonelective orthopedic surgeries in liver transplant patients. Methods: The study design is a retrospective cross-sectional study. Data extraction using SlicerDicer was used to identify patients who underwent liver transplantation and elective and non-elective orthopedic surgeries following transplantation from 2013-2022. Data collected included demographics, number of months following transplant, type of orthopedic surgery, and immunosuppression at time of orthopedic surgery. Primary outcomes included infection within 30 days of orthopedic surgery and death within 3 months. Results: A total of 87 patients were identified. The average patient age was 67.5 years at the time of orthopedic surgery. The mean length of time from transplantation to orthopedic surgery was 87 months. Elective surgeries comprised more of the population with 26 undergoing total knee arthroplasty (30%) and 19 undergoing total hip arthroplasty (22%). Non-elective surgeries included open reduction internal fixation (ORIF) and closed reduction internal fixation (CRIF) following acute fracture, comprising of 16 patients (18%). Infections within 30 days were identified in 4 patients, 2 of which underwent total hip arthroplasty. However, there is no significant association between infections within 30 days and type of surgery or immunosuppression at the time of surgery. Additionally, there were no patient deaths that resulted from infection. Conclusion: We evaluated outcomes following orthopedic surgeries in patients following liver transplantation. Our results support the safety and efficacy of these surgeries following liver transplantation.

Gastroenterology

Shahzil M, Fatima M, **Faisal MS**, Rehmani M, **Chaudhry AJ**, Khaqan MA, and **Faisal MS**. Efficacy of Submucosal Injection in Endoscopic Papillectomy for Ampullary Tumors: A Meta-Analysis. *Am J Gastroenterol* 2024; 119(10):S1157-S1158. Full Text

M. Shahzil, Penn State Health Milton S. Hershey Medical Center, Hershey, PA, United States

Introduction: Ampullary adenomas, originating from the ampulla of Vater (AoV), require complete resection due to their precancerous nature. Endoscopic papillectomy offers a less invasive alternative to surgery, but the use of submucosal injection (SI) in this procedure is not standardized, and its efficacy remains unclear due to the unique anatomy of the AoV. This meta-analysis evaluates the clinical efficacy of SI versus no injection before endoscopic papillectomy, focusing on complete resection rates and prevention of complications. Methods: This meta-analysis followed Cochrane and PRISMA guidelines, comparing submucosal injection versus no injection in endoscopic papillectomy for ampullary tumors. We searched PubMed, Embase, Scopus, and Cochrane CENTRAL databases up to May 2024, including RCTs and observational studies. Data extraction followed PICOS criteria using Excel, and statistical analyses were performed with RevMan using a random-effects model ($P < 0.05$). Results: From 203 screened studies, 4 studies with 322 patients undergoing endoscopic papillectomy were selected. The SI group included 134 patients, while the non-SI group had 116 patients. Primary outcomes assessed included en bloc resection (OR: 1.17; 95% CI: 0.49, 2.77), complete resection (OR: 0.55; 95% CI: 0.27, 1.15), and no evidence of residual tumor after long-term follow-up (OR: 0.55; 95% CI: 0.21, 1.42), with no significant differences between groups. Secondary outcomes showed no significant differences in positive deep resection margin (OR: 1.88; 95% CI: 0.62, 5.73), positive lateral resection margin (OR: 2.19; 95% CI: 0.71, 6.72), and overall positive resection margin (OR: 0.65; 95% CI: 0.19, 2.16). Pathologic findings of adenocarcinoma and adenoma were similar. Adverse events, including post-papillectomy bleeding, pancreatitis, perforation, cholangitis, and papillary stricture, showed no significant differences between the SI and non-SI groups. Conclusion: This meta-analysis provides comprehensive evidence indicating no significant benefit of submucosal injection (SI) over no injection in endoscopic papillectomy for ampullary tumors. The lack of significant differences in en bloc resection, complete resection, absence of residual tumors after long-term follow-up, and adverse events suggests that routine SI in endoscopic papillectomy may not offer additional clinical advantages. Further research and broader clinical evaluations are needed to optimize endoscopic techniques for treating ampullary tumors. (Table Presented).

Gastroenterology

Shahzil M, Hasan F, Khan S, Afzal N, **Jomaa D**, Sohail A, **Faisal MS**, Khaqan MA, **Dababneh Y**, and **Salgia R**. OPTIMAL TREATMENT STRATEGIES FOR HEPATOCELLULAR CARCINOMA: A META-ANALYSIS COMPARING TRANSARTERIAL CHEMOEMBOLIZATION (TACE) PLUS MICROWAVE ABLATION (MWA) VERSUS MICROWAVE ABLATION ALONE. *Hepatology* 2024; 80:S1496-S1497. Full Text

M. Shahzil, Penn State Health Milton S. Hershey Medical Center, United States

Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related deaths, with a rising incidence due to non-alcoholic steatohepatitis. Microwave ablation (MWA) is the preferred thermal ablation technique for its larger, more homogeneous ablation zones. Combining transarterial chemoembolization (TACE) with MWA enhances treatment efficacy by reducing heat-sink effects and delivering cytotoxic drugs to microscopic HCCs. This is the first metaanalysis comparing the efficacy of TACE plus MWA versus MWA alone in HCC patients, aiming to optimize treatment strategies for HCC. Methods: This metaanalysis adhered to Cochrane guidelines and PRISMA standards, comparing the effectiveness of TACE plus MWA versus MWA alone for HCC treatment. A comprehensive search was conducted across PubMed, MEDLINE, Embase, Scopus, and CENTRAL databases until May 2024. Inclusion criteria targeted RCTs and observational studies with adult HCC patients receiving TACE plus MWA or MWA alone. Data extraction followed PICOS criteria and was performed using Excel. Statistical analyses utilized RevMan with a random-effects model, considering results significant at $p < 0.05$. Results: Of 485 screened studies, seven studies with 971 HCC patients were included. The TACE plus MWA group had 352 patients, and the MWA group had 619. Primary outcomes assessed included primary effectiveness, overall survival rates, and recurrence/ progression-free survival rates. Primary effectiveness showed no significant improvement (OR: 1.80; 95% CI: 0.88, 3.66). One-year overall survival (OR: 1.14; 95% CI: 0.55, 2.35), three-year overall survival (OR: 0.93; 95% CI: 0.54, 1.59), and five-year overall survival (OR: 0.58; 95% CI: 0.28, 1.21) showed no significant differences. Recurrence/progression-free survival at one year (OR: 1.18; 95% CI: 0.73, 1.92) and three years (OR: 2.09; 95% CI: 0.63, 6.89) also showed no significant differences. Secondary outcomes included disease progression/recurrence (OR: 0.67; 95% CI: 0.43, 1.05) and mean survival time (MD: -4.33 months; 95% CI: -16.07, 8.04), both of which were not significantly different. Adverse events, including intra-abdominal bleeding (OR: 0.72; 95% CI: 0.25, 2.11), GI symptoms (OR: 1.54; 95% CI: 0.21, 11.08), overall adverse events (OR: 2.56; 95% CI: 0.24, 26.79), and fever (OR: 3.65; 95% CI: 0.88, 15.20), showed no significant differences. Conclusion: This meta-analysis shows that combining TACE with MWA does not significantly improve primary effectiveness, overall survival, or recurrence/progression-free survival rates compared to MWA alone in treating HCC. Both treatments have similar safety profiles. Future research should identify subpopulations that may benefit from combined therapy, conduct larger randomized controlled trials, and assess the impact of transarterial radioembolization (TARE) with ablation, given the increasing use of radiation-based HCC treatments in the US.

Gastroenterology

Shamaa O, **Chavarria-Viales M**, **Alhaj Ali S**, **Al Khouly M**, **Varban O**, and **Zuchelli T**. Management of Gastro-Jejunal Anastomotic Strictures: Comparing Endoscopic Outcomes in Primary vs Conversion Roux-en-Y Gastric Bypass Patients. *Am J Gastroenterol* 2024; 119(10):S1118-S1119. Full Text

O. Shamaa, Henry Ford Health, Detroit, MI, United States

Introduction: Conversion surgery from sleeve gastrectomy (SG) to Roux-en-Y gastric bypass (RYGB) is a common intervention for GERD and weight recurrence. There is limited data on post-surgical gastrojejunal anastomotic strictures (GJAS) endoscopic therapy outcomes in patients with sleeve gastrectomy to Roux-en-Y gastric bypass (SG-RYGB) conversion surgeries. Our study aims to compare the outcomes of primary RYGB (P-RYGB) and SG-RYGB GJAS when treated with through-the-scope balloon dilation (TTS BD) and lumen-apposing metal stent (LAMS). Methods: This is a single center retrospective study, that included patients diagnosed with GJAS post P-RYGB and SG-RYGB surgeries who underwent TTS BD or intraluminal LAMS placement. Data was collected between 2/1/2013 - 1/1/2023. Primary outcomes were technical success, clinical success, surgical revision & mortality.

Secondary outcomes included immediate clinical success and the number of endoscopic sessions needed to achieve clinical success. Results: A total of 22 patients were identified to have GJAS, 13 post P-RYGB (age 55 67) & 9 post SG-RYGB (age 45.5 66). Among the P-RYGB group, 4 patients were treated with TTS BD (median stricture diameter 5 mm) and 9 with LAMS (median stricture diameter 5.5 mm). Whereas within the 9 SG-RYGB patients, 7 received TTS BD (median stricture diameter 8.5 mm), and 2 underwent LAMS placement (median stricture diameter 7 mm). All 22 patients had a 100% technical success rate with no mortality or need for surgical revision. Half (n=2/4) of the P-RYGB patients had clinical success with TTS BD compared to 89% (n=8/9) of those who received LAMS. In SG-RYGB patients, almost half of those who received TTS BD (n=3/7) & LAMS stents (n=1/2) had immediate clinical success following first intervention. During the duration of the study, 4/7 (57%) TTS BD and 2/2 (100%) LAMS SG-RYGB patients maintained clinical success without symptom recurrence. One P-RYGB case experienced intraprocedural LAMS mis-deployment. Post-procedure adverse event rates were reported in 1 P-RYGB TTS BD patient & 3 P-RYGB LAMS patients (Table 1). Conclusion: This study demonstrates that both TTS BD and LAMS are effective in the management of GJAS following primary as well as conversion bariatric surgery. LAMS generally exhibited higher immediate and maintenance clinical success rates compared to TTS BD, especially in P-RYGB patients. Further multicenter research involving larger patient cohorts is warranted to optimize patient outcomes in this population. (Table Presented).

Gastroenterology

Shamaa O, **Faisal MS**, **Matin T**, **Khoshbin S**, **Cools K**, and **Watson A**. Suprainfected Heterotopic Pancreatic Tissue: A Rare Culprit of Recurrent Gastric Outlet Obstruction. *Am J Gastroenterol* 2024; 119(10):S1743-S1744. Full Text

O. Shamaa, Henry Ford Health, Detroit, MI, United States

Introduction: Pancreatic rest (PR) is an uncommon finding of ectopic pancreatic tissue that can be located throughout the gastrointestinal tract and is commonly asymptomatic. However, when symptoms develop, they can cause severe complications that include pancreatitis and gastrointestinal obstruction. Here we report a rare case of supra-infected pancreatic rest tissue in the gastric antrum, leading to recurrent gastric outlet obstruction. Case Description/Methods: A 30-year-old woman presents with a 6-month history of worsening abdominal pain, nausea and vomiting refractory to proton pump inhibitor therapy. Index upper endoscopy (EGD) showed a subepithelial nodule in the pylorus, with central umbilication and stenosis in the first portion of the duodenum (Figure 1A). The patient developed recurrent symptoms and underwent 2 EGDs, 1 and 7 months later with serial balloon dilations of the duodenal stenosis to 10 mm and 12.5 mm respectively. Due to persistent stenosis and recurrent symptoms, endoscopic ultrasound (EUS) was performed twice, initially showing a well-defined (23 x 12 mm, Figure 1B) subepithelial lesion in the gastric antrum consistent with pancreatic rest and a second (24 x 14 mm, Figure 1C) subepithelial lesion in the pylorus causing stenosis, fine needle aspiration (FNA) consistent with abscess. Repeat EUS 10 months later showed persistent intramural abscess (27 x 23 mm) with extrinsic compression on the pylorus, repeat FNA drainage was performed. Magnetic resonance imaging abdomen 1 month post-EUS FNA showed an 11 mm distal gastric intramural abscess (Figure 1d) and heterotopic pancreatic tissue emanating from the pancreatic head and extending along the stomach inferior to the abscess (Figure 1e). Patient was treated with multiple courses of antibiotics that resulted in symptom improvement, but continued to develop symptom recurrence after antibiotic discontinuation. Given severe symptoms with recurrent episodes refractory to medical therapy, she was referred to surgical oncology to evaluate for resection. Discussion: This case describes the rare development of recurrent gastric outlet obstruction due to a suprainfected PR. It highlights the significance of recognizing the location and pathologic involvement of PR lesions to help predict and appropriately counsel patients about the potential disease course. Our patient had transmural gastric pylorus involvement, contributing to a higher risk for obstruction. Surgical evaluation should be considered in patients with recurrent severe symptoms if refractory to medical and endoscopic treatment.

Gastroenterology
Singh B, **Ethakota J**, **Bai S**, **Ranjan N**, **Quereshi A**, **Ramanan S**, Sridhar N, Hau Koo T, Kaur G, **Maraj D**, **Zreik H**, **Santos R**, and **Bern M**. Uncanny Association Between Clostridioides difficile and Microscopic Colitis. *Am J Gastroenterol* 2024; 119(10):S1929. Full Text

B. Singh, Henry Ford Jackson Hospital, Jackson, MI, United States

Introduction: Chronic diarrhea is often misdiagnosed as irritable bowel syndrome with diarrhea, especially in women with anxiety, depression, or fibromyalgia. This case highlights the need for thorough evaluation of chronic diarrhea. Causes like bile salt diarrhea post-cholecystectomy, small intestinal bacterial overgrowth in diabetics or post-anastomotic surgery, chronic pancreatitis in type 1 diabetics, and giardiasis near water bodies should be considered. Celiac disease and inflammatory bowel disease should be explored especially with family history. After years of empiric treatment, a colonoscopy during an acute exacerbation of chronic diarrhea led to a diagnosis of microscopic colitis (MC), prompting the discontinuation of selective serotonin reuptake inhibitors (SSRIs), which are a known risk factor. Concurrently, Clostridioides difficile diarrhea, initially missed due to a negative antigen test, was correctly identified via polymerase chain reaction. MC and C. difficile have a reciprocal relationship, where one can predispose to the other. Case Description/Methods: A 47-year-old woman with anxiety, migraines, and chronic diarrhea post-cholecystectomy presented with worsening symptoms. She developed diarrhea after 2 courses of Augmentin for sinusitis, with a subsequent computed tomography revealing pancolitis. Initial stool cultures were negative. Despite a course of ciprofloxacin and Flagyl, her symptoms worsened post-treatment. Family history included Crohn's disease. Daily medications included Escitalopram and cholestyramine. She had leukocytosis, and stool studies including C. difficile toxin were negative. Due to high suspicion, a polymerase chain reaction for C. difficile was ordered and returned positive. Treatment with oral vancomycin improved her symptoms significantly. A follow-up colonoscopy with biopsies diagnosed lymphocytic colitis. SSRI discontinuation was advised, and a tapering course of Budesonide was initiated. Discussion: MC, including collagenous colitis and lymphocytic colitis, presents with chronic watery diarrhea. MC is associated with medications like proton pump inhibitors, SSRIs, and nonsteroidal antiinflammatory drugs. Diagnosis requires colonoscopy and biopsies, as the colon appears normal macroscopically. Treatment typically involves a budesonide taper. Persistent diarrhea or recurrent C. difficile infections warrant colonoscopy with random biopsies to check for MC. This case suggests a possible link between C. difficile infection and lymphocytic colitis, supported by recent studies. MC risk factors include older age, female sex, and smoking. Prior gastrointestinal infections, including C. difficile, are more common in MC patients.

Gastroenterology
Singh B, **Patel-Rodrigues P**, **Khan MZ**, Kaur G, **Bai S**, **Bern M**, and **Jafri SM**. A Rare Case of Immune Checkpoint Cholangitis. *Am J Gastroenterol* 2024; 119(10):S1711. Full Text

B. Singh, Henry Ford Jackson Hospital, Jackson, MI, United States

Introduction: Immune checkpoint inhibitor cholangitis (IMC) due to its rarity poses difficulties in diagnosis and treatment. IMC includes a range of biliary tract injuries with different clinical and pathological characteristics, from small-duct to large-duct involvement. Case Description/Methods: A 32-year-old man presented hospital with presyncope, nausea , and vomiting. Upon computed tomography, he was found to have multiple cryptogenic liver lesions. He had a history of lung adenocarcinoma on maintenance Keytruda. He had multiple admissions related to Keytruda complications which included pancreatitis requiring high-dose steroids, esophagitis, and gastritis (last esophagogastroduodenoscopy showing Severe hemorrhagic gastritis, gastric stenosis). A magnetic resonance cholangiopancreatography was obtained for cholestatic elevation of transaminases and showed intrahepatic and extrahepatic biliary dilatation with periductal enhancement. A liver biopsy was inconclusive. However, the findings could be associated with obstructive changes. The likely differentials were primary versus secondary sclerosing cholangitis. In the setting of prolonged use of pembrolizumab for 1.5 years and taking into consideration the timeline of symptoms, secondary sclerosing cholangitis was diagnosed. She was treated with steroids and keytruda and paclitaxel were discontinued with improvement in symptoms. Discussion: Immune checkpoint inhibitors(ICI) can affect any organ system, including the liver, causing cholangitis, although

this is less common than immune-mediated hepatitis. Cholangitis induced by ICIs is categorized into 3 types: small-duct, large-duct, and mixed. Small-duct cholangitis is likely underreported due to the need for liver biopsy for diagnosis. Its pathology includes bile duct loss, minor bile duct injuries, and mixed inflammatory cells, predominantly CD81 T cells, diffuse fibrosis in the extrahepatic bile duct with imaging showing nonobstructive dilatation or stenosis. For treatment, the Barcelona criterion is used, where alkaline phosphatase normalization indicates complete resolution, a 40% decrease suggests a partial response, and less than 40% is unsatisfactory. Steroids alone or with immunosuppression show similar results. It's crucial to differentiate ICI-induced cholangitis from cholangiocarcinoma, which doesn't respond to steroids, and IgG4-related disease, which does. Taxanes can produce a similar picture and may need discontinuation if ICI-related cholangitis is suspected.

Gastroenterology
Singh B, **Ramanan S**, Kaur G, Singh W, and **Bern M**. MASH 2B TRIALS-A SYSTEMATIC REVIEW. *Hepatology* 2024; 80:S1265. Full Text

B. Singh, Henry Ford Health Jackson, United States

Background: Non-alcoholic fatty liver disease (NAFLD), now termed metabolic dysfunction-associated fatty liver disease (MAFLD), is the leading cause of chronic liver disease in the U.S., encompassing conditions from simple steatosis to cirrhosis and hepatocellular carcinoma. Early symptoms like fatigue and abdominal pain are non-specific, often delaying diagnosis until advanced stages. Systemic insulin resistance leads to lipid accumulation in the liver, triggering inflammatory responses. The gut microbiome and gut-liver axis also play significant roles. Diagnosis uses the NAFLD Activity Score (NAS) and the NASH Clinical Research Network (CRN) fibrosis score to assess disease activity and progression. Treatments emphasize weight loss and lifestyle changes, with promising pharmacological options targeting insulin sensitivity, lipid metabolism, and inflammation. These include PPAR agonists, SGLT-2 inhibitors, GLP-1 inhibitors, and the recently approved Resmetirom. Current research focuses on phase 2b trials to evaluate the efficacy and safety of these treatments. Methods: This study follows PRISMA-2020 guidelines. Three researchers conducted a literature search across multiple databases for phase 2b trials from the past 5 years. Studies were selected using PICO criteria and data were extracted per the Cochrane Handbook. Quality assessment was done using the Cochrane Risk of Bias Tool (2.0). Results: This study includes 11 randomized control trials (RCTs), all double-blinded, with 10 being placebo-controlled, involving adults with histologically confirmed NASH. The trials ranged from 100 to 392 participants. PPAR agonists were tested in the EMMINENCE and NATIVE trials, with NATIVE showing significant fibrosis and NASH resolution at higher doses. FGF21 and FGF19 pathways were targeted in six trials. The Harmony trial with efruxifermin showed significant fibrosis improvement, while the Enliven trial with pegozafermin also demonstrated significant fibrosis reduction at higher doses. The Falcon trials with pegbelfermin did not achieve significant primary outcomes. Alpine 2/3 and Alpine 4 trials with aldafermin showed mixed results, with significant fibrosis improvement only in specific doses. The TANDEM trial, comparing Tropifexor and Cenicriviroc, focused on safety and efficacy, showing ALT, AST, and GGT reductions. ICONA trial with Icosabutate showed potential in NASH patients with T2DM. Belapectin, a galectin-3 inhibitor, did not significantly reduce portal pressure. Outcomes frequently measured NAS or SAF score improvements, highlighting potential in combined drug mechanisms and specific comorbidities. Conclusion: RCTs in NASH treatment showed mixed outcomes. Lanifibranor and icosabutate showed promise, especially in T2D patients. FGF21 analogues like efruxifermin improved fibrosis, while FGF19 trials had variable results. Further research is needed.

Gastroenterology
Singh B, **Zarrar Khan M**, **Patel-Rodrigues P**, **Ramanan S**, **Ahsan B**, and **Schairer J**. Iron Gut. *Am J Gastroenterol* 2024; 119(10):S3149. Full Text

B. Singh, Henry Ford Jackson Hospital, Jackson, MI, United States

Introduction: Gastric siderosis refers to the abnormal deposition of iron within the gastric mucosa associated withwith unclear etiology. Liver is the primary storage organ and once its capacity is saturated, iron can be deposited in other organs such as the heart, joints, and pancreas, leading to organ mdamage,

primarily deposited as hemosiderin. Clinical disorders such as hemochromatosis, gastritis, repeated blood transfusions, and liver diseases are linked to gastric siderosis. Factors like alcohol abuse, iron supplements, NSAIDs, and PPIs also contribute. Studies show oral iron supplementation and NSAIDs can lead to GS. Iron concentration from portocaval shunting may expose stomach cells, particularly in individuals with esophageal varices. Case Description/Methods: A 70-year-old woman with watery diarrhea and rectal urgency for 3 weeks with 7 pounds weight loss. She denied overt bleeding, or recent antibiotic use. Admitted with hemoglobin of 8.8 which was at her baseline, and creatinine 4.6. CT abdomen, Stool studies including Giardia/Cryptococcus, C. difficile toxin, and bacterial PCR were negative. Colonoscopy showed a normal macroscopic appearance with biopsies negative for microscopic colitis. Upper endoscopy showed pitted brown spots mucosa in the gastric body, antrum, duodenal bulb, and second part of duodenum (Figure 1). Biopsies were taken, with antral ones demonstrating antral mucosa with iron deposition in the glands and lamina propria. The iron deposits are highlighted by a Prussian blue stain. The patient had no elevation in transaminases, and further ferritin turned out to be in the 300s limiting our suspicion for hereditary hemochromatosis. In her case, oral iron usage was deemed to be the culprit for the disease. Discussion: Numerous clinical disorders, such as hemochromatosis, gastritis, repeated blood transfusions, and cirrhosis, more so with varices, have been linked to gastric siderosis. Abuse of alcohol, iron supplements, NSAIDs, and PPIs are also implicated. It has diverse endoscopic appearance, characterized as a yellow-brown staining of mucosa. Three primary patterns of iron deposition are as follows: (A) iron deposition in macrophages, stroma, and epithelium, probably linked to stomach irritation, or ulcers, (B) primarily extracellular deposition with some focal deposition in blood vessels, and epithelium; linked to Oral iron supplementation and (C) gastric glandular siderosis and is linked to multiple blood transfusions, cirrhosis, or systemic iron excess caused by hereditary hemochromatosis. (Figure Presented).

Gastroenterology

Toiv A, **Baldwin H**, and **Jafri SM**. Is Age Really Just a Number? A Comparison of Outcomes in Intestinal Transplant Recipients ,50 and 50 Years Old. *Am J Gastroenterol* 2024; 119(10):S1597. Full Text

A. Toiv, Henry Ford Hospital, Detroit, MI, United States

Introduction: With the continued development of therapeutic advances in surgical approaches and post-transplant immunosuppression that consistently improve transplant outcomes, the transplant community has been revising previously held notions regarding age criteria in the transplant evaluation. Historically, younger patients have been prioritized for transplantation due to concerns about posttransplant outcomes in older patients; however, emerging evidence suggests that the impact of age on transplant eligibility criteria may need to be reevaluated. Few studies have explored the impact of age on serious outcomes after intestinal transplantation (IT). This study aims to compare visceral transplant outcomes between IT recipients , 50 and ≥ 50 years old. Methods: We conducted a retrospective chart review of all patients who underwent IT at an academic transplant center from 2010 to 2023. The primary outcome was patient survival, analyzed with Kaplan- Meier survival analysis. Results: Among the 50 IT recipients, there were 21 IT recipients , 50years old and 29 IT recipients ≥50 years old (Table 1). The median age at transplant in the , 50 group was 37 years (range, 17-48) and in the ≥50 group was 55 years (range, 50-68). In both groups, the majority of transplants were exclusively IT, however they included multivisceral transplantation as well. Kaplan-Meier survival analysis (Figure 1) revealed that the , 50 group has a higher survival probability over time compared to the ≥50 group (P 5, 0.01). Although there was a greater incidence of reoperation within 1 and 3 months and the development of chronic kidney disease in the ≥50 group it did not reach statistical significance (P 5.0.05). No significant differences were observed between the groups for graft failure at 1 or 3 years or moderate-to-severe rejection at 1 or 3 years. Conclusion: Although recently published transplant literature has been highlighting that with carefully selected patients age does not impact transplant-related outcomes, this study found that IT recipients ≥50-year-old demonstrated significantly lower survival rates following IT compared to younger patients. Despite not reaching statistical significance, the higher incidence of reoperation within 3 months and the development of chronic kidney disease in the older group suggest that this may be due to potential age-related differences in post-operative complications. .

Gastroenterology
Toiv A, **Baldwin H**, and **Jafri SM**. Does Sex Matter? A Comparison of Outcomes in Men and Women Intestinal Transplant Recipients. *Am J Gastroenterol* 2024; 119(10):S1595-S1596. Full Text

A. Toiv, Henry Ford Hospital, Detroit, MI, United States

Introduction: Researchers are increasingly investigating the possible differences in transplant-related outcomes between men and women. However, few studies have explored whether patient sex is associated with serious outcomes after intestinal transplantation (IT). This study aims to compare visceral transplant outcomes between men and women transplant recipients. Methods: We conducted a retrospective chart review of all patients who underwent IT or multivisceral transplant (MVT) at an academic transplant center from 2010 to 2023. The primary outcome was patient survival, analyzed with Kaplan-Meier survival analysis. Results: Among the 50 IT recipients, there were 20 men and 30 women (Table 1). The median age at transplant was 50 years (range, 22-64). Of the transplants, 58% were exclusively IT, while 42% were MVT. Kaplan-Meier survival analysis (Figure 1) revealed no significant mortality difference between the groups when analyzed by sex (P =0.28) or when comparing IT alone to MVT (P 5.0.05 in all subgroups). Male IT recipients showed a higher need for reoperation within 1 month (P =0.01) but not within 3 months (P =0.44). No significant differences were observed between the sexes in graft failure at 1 or 3 years, moderate-to-severe rejection at 1 or 3 years, or the development of post-transplant chronic kidney disease. Conclusion: Although the literature has highlighted differences in transplant-related outcomes based on patient sex, this study found no significant survival or transplant-related differences between men and women IT and MVT recipients. These findings can help address sex-based disparities in transplant outcomes and inform clinicians as to whether sex is an important consideration for IT evaluations. .

Gastroenterology
Toiv A, **Harris K**, **Zarrar Khan M**, **Theisen BK**, **Varma AK**, **Fain C**, and **Kaur N**. Rare EBV-Positive Recurrent Post-Transplant Lymphoproliferative Disorder With Barely Detectable EBV Viremia: A Diagnostic Challenge. *Am J Gastroenterol* 2024; 119(10):S1985. Full Text

A. Toiv, Henry Ford Hospital, Detroit, MI, United States

Introduction: Post-transplant lymphoproliferative disorders (PTLD) are complications arising from post-transplantation immunosuppressive therapy. Epstein-Barr virus (EBV) viremia is often seen in PTLD, but it is not a diagnostic feature. We report a rare case of recurrent PTLD in a transplant recipient who had high EBV viremia in her first PTLD episode, however, her recurrent episode had barely detectable EBV viremia, delaying diagnosis. Case Description/Methods: A 26-year-old woman with a heart transplant (EBV donor1/recipient-) and Crohn disease presented to the emergency department with severe abdominal pain and bloody diarrhea. Her heart transplantation was 7 years previously and she was maintained on high-dose immunosuppression. Notably, she had been diagnosed with EBV-positive PTLD 4 years previously and successfully treated with rituximab. That PTLD presentation was diagnosed with substantial EBV viremia (> 700,000 copies/mL). At this presentation, she had been treated for recurrent inflammatory bowel disease (IBD) flares over the preceding months before her symptoms escalated. Initial laboratory tests revealed high C-reactive protein, low EBV viral load below 50 IU/mL, and no lymphocyte abnormalities on peripheral smear. Computed tomography abdomen revealed severe pancolonic wall thickening and fat stranding, with multiple prominent pericolonic lymph nodes. She was started on methylprednisolone for presumed IBD flare. Due to a lack of clinical response, colonoscopy was pursued on day 3 of admission and showed inflammation with deep continuous and circumferential ulcerations from the rectum to the sigmoid, with pronounced serpiginous ulcers in the sigmoid colon. Pathology analysis (Figure 1) of colonic biopsies revealed mucosal architectural distortion, Paneth cell metaplasia, and increased lamina propria plasmacytic inflammation. Further histologic staining revealed EBV-positive plasma cell hyperplasia with no evidence of cytomegalovirus or granulomata supporting a diagnosis of recurrent early PTLD. Discussion: This case illustrates the challenge of diagnosing rare gastrointestinal recurrent PTLD. Our patient's diagnosis was delayed because her symptoms resembled an IBD flare and she had barely detectable EBV, unlike her first PTLD episode. When evaluating a transplant recipient manifesting severe gastrointestinal symptoms, we recommend maintaining a

heightened suspicion for PTLD and adopting a low threshold for early endoscopy with biopsy analysis for EBV.

Gastroenterology
Toiv A, **Kumar V**, **Patel A**, and **Jafri SM**. Protocol for the Management of Hepatitis C Transferred Through Kidney Transplantation. *Am J Gastroenterol* 2024; 119(10):S1320. Full Text

A. Toiv, Henry Ford Hospital, Detroit, MI, United States

Introduction: The effectiveness of direct-acting antiviral (DAA) drugs for treating hepatitis C virus (HCV) infection may substantially increase the number of available organs for transplants by allowing organ transplantation from HCV-positive (HCV1) donors into HCV-negative (HCV-) recipients. This study describes the outcomes of HCV- recipients who received kidneys from HCV1 donors, highlighting the benefits of post-transplant DAA therapy. Methods: This was a single center retrospective case series of all HCV- recipients who underwent kidney transplantation with organs from HCV1 donors at our transplant center from October 2020 to May 2023. Results: There were 11 HCV- recipients who underwent deceased donor kidney transplantation (DDKT) with organs from HCV+ donors: 9 men (82%) and 2 women (18%). There was 1 patient who received both liver and kidney. The median age was 60 years (range 41-76). The mean organ wait time spent on dialysis was 1.9 years. All patients were confirmed HCV- by quantitative nucleic acid amplification test at the time of transplant, and 9 (82%) patients tested HCV+ after transplantation. Of these 9 HCV infections, 6 were genotype 1a, 1 was 1b, and 2 were 2b. Notably, 8 of these 9 patients received DAA therapy for 12 weeks (6 sofosbuvir/velpatasvir and 2 glecaprevir/pibrentasvir), and all 8 patients had undetectable virus at 8 weeks of treatment with no side effects requiring early treatment termination. Also, none developed graft rejection or glomerulonephritis from HCV infection, although 2 patients had delayed graft function that improved. Within 1 year of transplant, 2 of the 8 patients died due to comorbidities unrelated to HCV or transplant. The 1-year survival for all kidney transplant recipients at our center between 2021 and 2022 was 96%. Conclusion: All HCV- patients who received an HCV+ DDKT and were treated with DAA therapy for post-transplant HCV infection had complete resolution of HCV. Patients receiving an HCV+ DDKT underwent transplant much earlier than expected, at around 1.9 years of dialysis waiting (DDKT wait time for type O patients is 5 years in Michigan). Effective DAA therapy now allows kidneys from HCV1 donors to be a safe source of organs for transplantation.

Gastroenterology
Toiv A, **Nabaty R**, **Saleh Z**, **Saleem A**, **Heppell O**, **Rahman A**, **Watson A**, and **Piraka C**. Entangled Pathways: Duodenal Obstruction Caused by Celiac Artery Dissection. *Am J Gastroenterol* 2024; 119(10):S3040. Full Text

A. Toiv, Henry Ford Hospital, Detroit, MI, United States

Introduction: Spontaneous celiac artery dissection is a rare subtype of visceral arterial dissection. While it may be incidentally discovered in asymptomatic individuals, it typically manifests as acute, severe abdominal pain and symptoms indicative of intestinal ischemia. This case introduces a novel diagnosis of acute celiac artery dissection causing duodenal obstruction. Case Description/Methods: A healthy 61-year-old man with no significant past medical history presented with subacute worsening nausea and vomiting, leading to an inability to eat or drink. Upon presentation, his vital signs were within normal range, and his abdominal physical examination was benign. Initial laboratory studies yielded normal results. Computed tomography of the abdomen revealed a 6.8 x 3.6 cm lobulated collection beneath the duodenum, compressing the duodenum. MR-cholangiopancreatography revealed dilation and aneurysm of the celiac trunk accompanied by a heterogeneous hemorrhagic mass enveloping and externally constricting the duodenum, causing duodenal obstruction. Esophagogastroduodenoscopy identified a narrowed, edematous 5 cm segment of the duodenum beyond D2, with all biopsies demonstrating normal mucosa. Subsequent computed tomography-angiography revealed a celiac artery dissection with preserved flow and a 4 cm pancreaticoduodenal artery pseudoaneurysm. Interventional radiologists successfully embolized the pancreaticoduodenal pseudoaneurysm using microcoils. Anticipating that the obstructive process would improve after aneurysm microcoiling, clinicians did not place a duodenal stent.

Instead, the patient was treated conservatively with nasogastric decompression. After several days of monitoring, the obstruction improved, allowing the patient to be discharged with the ability to consume a liquid diet. The patient was eventually able to return to eating a normal diet. Discussion: To our knowledge, this is the first reported case of a patient with a celiac artery dissection and pancreaticoduodenal pseudoaneurysm leading to external duodenal compression and obstruction. This case underscores a need for broadening the differential diagnosis for duodenal obstruction to encompass pathologies associated with the surrounding vasculature. Furthermore, it supports a conservative approach to managing this compressive duodenal obstruction with aneurysm coiling, rather than placing a permanent duodenal stent.

Gastroenterology
Toiv A, **Saleem A**, **Obri M**, **O'Brien H**, and **Jafri SM**. ADVANCING LIVER TRANSPLANTATION INTO THE NEXT DECADE: LIVER TRANSPLANT OUTCOMES IN PATIENTS 70 YEARS OR OLDER. *Hepatology* 2024; 80:S974. Full Text

A. Toiv, Henry Ford Hospital, United States

Background: Since the introduction of direct-acting antivirals for hepatitis C virus, liver transplantation (LT) has undergone a change in patient demographics, with patients receiving increasingly more LT for other chronic liver diseases and at older ages. Historically, younger patients have been prioritized for LT due to concerns about post-transplant outcomes in older patients; however, emerging evidence suggests that the impact of age on transplant eligibility criteria may need to be reevaluated. This study describes the clinical characteristics and postoperative LT outcomes of patients ≥ 70 years compared to patients < 70 years old. Methods: Single center retrospective chart review of all patients who underwent LT at a high-volume academic transplant center between January 1, 2014, and September 26, 2023. Results: Of 999 liver transplant recipients (36% women; 64% men), 43 were ≥ 70 years old (median 71 y; range 70-75) and 956 were < 70 years old (median 58 y; range 16-69). The older group had more baseline comorbidities but a lower median MELD at LT (21 vs 25; p =.014). Indications for LT differed between groups; while the younger group had a higher rate of alcoholic cirrhosis (39% vs 14%; p = < .001), the older group had greater proportions of patients with metabolic dysfunction-associated steatohepatitis (51% vs 23%; p = <.001), primary biliary cholangitis (9.3% vs 2.8%; p= .040), and cryptogenic cirrhosis (14% vs 5%; p= .022). Older and younger patients had similar postoperative liver function laboratory values, biliary complication rates, need for further procedures, and hospital readmission. The older cohort had a significantly longer mean length of stay (25.5 vs 14.0 days; p= .002), an association that was confirmed on regression analysis (p < .001). Notably, no differences in mortality or graft failure at 1, 3, and 5 years were observed between older and younger LT recipients. Conclusion: LT recipients ≥ 70 years-old had positive post-transplant outcomes and similar patient and graft survival as patients < 70 years old, although older age was associated with a longer hospital stay. Overall, LT evaluation and eligibility age criteria may need to be reevaluated to be more age inclusive.

Gastroenterology
Trivedi P, **Gordon S**, Gulamhusein A, Villamil A, Lawitz E, Vierling J, Londono MC, Kremer A, Bowlus C, Proehl S, Zhuo S, Crittenden D, and McWherter C. LONG-TERM SAFETY OF SELADELPAR 10 MG WITH UP TO 5 YEARS OF TREATMENT IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS. *Hepatology* 2024; 80:S1823-S1824. Full Text

P. Trivedi, University of Birmingham, Toronto, Canada

Background: Seladelpar, a novel delpar (selective PPARdelta agonist), is in development for the treatment of primary biliary cholangitis (PBC). The phase 3, placebocontrolled RESPONSE study (NCT04620733) in PBC patients with an inadequate response or intolerance to ursodeoxycholic acid demonstrated significant improvements in cholestatic markers and pruritus with seladelpar over one year. Similar proportions of seladelpar and placebo-treated patients experienced adverse events (AEs) and serious AEs (SAEs). To assess long-term safety, data from all PBC patients exposed to seladelpar 10 mg in 6 studies with similar entry criteria were pooled. Methods: AE data from 2 placebo-controlled and 4 openlabel studies were pooled for all patients treated with seladelpar 10 mg as of 31 Jan 2024, beginning

with first exposure to seladelpar, including all exposure periods and excluding treatment gaps. Placebo exposure was pooled from the 2 placebo-controlled studies. Exposure-adjusted subject incidences of AEs, SAEs, and AEs of interest (defined as liver-, muscle-, renal-, and pancreatic-related AEs) were calculated. Results: As of the data cutoff, a total of 486 patients received seladelpar 10 mg: 355 were treated for ≥1 year, 170 ≥2 years, 66 ≥3 years, 36 ≥4 years, 10 ≥5 years. The exposure-adjusted subject incidence (per 100 patient-years) for seladelpar 10 mg was 48.3 for AEs, 8.0 for SAEs, 9.8 for Grade ≥3 AEs, and 6.1 for liver-related AEs. There were no treatment-related SAEs. Muscle, renal, and pancreatic AEs occurred in <7 patients per 100 patient-years. Placebo exposure included 152 patients: 117 were treated for ≥12 weeks, 84 for ≥6 months, and 57 for 12 months of placebo treatment in RESPONSE. The exposure-adjusted subject incidence (per 100 patient-years) for patients treated with placebo was 132 for AEs (rate reflective of shorter exposure time for placebo patients), 7.8 for SAEs, 12.2 for Grade ≥3 AEs, and 13.3 for liver-related AEs (with other AEs of interest occurring at lower rates). AEs leading to treatment discontinuation occurred in 2.9 patients per 100 patientyears in seladelpar patients and 5.6 per 100 patient-years in placebo patients. Conclusion: Analysis of a large safety database for seladelpar in PBC patients with exposure through 5 years indicated that seladelpar was well tolerated with a safety profile similar to placebo.

Gastroenterology
Trivedi PJ, Levy C, Kowdley KV, **Gordon SC**, Bowlus CL, Hurtado MCL, Hirschfield GM, Gulamhusien AF, Lawitz EJ, Villamil A, Cetina ALDG, Mayo MJ, Younes ZH, Shibolet O, Yimam KK, Pratt DS, Heo J, Morgera U, Andreone P, Kremer AE, Corpechot C, Goel A, Peyton A, Elbeshbeshy H, Crittenden DB, Heusner C, Proehl S, Zhou S, and McWherter CA. OP-1 LONG-TERM EFFICACY AND SAFETY OF OPEN-LABEL SELADELPAR TREATMENT IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS: INTERIM 2-YEAR RESULTS FROM THE ASSURE STUDY. *Ann Hepatol* 2024; 29. Full Text

Introduction and Objectives: Seladelpar reduces biochemical markers of cholestasis and pruritus in patients with primary biliary cholangitis. ASSURE (NCT03301506) is an ongoing, open-label, long-term Phase 3 trial of seladelpar in patients rolling over from Phase 3 RESPONSE (NCT04620733) or legacy studies (NCT03602560, NCT02955602, NCT03301506, and NCT04950764). We report interim 2-year efficacy and safety results. Patients / Materials and Methods: Patients with insufficient response/intolerance to ursodeoxycholic acid could enroll in ASSURE. Key endpoints were composite biochemical response (alkaline phosphatase [ALP] <1.67 × upper limit of normal [ULN], ALP decrease ≥15%, and total bilirubin ≤ULN) and ALP normalization. Pruritus was measured using numerical rating scale (NRS; 0–10). For patients enrolling from RESPONSE, baseline was entry to RESPONSE and analyzed as continuous seladelpar or crossover from placebo; legacy patients were analyzed separately with baseline defined as entry to ASSURE. Results and Discussion: As of 01/2024, 158 RESPONSE and 179 legacy patients received seladelpar 10 mg daily for up to 155 weeks. In RESPONSE, 61.7% of patients met the endpoint at 12 months (M) vs 20% for placebo. In ASSURE, 61.8% (6M) and 72.4% (12M) met the composite endpoint; 75% (6M) and 93.8% (12M) of placebo crossover patients met the endpoint. In RESPONSE, ALP normalized in 25% of seladelpar and 0 placebo patients at 12M. With continued treatment, 33.3% (6M) and 17.2% (12M) had ALP normalization; 26.9% (6M) and 50% (12M) of crossover patients had ALP normalization. In ASSURE, 6-month change from baseline in pruritus NRS was similar to RESPONSE: −3.8 and −3.7 in continuous and crossover patients, respectively. At 12M and 24M, 73.2% and 69.7% of legacy patients met the endpoint in ASSURE; 42.1% and 42.4% achieved ALP normalization, and reduction in pruritus NRS was −3.8 and −3.1, respectively. There were no treatment-related serious adverse events. Conclusions: Seladelpar treatment led to improvements in biochemical markers and pruritus, and was well tolerated with long-term use.

Gastroenterology
Vemulapalli K, **Khan MZ**, and **Al Shammari M**. Uncomplicated Diverticulitis Masquerading as Symptomatic Ovarian Cyst in a Young Female. *Am J Gastroenterol* 2024; 119(10):S1973. Full Text

K. Vemulapalli, Henry Ford Health, Detroit, MI, United States

Introduction: Diverticulitis is an overwhelmingly common diagnosis in the field of gastroenterology. However, it is currently a diagnosis of high suspicion only in elderly to middle aged patients. Signs and

symptoms of diverticulitis overlap with many alternative diagnoses. The differential is particularly broad in young female patients. Here we present a case of diverticulitis in a young female patient that was previously masquerading as symptomatic ovarian cyst. Case Description/Methods: A 19-year-old woman with prior history of symptomatic ovarian cyst requiring resection months prior presented with 4-day history of right lower quadrant pain associated with nausea and diarrhea. She denied fevers or chills. She reported symptoms consistent with recurrence of prior episodes of symptomatic ovarian cyst. Exam was pertinent for right lower quadrant tenderness. Vitals signs remarkable for initial tachycardia with lab work showed leukocytosis to 13.0, unremarkable liver profile, lipase, urinalysis and pregnancy testing. Computed tomography Abdomen Pelvis with contrast was performed and showed findings of wall thickening and pericolonic fast stranding with multiple colonic diverticula at the level of mid ascending colon to the hepatic flexure concerning for diverticulitis. She was started on amoxicillin-clavulanate and noted to have significant improvement. She was discharged with a 5-day course of antibiotics to follow-up outpatient for colonoscopy. Discussion: Acute diverticulitis is 1 of the leading gastrointestinal-related causes of hospitalization with diagnostic delay resulting in increased risk of associated complications including abscess formation, fistulation, and sepsis. Recent trends have demonstrated a rising incidence of diverticulitis in younger patients resulting in a disconnect between clinical suspicion and disease prevalence. Moreover, studies have indicated diverticulitis in younger patients can present with increased severity and likelihood of recurrence. Differential diagnoses of recurrent abdominal pain should remain broad even with prior diagnoses of gynecologic etiology. Guidelines for treatment are not standardized therefore early intervention and appropriate follow-up should be arranged to ensure adequate long-term care of affected patients (see Figure 1).

Gastroenterology

Vemulapalli K, **Khan MZ**, **Patel-Rodrigues P**, **Hammad T**, and **Watson A**. Intrapapillary Mucinous Neoplasm Complicated by Spontaneous Pancreaticogastric Fistula. *Am J Gastroenterol* 2024; 119(10):S1836-S1837. Full Text

M.Z. Khan, Henry Ford Health, Detroit, MI, United States

Introduction: Intraductal Papillary Mucinous Neoplasms (IPMNs) consist of a range of presentations varying in malignant potential. Mainly characterized by papillary growth and significant mucin secretion, IPMNs can present with various complications including obstructive jaundice or cholangitis. Rarely, IPMN can fistulize into the adjacent organs. Here we present the case of a patient found to have benign IPMN complicated by 20mm pancreatico-gastric fistula. Case Description/Methods: An 85-year-old woman with history of heart failure presented with several week history of progressive epigastric pain accompanied by poor appetite and nausea. She remained hemodynamically stable with lab work showing unremarkable liver enzymes, blood counts, and lipase. Computed tomography abdomen pelvis showed dilated pancreatic duct with communication to the stomach. Magnetic resonance cholangiopancreatography (MRCP) showed moderate intrahepatic and severe extrahepatic biliary ductal dilation with the main pancreatic duct dilated up to 20mm. A 20mm fistula between the pancreatic body duct to posterior wall of the stomach was noted. The patient underwent Esophagogastroduodenoscopy/endoscopic retrograde cholangiopancreatography (ERCP) which demonstrated a 20mm fistula with copious amounts of mucin pouring out of the lesser curvature opening. The main pancreatic duct was visualized with features of main duct IPMN. Biopsy demonstrated features consistent with low-grade IPMN. Sphincterotomy and balloon extraction of choledocholithiasis was performed. A fully covered metal stent was placed into the common bile duct to maintain biliary drainage. Multidisciplinary discussion was held with the patient's family, gastroenterology team, and oncology team and decision to pursue resection was deferred in favor of symptomatic care. The patient recovered well and was discharged to follow-up for outpatient ERCP for further stent management. Discussion: IPMN resulting in fistulation into the stomach is an exceedingly rare presentation that can mimic many other pathologies of abdominal pain. Our patient's presentation with non-specific symptoms of epigastric pain, nausea, and early satiety requires a high degree of suspicion for biliary pathology. The identification of such a diagnosis requires complex decision-making involving multidisciplinary insight as well as shared decision-making regarding the potential for malignancy and surgical versus conservative management (see Figure 1).

Gastroenterology

Venkat D, **Chaudhary AJ**, **Elshebiny H**, and **Jafri SM**. Incidence, Management, and Prognosis of Wilson's Disease. *Am J Gastroenterol* 2024; 119(10):S1263. Full Text

D. Venkat, Wayne State University, School of Medicine, West Bloomfield, MI, United States

Introduction: Wilson's disease is an autosomal recessive condition caused by mutation in the Wilson's disease protein (ATP7B) gene, which results in an excessive copper buildup in the body. In this study, we present a retrospective analysis of the incidence, prognosis, and management of Wilson's disease at an academic medical center. Methods: We evaluated medical records of all patients with Wilson's disease seen at an academic medical center over the past 10 years. Each patient's presentation, management, and overall disease course was reviewed. This includes demographics, laboratory testing, 24-hour copper urine testing, symptoms, hepatology evaluation, therapy, side effects, liver complications, transplantation, and mortality. Results: A total of 88 patients with Wilson's disease were included; 43% are older than 50 years at diagnosis, with mean age 46.6 (range 13 to 83); 55% were female. Of the 17 with an initial 24-hour urine copper test recorded at our center, 29% had urine copper greater than 100 mcg at first clinic visit. Of those with initial and most recent 24-hour urine copper testing documented, 78% showed decreased urine copper and 22% showed no change or increase in urine copper. In total, 51% were asymptomatic, 15% had only gastrointestinal (GI) symptoms, 22% had only neuropsychiatric symptoms, and 2% had both GI and neuropsychiatric symptoms, 52% had documented visits with hepatology forWilson's disease. Of those who saw hepatology, 23% had 1 follow-up visit each year, and 77% had 2 or more visits per year. Only 28% of patients had documented therapy. Of patients on treatment, 28% were placed on trientine only, 36% were on zinc only, 24% received a combination of trientine, zinc and/or penicillamine. For those taking medications, 24% demonstrated intolerance to medications. 16% required a liver transplant. In total, 26% of the patients had cirrhosis, and 11% received a transplant. The mortality rate was 11%, but none of the deaths were related to Wilson's disease. Conclusion: Wilson's disease is a complex condition in which follow-up and assessment of fibrosis and successful therapy are important. We found that a large number of patients did not have referral to hepatology in spite of the diagnosis. Further, only 28% of patients with diagnosis of Wilson's disease had documented therapy at any time. Closer attention is warranted to ensure treatment and follow-up of patients with this progressive condition.

Gastroenterology

Yilmaz Y, Yu ML, Alswat K, El-Kassas M, Buti M, Papatheodoridis G, Fernandez MIC, Eguchi Y, Duseja A, Keklikkiran C, Hamid S, Chan WK, **Gordon S**, Esmat G, Isakov V, Roberts S, Mendez-Sanchez NN, Fan JG, Gomez MR, George J, Singal A, Ahmed A, Lam B, Nader F, Henry L, Stepanova M, and Alqahtani S. FATIGUE IN CHRONIC HEPATITIS B (CHB) AND C (CHC) IS ASSOCIATED WITH IMPAIRMENT OF PATIENT-REPORTED OUTCOMES (PROS) AND WORK PRODUCTIVITY. *Hepatology* 2024; 80:S348-S349. Full Text

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Background: CHB and CHC infections are linked to impaired PROs. We sought to identify factors associated with fatigue and PROs in CHB and CHC. Methods: We analyzed clinical, demographic, and PRO data (FACIT-F, CLDQ or CLDQ-HCV, WPAI) from CHB and CHC patients enrolled in the Global Liver Registry™. Clinically overt fatigue was defined as a Fatigue Scale (FS) score of less than 30 on a 0-52 scale. Results: We included 2,888 patients: 1,561 CHB (age 47 ± 13 years, 60% male, 26% obese, 12% type 2 diabetes, 13% advanced fibrosis, 13% history of depression, 21% fatigue) and 1,327 CHC (age 50 ± 13 years, 47% male, 30% obese, 16% type 2 diabetes, 21% advanced fibrosis, 18% depression, 39% fatigue), recruited from 19 countries. Patients with CHB and fatigue were younger, more likely female, and more commonly obese, with higher rates of anxiety and depression (all $p < 0.01$). They also reported significant impairment in all PRO domains, with mean total CLDQ score (range 1-7) 4.14 (SD 0.90) vs. 5.77 (0.86), total FACIT (4 generic domains of FACIT-F, not including FS, range 0-108) 67.6 (14.5) vs. 87.7 (13.7), work productivity impairment (WPI) (range 0-1) 0.33 (0.29) vs. 0.11 (0.22) (all $p < 0.0001$). Multivariable analysis revealed that the association between lower PRO scores and fatigue in CHB remained significant, with an impairment magnitude of up to -23% of the PRO range size (all p<

0.01). Similarly to CHB, CHC patients with fatigue were more commonly female, obese, and had higher rates of type 2 diabetes, anxiety, and depression (all p< 0.05). They reported substantial impairment in PRO scores, with mean total CLDQ-HCV scores of 3.76 (SD 1.03) vs. 5.46 (0.99), mean total FACIT scores of 61.8 (14.1) vs. 85.6 (14.5), and mean WPI of 0.49 (0.32) vs. 0.17 (0.25) (all p <0.0001). Multivariable analysis showed that the association between lower PRO scores and fatigue in CHC was significant for all PROs, with an impairment magnitude of up to -33% (all p <0.01). Other predictors of lower PRO scores in both CHB and CHC included age, female sex, advanced fibrosis, nonhepatic comorbidities, and lack of regular exercise (p< 0.05). In the combined CHB and CHC sample, having CHB (reference: CHC) was independently associated with higher PRO scores in all but one domain and the total score of FACIT (up to +5%, p< 0.01). Conclusion: Our study highlights the significant burden of fatigue experienced in both CHB and CHC, which is associated with substantial impairment of PROs and work productivity.

Gastroenterology
Younossi Z, Buti M, Papatheodoridis G, Yilmaz Y, Yu ML, El-Kassas M, Alswat K, Fernandez MIC, Eguchi Y, Duseja A, Keklikkiran C, Hamid S, Chan WK, **Gordon S**, Roberts S, George J, Singal A, Ahmed A, Lam B, Nader F, Henry L, Stepanova M, and Alqahtani S. THE IMPACT OF SUPERIMPOSED METABOLICDYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE (MASLD) ON CLINICAL AND PATIENT-REPORTED OUTCOMES (PROS) PROFILE OF PATIENTS WITH CHRONIC HEPATITIS B (CHB) AND C (CHC). *Hepatology* 2024; 80:S200-S201. Full Text

Z. Younossi, Global NASH Council

Background: CHB, CHC and MASLD are common causes of liver disease. We aimed to assess clinical and PRO profiles of patients with CHB and CHC with and without superimposed MASLD using the Global Liver Registry™. Methods: Clinical and PRO (FACIT-F, CLDQ, WPAI) data were analyzed from CHB and CHC patients from GLR. Superimposed MASLD was defined as Hepatic Steatosis Index (HSI) ≥ 36 and presence of > 1 cardio-metabolic risk factor (overweight, type 2 diabetes, hypertension, hyperlipidemia). Results: We included 4,649 subjects: 2,063 CHB (48 ± 13 years, 57% male, 11% advanced fibrosis) and 2,586 CHC subjects (56 ±14 years, 47% male, 18% advanced fibrosis). Among CHB, 49% had superimposed MASLD. CHB patients with and without MASLD were similar in age, sex, and had similar rates of advanced fibrosis (defined as FIB-4 ≥ 2.67 or liver stiffness ≥ 12 kPa), biopsy-proven cirrhosis, and non-cardio-metabolic comorbidities (all p > 0.05). Despite this, CHB patients with MASLD had significantly lower PRO scores in the domains of Physical Well-Being and Fatigue of FACITF, and all six domains of CLDQ (all p <0.01); the greatest impairment was observed in the Fatigue domain of CLDQ (-6% of the score range size). In multivariate analysis, the presence of superimposed MASLD in CHB was independently associated with lower scores in these domains after adjustment for confounders (p <0.05). Among CHC, 47% had superimposed MASLD. CHC patients with MASLD were younger and more commonly female (p <0.01). However, they had similar rates of advanced fibrosis, biopsy-proven cirrhosis, and non-cardio-metabolic comorbidities (all p > 0.05). CHC patients with MASLD had lower PRO scores in Physical Well-Being domain of FACIT-F and all four domains of CLDQ-HCV (all p< 0.01); the greatest impairment was observed in Systemic Symptoms and Worry domains of CLDQ-HCV (-6% of the score range size). In multivariate analysis, presence of superimposed MASLD in CHC was independently associated with lower scores in CLDQHCV domains after adjustment for confounders (p< 0.05). In comparison to CHC+MASLD, CHB +MASLD were younger (48 vs. 54 years), more commonly male (58% vs. 39%) with lower rates of advanced fibrosis (10% vs. 18%) and select nonhepatic comorbidities, and had higher PRO scores in most domains (3/5 domains of FACIT-F, work productivity and activity impairment by WPAI) (p <0.05). Conclusion: Almost half of the patients with CHC or CHB had superimposed MASLD. The clinical profile between those with viral hepatitis with or without MASLD is similar but those with superimposed MASLD reported a significant impairment in their patientreported outcomes.

Gastroenterology
Younossi Z, Yilmaz Y, Yu LL, Isakov V, Castellanos Fernandez MI, Wong V, Eguchi Y, Romero-Gómez M, Duseja A, Bugianesi E, Chan WK, Alswat K, Hamid S, Singal A, Fan JG, Papatheodoridis G, **Gordon S**, El-Kassas M, Younes Z, Roberts S, Mendez-Sanchez NN, Keklikkiran C, Ahmed A, Lam B, Nader F, Henry L, Stepanova M, and Alqahtani S. PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) AND METABOLIC DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE (MASLD) HAVE SIMILAR CLINICAL, NON-INVASIVE TESTS (NITS) AND PATIENT-REPORTED OUTCOMES (PROS) PROFILE. *Hepatology* 2024; 80:S1279-S1280. Full Text

Z. Younossi, Global NASH Council, Riyadh, Saudi Arabia

Background: NAFLD was recently renamed as MASLD. Given changes in the definition, there have been concerns about the applicability of previous NAFLD evidence on MASLD. Our aim was to compare PROs and NITs between NAFLD and MASLD. Methods: Using our Global NASH Registry and NAFLD Databases, patients with established diagnosis of NAFLD and NASH were included. MASLD and MASH were defined according to the new criteria (Rinella, Hepatology 2023). We calculated the concordance of definitions for MASH and NASH or NAFLD and MASLD. We also evaluated NIT scores and PRO scores (by CLDQ-NAFLD or FACIT-F or WPAI instruments) according to NAFLD and MASLD. Results: 11,600 NAFLD patients were included (age 53 ± 12 years, 45% male, BMI 34.0 ±8.0, and T2D 48%). Of the entire NAFLD group, 97.2% fulfilled the criteria for MASLD; among participants with biopsy-proven NASH, 99.97% also met the definition of MASH. Subjects with MASLD and NAFLD had similar FIB-4 scores (1.58 ± 1.52 vs. 1.58 ± 1.51) and liver stiffness by transient elastography (12.0 ± 9.8 kPa vs. 11.8 ± 9.7 kPa). Of the entire NAFLD sample, 71% had PRO scores recorded. The CLDQ-NAFLD and FACIT-F scores were similar between MASLD and NAFLD groups: total CLDQNAFLD 5.16 ± 1.14 vs. 5.17 ± 1.14 (range 1-7), total FACIT-F 114.1 ± 26.2 vs. 114.5 ± 26.2 (range 0-160). However, for subjects with NAFLD who did not fulfil the criteria for MASLD (2.8% of all NAFLD), NIT scores were significantly lower (FIB-4 1.39 ± 1.32 vs. 1.58 ± 1.52, liver stiffness 5.73 ± 3.22 kPa vs. 12.0 ± 9.8 kPa) while their PRO scores were significantly higher (CLDQ-NAFLD 5.70 ± 0.84 vs. 5.16 ± 1.14, FACIT-F 125.1 ± 23.4 vs. 114.1 ± 26.2) in comparison to subjects with MASLD. In multivariate regression analysis, independent predictors of PRO scores were similar in patients with NAFLD and MASLD and included age, sex, enrollment setting (tertiary care vs. real-world), BMI, FIB-4 score, and the presence of nonhepatic comorbidities ($p < 0.05$). Conclusion: Over 97% of NAFLD patients meet the criteria for MASLD with similar NIT and PRO profile. NAFLD patients who do not meet MASLD criteria seem to have milder disease as manifested via lower NIT scores and higher PRO scores. These data provide evidence that NAFLD and MASLD, NASH and MASH can be used interchangeably.

Gastroenterology
Youssef RM, **Yanamandra A**, and **Jafri SM**. Outcomes of Liver Transplantation in Arab American Patients: A Single Center Experience. *Am J Gastroenterol* 2024; 119(10):S1339. Full Text

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Introduction: Arab American patients are a unique population poorly studied following liver transplantation. We aimed to evaluate the outcomes following liver transplant in self-identified Arab American Patients at a single academic center. Methods: This is a single-center qualitative study using a retrospective database of all patients who self-identify as Arab that received a liver transplantation. Patients were evaluated for demographics, clinical outcomes and disease recurrence. Results: Of the 28 patients included in our population, the average age at transplant is 56.3 (30.3 to 67.8) years of age and 71.4% of patients are male. The etiologies leading to cirrhosis are alcoholic cirrhosis (42.9%), hepatitis C (25.0%), hepatitis B cirrhosis (7.1%), autoimmune hepatitis (7.1%), primary sclerosing cholangitis (7.1%), nonalcoholic steatohepatitis (3.6%), cryptogenic cirrhosis (3.6%), and autoimmune cholangitis (3.6%). Survival at 1 year is 85.7%, at 3 years is 78.6%. Graft survival at 1 year is 85.7%, at 3 years is 78.6%. 7.1% of patients had histologic evidence of graft rejection and rejection occurred at a mean of 2.75 months post-liver transplant. 50% of patients with rejection survived to 1- and 3-years post-transplant. 10.7% of patients had histologic evidence of recurrent cirrhosis. 6 patients have died. Their etiology of cirrhosis varied with separate patients each having autoimmune hepatitis, hepatitis B, hepatitis C,

cryptogenic, nonalcoholic steatohepatitis, alcoholic cirrhosis respectively. The causes of death for each separately are cardiac arrest, cholangiocarcinoma, cholangiosarcoma, graft failure, angiosarcoma, graft versus host disease respectively. Of the deceased patients, 33.3% survived 1 year post-liver transplant, while 0.0% survived 3 years. 16.7% had recurrent cirrhosis. Conclusion: Arab Americans are a growing group of patients with potential differences in metabolic disease, underlying liver disease recurrence and complications. Survival is worse than expected, especially in the face of rejection. Further study of this population is needed for an understanding of risk factors to better care for these patients following liver transplantation.

Hematology-Oncology

Abusuliman M, Abusuliman A, Aboeldahb M, Salem A, Meribout S, Mohamed I, Ibrahim AM, **Nimri F**, **Sheqwara J**, and **Jafri SM**. A Rare Case of T-cell Post-Transplant Lymphoproliferative Disorder (PTLD) Found Following a Diagnosis of Hemophagocytic Lymphohistiocytosis in a Patient With History of Liver Transplantation. *Am J Gastroenterol* 2024; 119(10):S2813. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Post-Transplant Lymphoproliferative Disorder (PTLD) encompasses various lymphoid proliferative disorders arising after hematopoietic or solid organ transplantation and ranging from polyclonal lesions to lymphomas. It mostly arises from B-cell origin and is linked to Ebstein-Barr Virus (EBV) in the setting of post-transplant immunosuppression. T-cell PTLD is rare, and its association with EBV is even rarer. We herein report a rare case of T-cell PTLD complicated by Hemophagocytic Lymphohistiocytosis (HLH) in a patient with history of liver transplant Case Description/Methods: A 43-year-old patient with history of alcoholic cirrhosis status post liver transplant presented with progressive bilateral lower limb weakness a year after transplant. A magnetic resonance imaging (MRI) of the spine showed cauda equina enhancements. Lumbar puncture showed inflammation and was positive for EBV. She was started on ganciclovir and bortezomib, but developed fever and pleural effusion; thoracentesis revealed exudate positive for Streptococci. Despite placement of chest tube and completion of antibiotic course, she continued to have febrile episodes with negative infectious workup except for EBV viremia. She had hemophagocytosis on bone marrow biopsy, and splenomegaly on computed tomography (CT), meeting the criteria for HLH. Her liver enzymes were elevated and CT of the liver showed bilateral multiple rounded lobular hypo-attenuating collections, the largest measuring 17 mm (Figure 1). She underwent a liver biopsy which showed EBV-positive monomorphic T-cell lymphoproliferative disorder, consistent with peripheral T-cell Lymphoma, not otherwise specified. The patient was started on CHEOP (cyclophosphamide, doxorubicin, etoposide, vincristine and prednisone) Her course was complicated with pancytopenia and recurrent attacks of fever. She eventually passed away 2 months later from septic shock Discussion: PTLD is a rare complication post solid organ transplant that is related to immune suppression. It is classically EBV related, B cell lymphoproliferation. The incidence of PTLD is higher post cardiac lung or multi organ transplant because of the higher doses of immune suppressants needed in these cases, with only 5-11% occur following liver transplant. Peripheral T-cell lymphoma is a rare PTLD subtype that is rarely associated with EBV. Vigilance post transplant is key to recognize these rare cases and guide the treatment strategy, which is usually directed towards reducing immune suppression and chemotherapy.

Hematology-Oncology

Chiang AC, Garcia MEO, Carlisle J, Dowlati A, Reguart N, Felip E, Jost PJ, Steeghs N, Stec R, **Gadgeel S**, Loong HHF, Jiang W, Hamidi A, Parkes A, and Paz-Ares L. Tarlatamab for patients with small cell lung cancer: 6-8 hour outpatient vs 48 hour inpatient monitoring in cycle 1. *Immuno-Oncology Technol* 2024; 24. Full Text

Background: Tarlatamab, a bispecific T-cell engager (BiTE®) immunotherapy targeting delta-like ligand 3, has shown promising outcomes in previously treated small cell lung cancer (SCLC). We evaluated the safety of a reduced 6-8 hour (h) monitoring period with tarlatamab in an outpatient setting in the phase 1 DeLLphi-300 study. Methods: Patients (pts) with previously treated SCLC were enrolled in Part F evaluating 6-8 h outpatient monitoring for cycle 1 doses and received tarlatamab 10 mg Q2W dosing (1 mg on day 1, 10 mg on day 8 and 15 of cycle 1, and Q2W thereafter). Pts needed a caregiver and

remained within 1 h of study site or affiliated hospital for 72 h post-dose. Clinic visits on days 2, 3, 5, 9, 16, and 22 were required to mitigate risk of underreporting adverse events (AEs). The primary endpoint was safety and tolerability. Safety outcomes were compared to pts from Part A cohorts who received tarlatamab 10 mg Q2W dosing with 48 h inpatient monitoring for cycle 1 doses. AEs were classified per CTCAE v4.0 and cytokine release syndrome (CRS) graded per Lee DW et al, Blood 2014. Results: A total of 88 pts (66 years median age; 51% male; median 2 prior lines of therapy) were enrolled, including 30 in the outpatient group and 58 in the inpatient group. The outpatient vs inpatient groups had a similar incidence of treatment-related AEs (93% vs 100%) and serious AEs (20% vs 29%). CRS incidence and time to resolution were similar between groups (Table 1). In the outpatient group, 18 pts had 25 cycle 1 CRS events, all of which resolved. Of the 25 CRS events, 5 events required hospitalization and 2 events involved an emergency room visit. Immune effector cell–associated neurotoxicity syndrome was rare (outpatient: 3.3%; inpatient: 3.4%). The hospitalization rate for any AE in cycle 1 was similar between groups. [Formula presented] Conclusions: There were no major differences in safety outcomes following tarlatamab administration with 6-8 h outpatient versus 48 h inpatient monitoring in cycle 1. Clinical trial identification: NCT03319940.

Hematology-Oncology
Faddah R, **Walbert T**, **Snyder J**, **Gadgeel S**, **Philip P**, and **Lange L**. STREAMLINING THE STUDY INTAKE PROCESS AT THE CANCER CLINICAL AND TRANSLATIONAL RESEARCH OFFICE (CCTRO). *Neuro Oncol* 2024; 26:viii261. Full Text

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Challenges in the Protocol Intake/Activation process at the Henry Ford Cancer Center, particularly during the budget negotiation and coverage analysis (CA) phases, hamper operational efficiency and financial prospects. This study aimed to improve budget time and process efficiency. Process flow mapping, Value Stream Mapping (VSM), and cause-effect analysis using a fishbone diagram were used to identify and analyze key bottlenecks, focusing on the budget negotiation and CA phases. Budget negotiation took an average of 121.5 days in 2023 due to multiple procedures and a lack of standardized practices. Delays ranged from 127.75 days in August to a low of 69.84 days in November of 2023. The budget build process averaged 13.31 days, with an additional 7.57 days for approval, totaling 20.89 days. The CA phase had an average cycle time of 10.82 days (range 2-10 days). To improve approval times, it was recommended to implement an Electronic Document Management System to automate routing, signing, and tracking of budget and CA-related documents, standardized budget templates to streamline negotiations, a detailed electronic checklist to streamline task lists for document collection and budget negotiation, automated reminders for internal and external stakeholders to ensure timely submission of necessary documents, and timely submission policies enforced by a dedicated finance member on committees. Newly developed Key Performance Indicators (KPIs) such as 'time to collect documents,' 'time between committees,' and 'time for budget negotiation process,' along with a dual tracking system in Excel, were proposed to monitor and improve these metrics. The recommendations are expected to significantly enhance the efficiency of the Protocol Intake/Activation process. By reducing the budget negotiation phase to less than 60 days and optimizing the CA process, faster study initiation, better resource utilization, and improved responsiveness to research opportunities will be achieved. This study underscores the critical need to address operational challenges in clinical trial management to enhance CCTRO's capability to conduct timely and effective research.

Hematology-Oncology
Fahr L, **Benitz S**, Schreiner N, Straub T, Mutter J, Hamidach H, Mahajan UM, Beyer G, Steiger K, Terrasi A, Schotta G, Imhof A, Lauber K, Kleeff J, Michalski CW, Mayerle J, and Regel I. Irf3 and Irf7 induce epigenetic changes to promote pancreatic carcinogenesis. *Pancreatology* 2024; 24:e116-e117. Full Text

The interferon regulatory factors 3 and 7 (Irf3, Irf7) are transcription factors downstream of the TLR3 pathway. We discovered an overexpression of Tlr3, Irf3 and Irf7 in pancreatic acinar-to-ductal metaplasia (ADM) and tumor cells. Furthermore, ADM and tumor cells exhibit epigenetic modifications, including changes in chromatin accessibility of interferon-response genes. Own preliminary data show that Irf3/Irf7 depletion prevents tumor development in the pancreas in an inducible oncogenic Kras mouse model. In

this study, we want to investigate whether Irf3/Irf7-deficient ADM and pancreatic tumor cells lack an epigenetic tumor-promoting program which is essential for pancreatic tumorigenesis. Immunoblot and immunohistochemistry staining were used to detect changes in total histone modification levels in cerulein-treated Irf3/Irf7 knockout mice expressing an inducible Kras mutation. 3D-ADM cultures were performed to assess reprogramming abilities of Irf3/Irf7KO acinar cells. Moreover, we created Irf3/Irf7KO mouse tumor cells with CRISPR/Cas9 to determine changes in tumor cell characteristics. Tumor formation capabilities were tested in orthotopic and metastatic mouse models. Possible alterations of an epigenetic, tumor-promoting program were analyzed by RNA-seq, ATAC-seq and ChIP-seq for H3K27ac and H3K4me3 in Irf3/Irf7KO tumor cells. Cerulein treatment of inducible oncogenic Kras mice lacking Irf3/Irf7 results in ADM formation without further development of precursor lesions or tumors. Irf3/Irf7KO acinar cells exhibit reduced reprogramming abilities in 3D culture. Furthermore, the tumorigenic potential of Irf3/Irf7KO tumor cells is strongly reduced in vivo, with no tumor growth in an orthotopic and metastatic mouse model. Moreover, Irf3/Irf7KO tumor cells show a significantly less aggressive phenotype in vitro with decreased colony and sphere formation capacities and reduced invasive potential. Depletion of Irf3/Irf7 in tumor cells leads to decreased H3K27ac and higher H3K4me3 levels as well as increased expression and activity of histone deacetylases 1 and 2. Downregulated genes in Irf3/7KO ADM and tumor cells are associated with tumor-promoting programs such as migration, mitochondrial respiration and chromatin organization. Our findings indicate that the transcription factors Irf3 and Irf7 play a significant role in establishing an epigenetic signature that gives rise to an aggressive phenotype of the tumor cells and supports a tumor-promoting program.

Hematology-Oncology

Schreiner N, Fahr L, **Benitz S**, Zhou Q, Alnatsha A, Imhof A, Mahajan U, Mayerle J, Schotta G, and Regel I. Lysine Demethylase 5a (Kdm5a) regulates metabolic activity and tumorigenic potential of murine pancreatic cancer cells. *Pancreatology* 2024; 24:e94. Full Text

Background: Lysine Demethylase 5a (KDM5A) is a histone demethylase known for selective removal of tri-methylation from lysine 4 of histone 3 (H3K4me3), a modification linked to active transcription. Crucial cellular processes implicated in cancer progression, such as senescence, cell cycle regulation and motility are known to be tightly regulated by KDM5A. Own previous studies revealed deregulation of H3K4me3 modifications with concomitant increased expression of Kdm5a in murine pancreatic tumor cells, indicating an oncogenic role. We hypothesize that Kdm5a-mediated removal of H3K4me3 from specific target genes contributes to a more aggressive tumor phenotype. Methods: A knockout of Kdm5a (K5KO) was generated in murine pancreatic tumor cells utilizing the CRISPR/Cas9 system. Phenotypic characterization of K5KO cells included assays for colony formation, proliferation, migration, cell cycle, cancer stem cell potential, and respiratory activity. Transcriptional changes were assessed via RNA-seq, while ChIP-seq was performed to evaluate the abundance of H3K4me3 and H3K4me1. Metabolomic analyses was conducted to verify alterations of metabolites in pathways of interest. The tumor formation capacity of K5KO was investigated using orthotopic and metastatic mouse models. Results: Deletion of Kdm5a in murine pancreatic cancer cells resulted in a pronounced increase of H3K4me3 levels, accompanied by transcriptional changes leading to an upregulation of genes involved in carbohydrate metabolic processes. On the other hand, genes regulating oxidative stress are downregulated in K5KO tumor cells. K5KO clones exhibited significant reduction in proliferation, migration, colony formation and the expression of cancer stem cell markers. Furthermore, they displayed changes in the oxygen consumption and extracellular acidification rate, accompanied by a significant upregulation of the metabolites within the TCA cycle and downregulation in the Glycolysis pathway. Experiments conducted in vivo displayed a complete loss of tumor-forming capacity of K5KO cells. Conclusions: Our findings corroborate a pro-tumorigenic role of Kdm5a for pancreatic cancer. We demonstrated that Kdm5a alters H3K4me3 modifications and regulates the metabolic activity and aggressiveness of pancreatic cancer cells in vitro and in vivo. K5KO leads to H3K4me3 accumulation and an epigenetic reprogramming, shifting the tumor cellś metabolic reliance from glycolysis to oxidative phosphorylation.

Hematology-Oncology

Theisen B, **George M**, **Loveless I**, and **Steele N**. Quantifying Tertiary Lymphoid Structures in Resected Pancreatic Ductal Adenocarcinoma in Clinical Practice - A Feasibility Study Demonstrating a Correlation with Survival. *Lab Invest* 2024; 104(3):S1862-S1863. Full Text

[Theisen, Brian] Henry Ford Hosp, Detroit, MI 48202 USA. [George, Madison; Loveless, Ian] Michigan State Univ, E Lansing, MI 48824 USA. [Steele, Nina] Henry Ford Hlth Syst, Detroit, MI USA. University; Henry Ford Health System; Henry Ford Hospital

Hospital Medicine
Ali SA, **Khadra M**, **Sitto M**, **Graifman M**, and **Gietzen J**. Semaglutide's Hidden Perils: A Rare Case of Malnutrition and Wernicke Encephalopathy. *Am J Gastroenterol* 2024; 119(10):S2964. Full Text

S.A. Ali, Henry Ford Hospital, Detroit, MI, United States

Introduction: With increasing use, concerns about semaglutide's long-term effects have been raised due to its potential to cause extended malnutrition, which can lead to vitamin deficiencies such as thiamine even without a history of alcohol use. We report a rare case of semaglutide-associated Wernicke Encephalopathy (WE) in an older adult with numerous comorbidities. Case Description/Methods: A 74-year-old woman with history of ischemic stroke, coronary artery disease, hypertension, hypothyroidism, depression, & class 2 obesity (body mass index 35 kg/m2) presented to the emergency department with generalized weakness after 3 days of low oral intake & decreased appetite. She was adherent to her medications, including semaglutide initiated 6 months & subsequently stopped 2 months prior (following 47 pounds weight loss) due to nausea, vomiting, abdominal pain, fatigue, lightheadedness, generalized weakness, & decreased bowel movements with the 0.5 mg dose, resulting in 3 hospitalizations. She exhibited changes in mental status, oriented to person & place but not to time or situation. Notable findings included incidental COVID-19 infection, vertical & horizontal nystagmus, & diffuse areflexia. Diagnostic imaging revealed right frontal lobe encephalomalacia & chronic micro-idiopathic alterations, while electroencephalogram indicated mild cerebral dysfunction. Thyroid stimulating hormone, vitamin B12, ammonia, & infectious/paraneoplastic/autoimmune workup were negative. She was treated with IV immunoglobulin for possible COVID-19-induced encephalopathy without improvement. Ultimately, her symptoms were attributed to WE & axonal neuropathy due to protein-calorie malnutrition & multiple vitamin/mineral deficiencies (zinc & vitamins B6, C, D, A). Treatment with IV thiamine was empirically initiated & continued despite a normal serum thiamine level, but her cognitive condition remained poor, leading to a diagnosis of WE possibly complicated by Korsakoff syndrome. She was ultimately discharged to hospice care. Discussion: This case underscores the need for awareness of the risks associated with semaglutide, along with the diagnostic challenges in recognizing WE as a complication of semaglutide-induced nutritional deficiency. While traditionally linked to alcohol use, WE should be considered when patients present with prolonged dietary deficiencies, altered mental status, & oculomotor abnormalities even in the setting of normal serum thiamine. Diagnosis should be made promptly & treatment given empirically to reduce the risk of lasting complications.

Hospital Medicine
Bai S, **Singh B**, **Ethakota J**, **Tariq H**, and **Rahman A**. Unmasking the Silent Invader: Tuberculosis Colitis. *Am J Gastroenterol* 2024; 119(10):S1928-S1929. Full Text

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Introduction: Gastrointestinal tuberculosis (TB) is a prominent form of extrapulmonary TB that presents diagnostic challenges due to symptom overlap with other gastrointestinal conditions and the limited accuracy of current diagnostic tests. There is a critical need for increased awareness of this disease, particularly in regions with low disease prevalence such as developed countries. Left untreated, gastrointestinal TB can result in considerable morbidity, requiring prolonged hospital stays and sometimes surgical intervention. Early and accurate diagnosis followed by prompt initiation of therapy is crucial in preventing these complications. This detailed case study focuses on TB colitis, highlighting its clinical features, diagnostic approaches, and management protocol of extended drug resistant tuberculosis. Case Description/Methods: We present the case of a 36-year-old immigrant from Honduras who initially presented with rectal bleeding, night sweats, and a notable weight loss of 30 pounds over 8 weeks. Colonoscopy identified Acid-fast bacilli (AFB)-positive granulomatous colitis, prompting a multidisciplinary diagnostic approach that included imaging studies, colonoscopy and microbiological

confirmation. Discussion: This case underscores the importance of considering tuberculosis (TB) in the differential diagnosis of gastrointestinal symptoms. TB can affect the digestive tract, presenting similarly to conditions like Crohn's disease. Colonoscopy with deep biopsy is crucial for tissue diagnosis, revealing characteristic ulcerative and hypertrophic lesions. Polymerase chain reaction (polymerase chain reaction) significantly enhances diagnostic sensitivity and specificity compared to traditional methods. Treatment involves anti-TB medication, with follow-up colonoscopy showing gut response within 3-4 weeks. Surgical intervention may be necessary for complications such as stricture formation. Timely recognition and management are essential to prevent morbidity associated with TB colitis, especially in atypical presentations. Increasing clinician awareness is critical for improving diagnostic accuracy and ensuring prompt initiation of appropriate therapy (see Figure 1).

Infectious Diseases

Fichtenbaum CJ, Malvestutto CD, Watanabe MG, Smith ED, Ribaudo HJ, McCallum S, Fitch KV, Currier JS, Diggs M, Aberg JA, Lu MT, Valencia J, Gomez-Ayerbe C, **Brar I**, Madruga JV, Bloomfield GS, Douglas PS, Zanni MV, Grinspoon SK, and Investigators R. Abacavir is associated with elevated risk for cardiovascular events in the REPRIEVE trial. *J Int AIDS Soc* 2024; 27:89-90. Full Text

[Fichtenbaum, C. J.] Univ Cincinnati, Internal Med Infect Dis, Cincinnati, OH USA. [Malvestutto, C. D.] Ohio State Univ, Med Ctr, Columbus, OH 43210 USA. [Watanabe, M. G.; Smith, E. D.; Ribaudo, H. J.; McCallum, S.] Harvard TH Chan Sch Publ Hlth, Ctr Biostat AIDS Res, Boston, MA USA. [Fitch, K. V.; Diggs, M.; Zanni, M. V.; Grinspoon, S. K.] Harvard Med Sch, Massachusetts Gen Hosp, Metab Unit, Boston, MA 02115 USA. [Currier, J. S.] Univ Calif Los Angeles, David Geffen Sch Med, Los Angeles, CA 90095 USA. [Aberg, J. A.] Icahn Sch Med Mt Sinai, Div Infect Dis, New York, NY 10029 USA. [Lu, M. T.] Harvard Med Sch, Massachusetts Gen Hosp, Cardiovasc Imaging Res Ctr, Boston, MA 02115 USA. [Valencia, J.] Asociac Civil Impacta Salud & Educ, Lima, Peru. [Gomez-Ayerbe, C.] Hosp Univ Virgen Victoria, Malaga, Spain. [Brar, I.] Henry Ford Hosp, Detroit, MI 48202 USA. [Madruga, J. V.] Ctr Referencia & Treinamento DST AIDS, Sao Paulo, Brazil. [Bloomfield, G. S.] Duke Univ, Sch Med, Duke Global Hlth, Durham, NC USA. [Douglas, P. S.] Duke Univ, Sch Med, Duke Clin Res Inst, Durham, NC USA. of Ohio; Ohio State University; Harvard University; Harvard T.H. Chan School of Public Health; Harvard University; Massachusetts General Hospital; Harvard Medical School; University of California System; University of California Los Angeles; University of California Los Angeles Medical Center; David Geffen School of Medicine at UCLA; Icahn School of Medicine at Mount Sinai; Harvard University; Massachusetts General Hospital; Harvard Medical School; Hospital Virgen de la Victoria; Henry Ford Health System; Henry Ford Hospital; Duke University; Duke University

Background: Major adverse cardiovascular events (MACE) are more common in people with HIV (PWH). In REPRIEVE, pitavastatin reduced MACE by 35% among PWH with low-to-moderate traditional risk. We evaluated the role of prior and current use of antiretroviral agents (ART) on the development of MACE. Methods: The trial enrolled PWH age 40–75 years on ART for at least 180 days, with a CD4 count >100 c/mm3 and low-moderate CVD risk. ART history was collected at baseline, including duration of exposure to select agents. Analyses in the REPRIEVE ITT population were performed for first MACE (including MI, TIA/stroke, revascularization, CV death), with median follow-up of 5.6 years. Cox proportional hazards models stratified by treatment group were used to account for treatment group differences. Effects of ART exposure were estimated in models unadjusted and adjusted for entry risk factors. Results: Among 7,769 participants, 31.1% were natal female and 65.2% non-White. Median age was 50 years, LDL 108 mg/dL, 10-year ASCVD risk score 4.5%, CD4 621 cell/mm3 (447,826 c/mm3) with 88% having an HIV viral load <400 copies/mL. The median duration of ART use was 9.5 years (5.3,14.8 years) and varied by Country. Overall, 22% reported prior exposure to abacavir (ABC), 86% to Tenofovir (TDF), 49% to Thymidine analogs (AZT/d4T), and 47% to protease inhibitors (PIs). At study entry 13% were using ABC, 61% TDF, 10% AZT/d4T, and 26% PIs. Entry regimens included 2 NRTIs plus an NNRTI–47%, INSTI–25%, or a PI–19%. In adjusted analyses including the baseline regimen, both former and current use of ABC was associated with higher incidence of MACE (Figure). Former or current use of other ART agents was not associated with MACE (data not shown). Conclusions: Former and current use of abacavir was associated with a higher incidence of subsequent major adverse cardiovascular events in the REPRIEVE trial.

Infectious Diseases

Singh H, **Bachour C**, **Metcalf D**, **Luthra K**, and **Kak V**. Hyponatremia as a Predictive Marker of Mortality in Hospitalized COVID- 19 Patients: A Healthcare System Analysis. *Am J Respir Crit Care Med* 2024; 209. Full Text

H. Singh, Internal Medicine, Henry Ford Jackson Hospital, Jackson, MI, United States

Rationale: There is documented evidence of the association between hyponatremia and mortality in hospitalized patients, including patients admitted with coronavirus disease-2019 (COVID-19) pneumonia. One of the proposed mechanisms of hyponatremia in COVID-19 is the syndrome of inappropriate antidiuretic hormone (SIADH) due to circulating cytokines such as IL-6. These cytokines are proposed to be associated with lung inflammation and correlate with respiratory failure and in-hospital mortality. Immunomodulators, tocilizumab and baricitinib, acting against the cytokine response, are known to reduce mortality in hospitalized COVID-19 patients. This study was undertaken to associate the severity of hyponatremia with in-hospital mortality in patients admitted with COVID-19 in multiple hospitals over a single health system network. Methods: After obtaining appropriate institutional review board (IRB) approval, a retrospective chart review was conducted from 03/01/2020 to 06/01/2021, which included all admitted patients with positive COVID-19 polymerase chain reaction tests at the time of admission. Individuals less than 18 years of age, incarcerated, and pregnant patients were excluded. Performance analytics and improvement (PAI) tool was used to extract patient records. The patients were categorized based on their admission sodium values into the following groups: normal sodium (>=136 mEq/L), mild hyponatremia (131 to 135 mEq/L), moderate hyponatremia (121 to 130 mEq/L), and severe hyponatremia (<=120 mEq/L). Primary and secondary outcomes calculated were hospital mortality and length of stay. IBM SPSS software was used to perform the data analysis. Chi-square tests and ANOVA tests were run to evaluate these outcomes. Results: Data for 2561 patients was extracted using the above method. 14 cases with severe hyponatremia were not included because of the small case count and its minute impact on the analysis and the interpretation of the results. Hence, 2547 patients were analyzed in this study. The percentage of in-hospital mortality in patients with normal sodium, mild hyponatremia, and moderate hyponatremia was found to be 8.7% (109/1260), 8.9% (84/945), and 15.8% (54/342) respectively; with Chi-Square p-value of <0.001 comparing mortality between the moderate hyponatremia group with the rest of the individual groups. Hospital length of stay of groups with normal sodium, mild hyponatremia, and moderate hyponatremia was 8.03, 7.99, and 9.44 days, respectively, with ANOVA F-Test P-value of 0.012. Conclusion: Admission hyponatremia of <130 mEq/L in COVID-19 patients is associated with a higher in-hospital mortality. Hence, admission sodium level may be used as a prognosticating factor and possible variable in the future COVID-19 treatment trials.

Internal Medicine

Abdallfatah A, Elhawary A, Ahmed OT, Elfert K, Mohamed I, Razzak IA, Abdalla M, **Abusuliman M**, Sethi A, Salem AE, Abdelhalim O, Gayam VR, Eskaros SL, and Boulay BR. The Efficacy of Hemospray in Managing Bleeding Related to Gastrointestinal Tumors: Systematic Review and Meta-analysis. *Am J Gastroenterol* 2024; 119(10):S703. Full Text

A. Elhawary, Icahn School of Medicine at Mount Sinai, Queens, NY, United States

Introduction: Gastrointestinal (GI) bleeding stemming from malignant tumors is increasingly recognized due to advancements in oncology and detection methods. Traditional endoscopic hemostatic techniques have shown variable success rates in managing hemorrhagic GI neoplasms. Hemospray, an emerging endoscopic hemostatic powder, offers promise in treating upper GI bleeding, potentially extending its utility to neoplastic bleeding sites. This meta-analysis aims to evaluate Hemospray's efficacy in managing bleeding related to gastrointestinal tumors. Methods: Database search including Embase, Scopus, Web of Science, Medline/PubMed, and Cochrane was done until January 03, 2024, using Boolean search strategies with the terms 'Hemospray' OR 'Hemostatic powder' OR 'TC 325') AND ('Gastrointestinal bleeding' OR 'GI bleeding') AND ('Malignancy' OR 'Neoplasm' OR 'Cancer'. Inclusion criteria encompassed studies focusing on malignancyrelated GI bleeding and interventions utilizing Hemospray. Comparative studies contrasted Hemospray with standard endoscopic treatments (SET), while non-comparative studies assessed Hemospray's efficacy independently. The risk of bias was assessed using

appropriate tools, and statistical analyses were performed using Review Manager and open Meta analyst software. Results: Initial searches yielded 327 articles, with 19 included in the meta-analysis, comprising 930 patients. Hemospray demonstrated higher rates of immediate hemostasis compared to SET (OR: 17.14, 95% CI: 4.27-68.86), with consistent outcomes across studies. Rebleeding rates at 14 and 30 days were comparable between Hemospray and SET groups, suggesting similar efficacy in long-term hemostasis. Hemospray showed a significantly lower need for non-endoscopic hemostasis compared to SET (OR: 0.51, 95% CI: 0.30-0.87), indicating a potential reduction in supplementary interventions. Safety assessments revealed no confirmed adverse events directly linked to Hemospray. Conclusion: This meta-analysis highlights Hemospray's efficacy in achieving immediate hemostasis in GI tumor-related bleeding, with potential benefits in reducing supplementary interventions and improving patient outcomes. Despite comparable rebleeding rates, Hemospray emerges as a valuable adjunctive therapy in managing malignant GI bleeding (see Figure 1).

Internal Medicine

Aboeldahb M, Marwan M, Abdallfatah A, Abosheaishaa H, **Abusuliman M**, Abdelwahed AH, Ali K, Ismail A, Eldesouki M, Hassan MA, and Rahman H. Efficacy and Safety of Seladelpar in Primary Biliary Cholangitis: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Am J Gastroenterol* 2024; 119(10):S1372. Full Text

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Introduction: Primary biliary cholangitis (PBC) is a chronic progressive condition that causes the inflammation and destruction of bile ducts. Thus, leading to cholestatic liver disease. Although there is currently no curative treatment for PBC, medications can be utilized to slow the progression of the disease. Seladelpar is a peroxisome proliferator-activated receptor delta (PPARd) agonist that has been shown to exert beneficial effects in liver disease and reduce total bile acid levels. It also possesses anti-inflammatory activity, inhibiting the activation of macrophages and the release of inflammatory mediators. The aim of this systematic review and meta-analysis is to assess the safety and efficacy of Seladelpar in patients with PBC. Methods: We searched PubMed, EMBASE, WOS, Scopus, and Cochrane Central from inception till April 29, 2024 for randomized controlled trials (RCTs) exploring the use of Seladelpar in PBC. Data extraction included study characteristics, patient demographics, and outcomes of interest. Statistical analysis was performed using RevMan version 5.4. Heterogeneity was assessed using I2 statistics. Pooled odds ratios (OR) and mean difference (MD) were used to assess the reduction in alkaline phosphatase (ALP), bilirubin, risk of pruritus, and nausea, adopting a random-effects model. The risk of bias was assessed using Rob 2.0. Results: Three studies with 499 patients, of whom 333 received Seladelpar, were included in this meta-analysis. Our meta-analysis found a significant reduction in ALP levels in patients who received Seladelpar when compared to those who received placebo (MD: -42.32, 95% CI [-52.18 to -32.46]; P<0.00001). On the other hand, there was no significant decrease in bilirubin levels in individuals treated with Seladelpar compared to the placebo group (MD: -0.04, 95% CI [-0.13 to 0.05]; P = 0.39). The incidence of nausea in the Seladelpar group was comparable with that in the placebo group (OR 1.53, 95% CI [0.67 to -3.50]; P = 0.31). Furthermore, there was no statistically significant difference in the incidence of pruritus between the Seladelpar group and the placebo group (OR 0.53, 95% CI [0.20 to 1.40]; P = 0.20). Conclusion: Seladelpar appears to be a promising and well tolerated treatment for PBS. However, it does not seem to significantly decrease bilirubin levels. Thus, larger multicenter trials are needed to further explore and confirm the safety and efficacy of Seladelpar in PBC.

Internal Medicine

Abosheaishaa H, Abdallfatah A, Abdelhalim O, Abdelghany A, Tahhan IS, Beran A, Amer MAM, Razzak IA, Mohamed I, Salem AE, Nassar M, **Abusuliman M**, Abomhya A, Bahbah AA, and Andrawes S. Efficacy and Safety of Sodium Alginate as an Injection Solution in Endoscopic Submucosal Dissection: A Systematic Review and Meta-Analysis. *Am J Gastroenterol* 2024; 119(10):S1104-S1105. Full Text

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Introduction: The increasing incidence of gastrointestinal (GI) tumors, such as colorectal and esophageal cancers, highlights the need for effective treatment methods. Endoscopic submucosal dissection (ESD) has emerged as a preferred technique due to its low local recurrence rates. This study evaluates the safety and efficacy of sodium alginate as a submucosal injection solution in ESD. Methods: A systematic search of Embase, Scopus, Web of Science, Medline, and Cochrane databases up to April 17, 2034, identified randomized controlled trials (RCTs) and observational studies on sodium alginate for ESD in GI adenomas and early-stage neoplastic lesions. Data extraction and analysis were independently conducted by 2 reviewers, with consensus resolving discrepancies. Statistical analyses were performed with Comprehensive Meta-analysis software. Results: Five studies involving 255 patients were included in this analysis. Overall en-bloc resection rates for sodium alginate were 97% [95% CI (93%-99%); I2:0%]. En-bloc resection subgroup analysis revealed 97% [95% CI (93%-99%); I2:0%] for 0.6% sodium alginate and 95% [95% CI (70%-99%); I2: 0%] for 0.4% sodium alginate. Delayed bleeding rates for sodium alginate were 5% [95% CI (1%-20%); I2: 65.2%]; however, after subgroup analysis delayed bleeding was 2% [95% CI (1%-6%); I2: 0%] for 0.6% sodium alginate and 22% [95% CI (8%-49%); I2:0%] for 0.4% sodium alginate. Perforation rates for 0.6% sodium alginate were 1% [95% CI (0%-5%); I2: 0%]. Procedure times were 60.86 minutes [95% CI (45.06-76.67); I2: 85.31%] for sodium alginate, 45.77 minutes [95% CI (32.94-58.59); I2:80.71%] for 0.6% sodium alginate, 85.38 minutes [95% CI (61.29-109.47); I2:24.90%] for 0.4% sodium alginate. Conclusion: This study demonstrates that sodium alginate is an effective and safe submucosal injection solution for ESD, offering several advantages over traditional solutions. Sodium alginate provides higher en-bloc resection rates and lower adverse event rates, along with a reliable submucosal cushion that enhances mucosal elevation and stability during ESD. Its properties, including excellent water retention and viscoelasticity, contribute to better mucosal elevation. Injectable sodium alginate hydrogels (ISAHs) also exhibit self-healing abilities and antioxidant activity. Additionally, sodium alginate is cost-effective and has a proven safety profile. These findings suggest sodium alginate, especially at a 0.6% concentration, is a viable and effective alternative for ESD procedures. (Figure Presented).

Internal Medicine

Abosheaishaa H, Abdallfatah A, Sethi A, Aboeldahb M, Abdelghany A, Ismail A, Mohamed I, Salem AE, Nassar M, **Abusuliman M**, Abdelhalim O, and Bilal M. Dexmedetomidine as an Adjunctive Sedative in Patients Undergoing Endoscopic Submucosal Dissection: A Systematic Review and Meta-analysis. *Am J Gastroenterol* 2024; 119(10):S1115-S1116. Full Text

A. Sethi, Icahn School of Medicine at Mount Sinai, New York, NY, United States

Introduction: Endoscopic submucosal dissection (ESD) allows for curative en-bloc resection of dysplastic gastrointestinal (GI) tract lesions. However, it is associated with postoperative adverse events (AEs) such as pain, bleeding, and perforation. Dexmedetomidine, an a2-receptor agonist, has emerged as a promising adjunct sedative for ESD under moderate sedation, offering anxiolysis and analgesia. We conducted a systematic review and meta-analysis to evaluate its efficacy and safety for use in ESD. Methods: A comprehensive systematic search was conducted across multiple databases, including Embase, Medline, Scopus, and Web of Science. Studies that involved ESD utilizing dexmedetomidine as an adjunctive medication in combination with other sedatives, were included. Data extraction and risk of bias assessment were independently performed by 2 reviewers. Meta-analysis was carried out with RevMan using a random-effects model. Results: Eight studies were included in the final analysis. Dexmedetomidine showed no significant difference in en-bloc or complete resection rates compared to controls. Sedation and procedure times were similar between the 2 groups as well. Dexmedetomidine significantly reduced restlessness (OR 0.15, 95% CI:0.07 to 0.29) and increased bradycardia (OR 7.15, 95% CI 3.17 to 16.11) compared to controls. Upon subgroup analysis, Dexmedetomidine plus Propofol, and Dexmedetomidine plus Midazolam, revealed the same findings regarding restlessness and bradycardia compared to controls which confirmed the adjunctive effects of Dexmedetomidine. Conclusion: Dexmedetomidine as an adjunctive sedative appears safe and effective in ESD, reducing restlessness without significant adverse events. The risk of bradycardia is increased, which may be reflective of reduced physiological stress. Future studies should explore optimal dosing and compare Dexmedetomidine with other sedatives in diverse populations. (Figure Presented).

Internal Medicine

Abosheaishaa H, Elfert K, Olimy A, Mohamed I, **Abusuliman M**, Salem A, Ismail A, and El-Kassas M. THE RISK OF PORTAL VEIN THROMBOSIS IN PATIENTS WITH PORTAL HYPERTENSION TAKING BETA-BLOCKERS: A RETROSPECTIVE COMPARATIVE STUDY FROM A MULTIINSTITUTIONAL DATABASE. *Hepatology* 2024; 80:S3. Full Text

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Background: Portal vein thrombosis (PVT) involves the obstruction or narrowing of the portal vein due to a blood clot and is commonly associated with liver cirrhosis and portal hypertension. Beta-blockers are frequently prescribed to manage portal hypertension, but their role in the development of PVT is not well understood. This study aims to assess the risk of developing PVT in patients with portal hypertension and liver cirrhosis who are taking beta-blockers compared to those who are not. Methods: This retrospective cohort study used the TriNetX database, which includes electronic health records from over 110 million patients in 63 US healthcare organizations. The study population consisted of adult patients (≥ 18 years) with portal hypertension and liver cirrhosis who underwent esophagogastroduodenoscopy with band ligation of esophageal varices, excluding those with liver cell carcinoma. Two cohorts were defined: one receiving beta-blockers (propranolol, carvedilol, or nadolol) and one not receiving beta-blockers. The primary outcome was the incidence of PVT (ICD-10-CM code I81), and the secondary outcome was mortality. Baseline characteristics were balanced using one-to-one propensity score matching (PSM). Outcomes were analyzed using adjusted odds ratios (aOR) with 95% confidence intervals (CI), considering p-values < 0.05 as statistically significant. Results: Before PSM, the beta-blocker cohort included 15,754 patients, and the control cohort included 8,783 patients. After PSM, each cohort had 6,970 patients with similar baseline characteristics. Before PSM, 8.64% of the beta-blocker cohort developed PVT compared to 4.72% in the control group (aOR 1.911, 95% CI 1.693-2.156). After PSM, 8.85% of the beta-blocker cohort developed PVT compared to 4.74% in the control group (aOR 1.951, 95% CI 1.686- 2.257). Mortality was higher in the beta-blocker cohort both before PSM (23.9% vs. 17.37%, aOR 1.494, 95% CI 1.397-1.597) and after PSM (22.8% vs. 18.6%, aOR 1.292, 95% CI 1.190-1.403) . Conclusion: Beta-blocker use in patients with portal hypertension and liver cirrhosis is associated with a significantly higher risk of developing PVT and increased mortality. Further research is needed to explore these associations and assess the safety of beta-blockers in this patient population. (Figure Presented).

Internal Medicine

Abusuliman M, Abusuliman A, Aboeldahb M, Salem A, Meribout S, Mohamed I, Ibrahim AM, **Nimri F**, **Sheqwara J**, and **Jafri SM**. A Rare Case of T-cell Post-Transplant Lymphoproliferative Disorder (PTLD) Found Following a Diagnosis of Hemophagocytic Lymphohistiocytosis in a Patient With History of Liver Transplantation. *Am J Gastroenterol* 2024; 119(10):S2813. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Post-Transplant Lymphoproliferative Disorder (PTLD) encompasses various lymphoid proliferative disorders arising after hematopoietic or solid organ transplantation and ranging from polyclonal lesions to lymphomas. It mostly arises from B-cell origin and is linked to Ebstein-Barr Virus (EBV) in the setting of post-transplant immunosuppression. T-cell PTLD is rare, and its association with EBV is even rarer. We herein report a rare case of T-cell PTLD complicated by Hemophagocytic Lymphohistiocytosis (HLH) in a patient with history of liver transplant Case Description/Methods: A 43-year-old patient with history of alcoholic cirrhosis status post liver transplant presented with progressive bilateral lower limb weakness a year after transplant. A magnetic resonance imaging (MRI) of the spine showed cauda equina enhancements. Lumbar puncture showed inflammation and was positive for EBV. She was started on ganciclovir and bortezomib, but developed fever and pleural effusion; thoracentesis revealed exudate positive for Streptococci. Despite placement of chest tube and completion of antibiotic course, she continued to have febrile episodes with negative infectious workup except for EBV viremia. She had hemophagocytosis on bone marrow biopsy, and splenomegaly on computed tomography (CT), meeting the criteria for HLH. Her liver enzymes were elevated and CT of the liver showed bilateral multiple rounded lobular hypo-attenuating collections, the largest measuring 17 mm (Figure 1). She

underwent a liver biopsy which showed EBV-positive monomorphic T-cell lymphoproliferative disorder, consistent with peripheral T-cell Lymphoma, not otherwise specified. The patient was started on CHEOP (cyclophosphamide, doxorubicin, etoposide, vincristine and prednisone) Her course was complicated with pancytopenia and recurrent attacks of fever. She eventually passed away 2 months later from septic shock Discussion: PTLD is a rare complication post solid organ transplant that is related to immune suppression. It is classically EBV related, B cell lymphoproliferation. The incidence of PTLD is higher post cardiac lung or multi organ transplant because of the higher doses of immune suppressants needed in these cases, with only 5-11% occur following liver transplant. Peripheral T-cell lymphoma is a rare PTLD subtype that is rarely associated with EBV. Vigilance post transplant is key to recognize these rare cases and guide the treatment strategy, which is usually directed towards reducing immune suppression and chemotherapy.

Internal Medicine

Abusuliman M, Abusuliman A, **Jamali T**, **Nimri F**, **Malick AN**, Salem A, Meribout S, and **Elatrache M**. A Rare Case of Carney-Stratakis Syndrome With a Large Gastrointestinal Stromal Tumor (GIST) Masquerading as a Pancreatic Mass. *Am J Gastroenterol* 2024; 119(10):S2629-S2630. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Carney-Stratakis syndrome (CSS), a rare familial syndrome of paraganglioma and gastrointestinal stromal tumor (GIST), is attributable to germline mutations in the succinate dehydrogenase genes SDHB, SDHC, and SDHD genes. It is a morbid disease with distinct clinical presentations and genetic heterogeneity that can contribute to underdiagnosis. We present a distinctive case of CSS in a 39-yearold woman. Case Description/Methods: A 39-year-old woman presented with worsening epigastric pain, loose clay-colored stool, early satiety and bloating. She had a history of endometriosis with excision of abdominal wall endometriosis and excision of a left paraganglioma. She has family history of paraganglioma, genetic testing performed on the patient during that time showed heterozygous c.136C .T (p.Arg46X) disease associated sequence variant in the SDHB gene which is associated with hereditary paraganglioma. Abdominal computed tomography (Figure 1) showed a large solid and cystic mass spanning along the entire length of the pancreas, extending to the left upper quadrant with mass effect on the greater curvature of the stomach, spleen, and splenoportal confluence; measuring 16.8 x 7.1 x 7.2 cm. Magnetic resonance of the abdomen showed a large heterogeneous mass within the lesser sac abutting the pancreatic neck measuring 12.1 x 8.6 x 8.0 cm. Urine and plasma metanephrines were within normal limit. Patient underwent Endoscopic Ultrasound-guided fine needle biopsy (EUS-FNB) of the lesion with a 22 gauge Franseen-tip needle. Morphology and immunoprofile of the sample were compatible with GIST, epithelioid variant. Staining and molecular analysis for SDHB showed partially loss nuclear stain. Considering the patient's known history of paraganglioma, she was diagnosed with CSS. Because the tumor was very extensive and not surgically resectable, treatment with Sunitinib was initiated. She was seen 2 months later with good general condition, with intermittent abdominal pain controlled with Ibuprofen. Genetic counselling for her 3 children was recommended. Discussion: CSS is a rare hereditary syndrome with a 50% risk of transmission to the offspring. GIST is integral to CSS diagnosis. While most GISTs arise from a mutation in KIT or platelet-derived growth factor receptor alpha, about 7.5% of GISTs involve SDH gene mutations, including those arising as part of CSS. In this case, EUS-guided FNB of the lesion provided a definitive diagnosis, benefiting both the patient and descendants who might share the condition. (Figure Presented).

Internal Medicine

Abusuliman M, Abusuliman A, **Rehman S**, Abosheaishaa H, Salem A, Elfert K, **Saleem A**, **Alomari A**, Meribout S, Ibrahim AM, and **Jafri SM**. Correlation Between Transient Elastography and Liver Biopsy in MASLD. *Am J Gastroenterol* 2024; 119(10):S1329-S1330. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: The escalating prevalence of metabolic syndrome has led to a parallel rise in NAFLD, thus identifying worsening fibrosis is crucial. Liver biopsy, though the gold standard, is invasive and prone to sampling error. Serologic markers and imaging modalities have limitations in distinguishing MASLD from

MASH. Transient Elastography detects hepatic fibrosis effectively. Developing non-invasive methods to distinguish MASLD from MASH is crucial for disease monitoring. Our study aimed to evaluate the concordance of Fibroscan (transient elastography) in predicting degree of fibrosis when compared to Liver Biopsy in patients suspected of having MASLD. Methods: We evaluated patients with metabolic liver disease presenting to a single tertiary center between 2015 and 2020 who underwent confirmatory liver biopsy to assess diagnosis and degree of fibrosis. Baseline characteristics and procedural data were collected. Results: Forty-five patients were included in the study, Baseline characteristics are shown in Table 1. The Spearman correlation coefficient for the association between the estimate of fibrosis on liver biopsy versus the estimate of fibrosis on Fibroscan was 0.249 (P5 0.032), indicating a strong positive monotonic relationship between the 2 variables. The Spearman correlation coefficient for the association between the estimate of fibrosis on liver biopsy versus the estimate of fibrosis on Fib-4. was 0.341 (P = 0.004). The Spearman correlation coefficient for the association between the estimate of fibrosis on liver biopsy versus the estimate of fibrosis on MASLD fibrosis score was 0.400 (P5 0.014). For F0-1, 94% of patients had the same degree of fibrosis on Fibroscan and liver biopsy, 6% had higher degrees of fibrosis on liver biopsy. There were 89% of patients with F2 had the same degree of fibrosis on Fibroscan and liver biopsy, 11% had higher degrees of fibrosis on liver biopsy. Eighty-seven percent of patients with F3 had the same degree of fibrosis on Fibroscan and liver biopsy, 13% had higher degrees of fibrosis on liver biopsy. For F4 100% of patients had the same degree of fibrosis on Fibroscan and liver biopsy. Conclusion: Fibroscan, Fib-4, and MASLD fibrosis score are all valuable methods to accurately estimate fibrosis in patients with MASLD with results comparable to liver biopsy. Fibroscan is a safe, non-invasive, and accurate method for predicting the degree of fibrosis compared to Liver Biopsy in patients suspected of having MASLD.

Internal Medicine

Abusuliman M, Abusuliman A, **Rehman S**, Salem A, Abosheaishaa H, Mohamed I, Aboeldahb M, Ibrahim AM, and **Jafri SM**. Pregnancy Outcomes Following Triple Organ (Small Bowel, Liver, and Pancreas) Transplantation. *Am J Gastroenterol* 2024; 119(10):S3043-S3044. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Compared to other solid organ transplants, intestinal transplant is relatively novel, and occurrences of successful pregnancies following this procedure are considerably less common. Literature shows only 10 documented cases of successful pregnancy after intestinal transplantation, and to date, only 1 of which was a triple organ (intestine, liver, pancreas) transplant.We present an extremely rare case of successful pregnancy post triple gastrointestinal organ transplant. Case Description/Methods: 20-year-old, 31-week-pregnant woman was evaluated by our Hepatology team for elevated liver enzymes on routine checkup. The patient had a history of small bowel, liver, and pancreas transplant at age 1 due to complicated gastroschisis at birth, and hospitalization from birth to age 4 years. She had no history of rejection and has had an uncomplicated post-transplant course. Prior to pregnancy, immune suppression was maintained with tacrolimus, sirolimus and prednisone. Sirolimus and prednisone were discontinued when the patient became pregnant, with continuation of tacrolimus 5 mg twice a day, with reported medication compliance. Labs showed elevated liver enzymes: aspartate aminotransferase= 275 IU/L, alanine transaminase =228 IU/L, total bilirubin= 1.8 mg/dL, and FK level < 2, despite reported compliance. Ultrasound imaging revealed normal liver transplant and normal directional flow. Virology panel came back negative. Prednisone 10 mg daily was added. The patient then developed acute kidney injury, Cr:1.37, pulmonary edema, and FK went supra-therapeutic reaching 13.7 so it was held at that time. The patient was diagnosed with preeclampsia with severe features and was taken for an uncomplicated C-section. The baby was admitted to pediatric intensive care unit for preterm labor with initial respiratory insufficiency that later improved with no complications, discharged home 3 weeks later.A month later, liver function tests (LFTs) were elevated with concern for rejection. The patient had a low tacrolimus level, reporting she was taking 3 mg daily instead of twice a day. High dose steroid (1 gm solumedrol for 3 days) was given, with improvement of LFTs after 2 doses. Tacrolimus was increased to 3 mg twice a day and sirolimus was restarted. The patient is currently on tacrolimus and sirolimus with normal LFTs. Discussion: Triple gastrointestinal organ transplant procedure is uncommon, and achieving a successful pregnancy afterward is even rarer. Challenges presented by pregnancy is to maintain

stability of the graft, prevent infection, ensure good nutritional support and monitor fetal wellbeing and growth (see Table 1).

Internal Medicine
Abusuliman M, Abusuliman A, Saad N, **Rehman S**, Ibrahim AM, **Jamali T**, **Shamaa O**, **Jafri SM**, and **Elatrache M**. A Rare Case of Pulmonary Sclerosing Pneumocytoma Diagnosed by Endoscopic Ultrasound (EUS). *Am J Gastroenterol* 2024; 119(10):S2628-S2629. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Pulmonary sclerosing pneumocytoma (PSP), formerly known as pulmonary sclerosing hemangioma, is a rare benign lung tumor with malignant potential. It mostly affects middle- aged women of Asian descent and is usually incidentally found, as most patients do not exhibit obvious medical symptoms. Cytological and immunohistochemical analysis is essential for definitive diagnosis of PSP. Analysis is typically performed on biopsy specimen obtained via image-guided fine needle aspiration (FNA) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). We present a case of a middle-aged woman diagnosed with PSP via Endoscopic Ultrasound (EUS)-guided FNA of a pulmonary nodule. To our knowledge, there are no reports of cases of PSP diagnosed with EUS-FNA. Case Description/Methods: A 54-year-old white woman, who is an ex-smoker with a family history of lung cancer, presented with right clavicle swelling after shoulder injury. A chest x-ray incidentally revealed a soft tissue mass seen on the lateral view just anterior to the xiphoid. Cross-sectional imaging of the chest showed a 14 mm para-mediastinal nodule extending to the mediastinal pleura in the medial basal segment of the right lower lobe in close proximity to the distal esophagus (Figure 1). Due to proximity to the esophagus, this area was felt to be accessible with EUS. Endosonographic examination revealed a 17 mm by 10 mm extramural well-defined hypoechoic lesion with a microcystic component outside the distal esophageal wall and abutting it. EUS-guided FNA of the lesion was performed. Histopathological examination revealed atypical alveolar type 2-like pneumocytes concerning for Sclerosing Pneumocytoma. The patient underwent wedge resection and is currently undergoing surveillance imaging. Discussion: PSP is a rare, slow-growing benign lung tumor with malignant potential. Most patients are asymptomatic on presentation. Diagnosis is frequently incidental, and a definitive diagnosis requires histopathological examination. EUS-FNA can be a safe and minimally invasive tool to aid in the diagnosis of this rare condition when it is in close proximity to the gastrointestinal tract. Our case highlights the utility of EUS-FNA in diagnosis and management of unique mediastinal and lung lesions outside of the GI tract. (Figure Presented).

Internal Medicine
Abusuliman M, Abusuliman A, **Saleem A**, **Alomari A**, Abosheaishaa H, **Nimri F**, **Jamali T**, and **El-Nachef N**. A Rare Presentation of Cytomegalovirus (CMV) Colitis as a Colonic Mass. *Am J Gastroenterol* 2024; 119(10):S1995. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Cytomegalovirus (CMV) infection affects the gastrointestinal tract in both immunocompromised and immunocompetent individuals. While commonly manifesting as ulcerative lesions, instances of CMV-induced mass lesions in the gastrointestinal tract are rare, and have only been described in a handful of cases. We herein report a rare presentation of CMV as a discrete colonic mass in a patient presenting with hematochezia. Case Description/Methods: A 54-year-old woman with end state renal disease on hemodialysis, hypertension, and sarcoidosis (on azathioprine), presented to the emergency roomwith rectal bleeding ongoing for a few months.A month prior she was hospitalized for diarrhea and abdominal pain. Abdominal computed tomography at the time was concerning for ischemic vs infectious colitis. She was scheduled for an outpatient colonoscopy. In the emergency room, the patient was hypotensive, and her hemoglobin dropped from 8.4 g/dl to 6.5 g/dl. She had a normal white blood cells and CD4 T-cell count. Computed tomography showed colitis from the cecum to the distal transverse colon. Stool studies ruled out C. difficile/common bacterial infections. She underwent a colonoscopy which showed 3 x 4 cm protruding mass in the ascending colon contiguous with the ileocecal valve. The lesion was villous and characterized by superficial ulceration, friability, and scarring,

with an adjacent area of ulceration and erythema on a nearby colonic fold (Figure 1). Biopsies revealed severely active nonspecific colitis in the ascending and transverse colon with positive CMV staining. The patient was started on ganciclovir IV 1.25 mg/kg 3 times weekly (renal dose adjusted) for 3 weeks. On follow up 3 weeks later, her other symptoms resolved and CMV levels were undetected. She still complained of abdominal pain, so the decision was to continue Valganciclovir for 6 weeks with regular monitoring. Follow up 2 months later showed hemoglobin improvement to 11.4 g/dl, with resolution of all symptoms. Discussion: While colonic masses are commonly attributed to neoplasms, infectious causes like CMV must be considered. Gastrointestinal symptoms of CMV when present are usually in patients with low white blood cell and CD4 counts, with HIV/AIDS or transplantation being the 2 greatest risk factors, but suspicion should be considered in individuals on immunosuppressants for rheumatological conditions as well, even with normal counts. Identification of CMV warrants medical intervention, resulting in clinical improvement and potential resolution of the mass.

Internal Medicine

Abusuliman M, **Jamali T**, Abusuliman A, **Nimri F**, **Rehman S**, **Hammad T**, and **Pompa R**. One Lesion at a Thyme: Oligometastatic Thymoma to the Liver. *Am J Gastroenterol* 2024; 119(10):S2812-S2813. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Thymomas are rare slowly growing tumors that can infiltrate directly through contiguity. They account for 40% of all mediastinal masses, resulting from neoplastic transformation of thymus epithelial cells. They mostly affect the surrounding structures via direct invasion. Extra-thoracic metastasis of thymomas is exceedingly rare, and the exact incidence is not known. Available literature revealed a total of 50 cases of extra-thoracic metastasis of thymoma. Of these have been 18 cases with liver metastasis,10 with simultaneous liver and other organs metastasis, and only 8 with solely liver metastasis. We herein report the first endoscopic ultrasound (EUS)-guided biopsy of metastatic thymoma solely to the liver Case Description/Methods: An 89-year-old man presented to his primary physician with urinary retention. Computed tomography (CT) scan incidentally noted a 6.8 x 5.2 cm heterogeneous mass in the aortopulmonary window suspicious for primary mediastinal malignancy or metastatic disease and an indeterminate 1.9 cm lesion in the left hepatic lobe. Abdominal Magnetic resonance imaging confirmed a 1.9 cm lesion in the left hepatic lobe concerning malignancy (Figure 1B). The mediastinal mass was biopsied, and pathology showed features consistent with Thymoma type B2. Gastroenterology team were consulted for an endoscopic ultrasound-guided biopsy of the liver lesion. The lesion appeared hypoechoic, heterogenous, and solid with well-defined borders, 16 mm 320 mm in diameter (Figure 1A). Pathology findings were consistent with metastatic thymoma. PET-CT confirmed a hypermetabolic anterior mediastinal mass and segment III liver mass consistent with metastatic thymoma. Radiation therapy was recommended as the patient was a poor candidate for surgery or chemotherapy given his advanced age and comorbidities Discussion: Extra-thoracic dissemination of thymomas is an extremely rare occurrence of these already rare tumors (Table 1). EUS-guided liver biopsy is a useful tool for diagnosis and easy access to metastatic lesions in the liver, and also morphologically characterize the lesion, avoiding more invasive diagnostic methods.

Internal Medicine

Abusuliman M, Jamali T, Nimri F, **Chaudhary AJ**, **Saleem A**, **Faisal MS**, **Alomari A**, **Rehman S**, Elfert K, Salem A, Meribout S, Abosheaishaa H, Ibrahim AM, **Shamaa O**, **Salman Faisal M**, **Watson A**, **Pompa R**, **Dang D**, **Elatrache M**, **Piraka C**, **Singla S**, and **Zuchelli T**. Adverse Events Associated With LAMS With and Without Plastic Stents Placement During Different EUS-Guided Interventions. *Am J Gastroenterol* 2024; 119(10):S1139-S1141. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Endoscopic ultrasound (EUS) guided lumen apposing metal stent (LAMS) has been used increasingly in lieu of surgery for multiple conditions, due to the novelty of the intervention, data on adverse events (AE) is scarce. We conducted this study to better understand and quantify the AE rates associated with LAMS placement, and plastic stent placement along with LAMS. Methods: Patients who

underwent attempted EUS-guided LAMS interventions from 2015 to 2023 were identified from a single quaternary care hospital (Henry Ford Hospital) endoscopic procedure database. Retrospective demographic, clinical, and procedure-related data (including AE data using a modified version of the American Society for Gastrointestinal Endoscopy lexicon for endoscopic AE) was collected from the medical record. Results: Out of 243 patients, 133 (54.7%) were male and 159 (65.4%) were white, with a mean age of 53.7 ± 15.9 years. The primary indication for lumen-apposing metal stents (LAMS) was pancreatic fluid collections in 170 (70%) patients, with cyst-gastrostomy being the most common intervention in 159 (65.4%) patients. The technical success rate of LAMS placement was 97.5%, while the clinical success rate, defined as an improvement in clinical outcomes, was 93%. A total of 96 (39.5%) patients experienced adverse events (AEs), with 48 (19.7%) having early AEs (occurring < 48 hours post-procedure) and 70 (28.8%) having late AEs (occurring >48 hours and < 30 days post-procedure). Abdominal pain was the most common early and late AE, affecting 28 and 25 patients, respectively. Plastic stents were placed alongside LAMS in 176 patients, of whom 85 (48.3%) experienced complications. The combination of plastic stent placement and LAMS was associated with a significantly higher overall risk of AEs (48.3% vs. 29.9%, P=0.009) and a higher risk of delayed AEs (33% vs. 17.9%, P=0.021). Multivariate analysis revealed that LAMS dilation without plastic stent placement resulted in a significantly higher rate of stent occlusion compared to LAMS dilation with plastic stent placement (7.3% vs. 0.8%, P=0.021). Additionally, LAMS dilation alone was associated with a higher rate of abdominal pain than when combined with stent placement (14.5% vs. 5.5%, P=0.027). Conclusion: LAMS has been demonstrated to have high technical and clinical success rates. Pairing of LAMS dilation and plastic stent placement may have beneficial effects on stent occlusion. More studies are needed to investigate the safety profile of LAMS. (Table Presented).

Internal Medicine

Abusuliman M, **Nehme J**, Abusuliman A, **Alomari A**, **Saleem A**, Meribout S, Salem A, Ibrahim AM, and Abosheaishaa H. The Sinister Entity Subdued: Conservative Management for Left-Sided Portal Hypertension. *Am J Gastroenterol* 2024; 119(10):S2442. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Sinistral portal hypertension is a rare cause of upper gastrointestinal (GI) bleeding. It arises from a pancreatic source that leads to compression of the pancreatic vein, increasing the pressure in the left portal venous system, and resulting in gastric varices. Treatment typically involves splenectomy to alleviate pressure in the left portal venous system. We present a rare case of bleeding isolated gastric varices due to sinistral portal hypertension that was managed conservatively without need for surgery. Case Description/Methods: A 39-year-old male presented with hematemesis, melena, and pallor. He had history of Alcohol use disorder, chronic pancreatitis complicated by pancreatic abscess. His hemoglobin on presentation was 3.3 g/dl (Table 1). Computed tomography (CT) imaging was negative for GI bleed but showed splenic vein occlusion with mild gastric wall varices and an embolus in the right lower lobe pulmonary artery. Bedside esophagogastroduodenoscopy (EGD) revealed normal esophagus and duodenum, blood residue in the stomach but no gastric or fundal varices. The patient was started on Octreotide and PPI. His hospital course was complicated by right leg deep vein thrombosis (DVT); However, anticoagulation was held till stabilization of hemoglobin. He was evaluated by Interventional Radiology (IR) and IVC filter was placed. The patient's hemoglobin continued to drop despite pRBCs transfusion, PPI, with slow improvement of melena. EGD was repeated, revealing type 1 Isolated Gastric Varices (IGV 1) with minimal oozing of blood. IR reported the patient was a poor candidate for BRTO. Surgery evaluated the patient, but given stable Hb, clinical stability on conservative management, and history of pancreatitis increasing risk of surgery, they deferred management to the outpatient setting with follow up in 1 month for elective splenectomy. The patient remained stable. pRBC transfusions were held despite Hgb < 7 given lack of symptoms and was deemed medically stable for discharge. He was then seen in clinic a month and 3 months later, denied any melena or hematemesis with stable hemoglobin and it was decided that there is no need for elective surgery. Discussion: Sinistral portal hypertension presents significant risk of severe upper GI bleeding, typically managed with splenectomy or splenic embolization. In this case, successful management was achieved through conservative treatment, emphasizing the need for individualized, tailored management approaches. (Figure Presented).

Internal Medicine

Adil SA, **Chaudhary AJ**, **Tang J**, and **El-Nachef N**. Infliximab-Associated Takotsubo Cardiomyopathy in a Patient With Ulcerative Colitis. *Am J Gastroenterol* 2024; 119(10):S2536. Full Text

S.A. Adil, Henry Ford Health, Shelby Township, MI, United States

Introduction: Tumor Necrosis Factor-alpha (TNF-α) inhibitors have been associated with heart failure, myocarditis, and acute myocardial infarction (MI). Takotsubo (stress-induced) cardiomyopathy (TC) is characterized by transient regional systolic dysfunction and mimics MI but without evidence of obstructive coronary artery disease. While emotional stressors are commonly implicated in TC, there is increasing recognition of pharmacological triggers. Data, however, is scarce on the association of anti-TNF therapy with TC. Here, we present a case of a 53-year-old woman with ulcerative colitis admitted to our hospital with TC, thought to be related to infliximab. Case Description/Methods: A 53-year-old woman with a history of left sided ulcerative colitis for 2 years had recently undergone escalation of therapy for colitis due to breakthrough symptoms despite maximum mesalamine therapy. She was started on infliximab 5mg/kg and underwent standard induction doses at week 0,2,6 and received 1 maintenance dose which resulted in clinical remission. However, she presented to the emergency department 19 days after her fourth infusion with complaints of chest pain, dyspnea, and diaphoresis. On arrival, her vital signs and electrocardiogram were normal, but her highsensitivity troponin levels were elevated, peaking at 2180 ng/L. A computed tomography scan was negative for pulmonary embolism, while an echocardiogram revealed regional wall motion abnormalities concerning for TC. Subsequent cardiac catheterization demonstrated non-obstructive coronary artery disease and a diagnosis of TC was confirmed. Upon review of her clinical and medication history, the inpatient cardiology team felt infliximab was a possible culprit for her presentation, although a definitive relationship could not be established. After discharge, she followed up with her gastroenterologist, who discontinued infliximab and started her on vedolizumab therapy for her ulcerative colitis. Discussion: TNF-α inhibitors are widely used in the management of inflammatory bowel disease (IBD) but are seldom implicated in cardiovascular adverse events. In our case, the temporal relationship between the initiation of infliximab and the development of TC raises suspicion for a potential association. Although rare, it is important for clinicians to remain cognizant of potential cardiovascular adverse events in patients with IBD who are undergoing biologic therapy, especially if they have existing cardiac risk factors. Switching to a different drug class should be considered.

Internal Medicine

Ahmed Z, Campbell C, Stanley S, **Ali F**, Hassan M, Nawras A, and Kobeissy A. Navigating Rare Waters: Chylous Ascites Following Robotic Bilateral Nephrectomy in an Elderly Patient. *Am J Gastroenterol* 2024; 119(10):S2863. Full Text

C. Campbell, University of Toledo, College Medicine and Life Sciences, Toledo, OH, United States

Introduction: There are many etiologies responsible for ascites in elderly patients. A relatively uncommon subtype is chylous ascites, defined as the accumulation of triglyceride-rich peritoneal fluid in the peritoneal cavity. The most common underlying causes of chylous ascites are lymphatic obstruction and trauma to the lymphatic vessels. We report a case of a patient with new-onset chylous ascites approximately one month after undergoing robotic bilateral native nephrectomy Case Description/Methods: A 71-year-old man with a history of autosomal dominant polycystic kidney and liver disease, hypertension, and bilateral native nephrectomy was admitted for uncontrolled hypertension. On initial evaluation, the patient was noted to have a distended abdomen with palpable fluid thrill and shifting dullness. CT scan showed massive abdominal ascites extending into the pelvis. RUQ ultrasound showed no evidence of portal or hepatic venous thrombosis. Ultrasound-guided paracentesis was performed, which yielded 5.8 liters of fluid and a serum albumin-ascites ratio of 0.5. Peritoneal fluid analysis was significant for 548 nucleated cells with 0 neutrophils and a fluid triglyceride level of 554 mg/dL. Given the patient's recent bilateral nephrectomy, it was suspected that his ascites were secondary to injury to lymphatic vessels during surgery. The dietary team was consulted in the hospital, and the patient was advised to follow a non-fat, high-protein diet with 5 mg medium-chain triglycerides to prevent essential fatty acid deficiency Discussion: Chylous ascites is relatively rare, making up approximately 1 in 20,000

cases of ascites. Most common causes include iatrogenic injury to lymphatic vessels and lymphatic obstruction. Up to 11% of retroperitoneal surgeries can result in this condition, as the lymphatic vessels near the cisterna chyli and the para-aortic lymph nodes are often damaged. However, the incidence of chylous ascites, specifically after nephrectomy, ranges from 0.013% to 5.9%. Management is typically conservative and most commonly involves a low-fat, high-protein diet supplemented with medium-chain fatty acids, though TPN is also often considered.

Internal Medicine
Al-Nabolsi A, **Chaudhary AJ**, **Jamali T**, **Caines AN**, and **Elatrache M**. Esophagitis in a Post-Liver Transplant Patient: A Case of Cytomegalovirus and Herpes Simplex Virus-1 Coinfection. *Am J Gastroenterol* 2024; 119(10):S2222-S2223. Full Text

A. Al-Nabolsi, Corewell Health Farmington Hills, Dearborn, MI, United States

Introduction: Infectious esophagitis is the third most common cause of esophagitis, after gastroesophageal reflux disease and eosinophilic esophagitis. Common infectious organisms include candida, herpes simplex virus (HSV) and cytomegalovirus (CMV). While the occurrence of CMV esophagitis is rare in CMV infected patients, there remains minimal reported cases regarding CMV/HSV esophagitis coinfection. We present a rare case of CMV/HSV esophagitis successfully treated with antivirals. Case Description/Methods: A 59-year-old woman with history of primary sclerosing cholangitis, who underwent orthotopic liver transplantation from a CMV seropositive donor 6 years ago, and achalasia secondary to scleroderma, treated with esophageal perusal endoscopic myotomy (EPOEM) one year ago, presented with a one-week history of dysphagia. The patient's immunosuppressive therapy at the time of presentation included prednisone, tacrolimus, and mycophenolate. The patient had negative CMV serology prior. An esophagogastroduodenoscopy (EGD) revealed severe esophagitis with extensive serpiginous and confluent non-bleeding ulceration (Figure 1A, B, C). Biopsies from the ulcer bed as well as ulcer edges confirmed CMV and herpes simplex virus-1 (HSV-1) co-infection. CMV quantitation in the blood was 9,523 IU/mL, subsequently becoming undetectable following treatment with valganciclovir. Mycophenolate was temporarily discontinued during treatment for CMV and HSV esophagitis. A repeat EGD performed 2 months later showed esophageal ulcers with no recent bleeding stigmata (Figure 1D). Biopsies revealed candida esophagitis with ulceration, and notably, CMV/HSV testing was negative. Discussion: CMV/HSV co-infection in the esophagus is very rare and can be associated with higher complication rates including perforation and bleeding. Thus, in immunocompromised hosts with esophagitis, a high index of suspicion for these conditions can help with targeting of appropriate biopsies of the esophagus to yield accurate and early diagnoses, allowing for rapid treatment.

Internal Medicine
Al-Suraimi A, **Almajed MR**, **Heil H**, **O'Neill B**, **Villablanca P**, **Parikh S**, **Gonzalez PE**, **Lee J**, **Zweig B**, **Wyman J**, **Frisoli T**, **O'Neill W**, and **Wang D**. Isolated Mitral Regurgitation Versus Multivalvular Disease in Patients Undergoing Mitral Valve Transcatheter Edge-toEdge Repair: A Comparison of Cardiac Function and Structure. *JACC Cardiovasc Interv* 2024; 17(4):S60-S60. Full Text

[Al-Suraimi, A.; Almajed, M. R.; O'Neill, B.; Villablanca, P.; Parikh, S.; Gonzalez, P. Engel; Lee, J.; Zweig, B.; Wyman, J.; Frisoli, T.; O'Neill, W.; Wang, D.] Henry Ford Hosp, Detroit, MI USA. [Heil, H.] Wayne State Univ, Detroit, MI USA.

Internal Medicine
Alhaj Ali S, **Dawod S**, **Alomari A**, **Omeish H**, **Cobty K**, **Shamaa O**, **Todd S**, **Williams C**, and **Jafri SM**. Hepatology Management of Adults with Fontan Circulation: An Interdisciplinary Protocol. *Am J Gastroenterol* 2024; 119(10):S1235-S1236. Full Text

S. Alhaj Ali, Henry Ford Hospital, Detroit, MI, United States

Introduction: The Fontan procedure is a palliative treatment for complex congenital heart disease that reduces cardiac output and raises venous pressure, leading to hepatic and cardiac complications. This study describes the clinical course and current management of adult patients with Fontan circulation

under an interdisciplinary protocol. Methods: A retrospective review was done on adult patients with Fontan circulation after data collection on fibrosis evaluation, laboratory/imaging surveillance, and clinical follow-up. Monthly meetings helped establish the protocol and review challenging cases. Data was analyzed for describing hepatic, oncologic, cardiac, and renal outcomes. Results: Forty-three patients were included, average age 30.4 ± 7.2 years. Lateral tunnel (60.5%) and extracardiac (30.2%) Fontan were predominant; 46.5% were fenestrated. Indications included arterial malposition (25.6%), tricuspid atresia (23.3%), and hypoplastic left heart (20.9%). Elevated liver enzymes and total bilirubin were noted in 23% and 13.9%, respectively. Transient elastography (TEG) was done on 31 patients showing median stiffness of 14.3 kPa, with 51.7% having F4 fibrosis and 37.9% F3. All patients underwent liver Ultrasound or Magnetic resonance imaging within the last 2 years, revealing cirrhosis in 34.9% and congestion in 23.3%. Despite lacking imaging evidence of fibrosis, 21 had F2 or higher fibrosis on TEG. Liver biopsies in 13 patients showed congestion (53.8%), no/mild fibrosis (23.1%), and cirrhosis (15.9%). 4 patients had congestion without advanced fibrosis, despite advanced TEG or imaging findings. Cirrhotic complications included varices (11.9%) and ascites (7%). There were no cases of hepatocellular carcinoma or hepatic encephalopathy, and 1 patient was referred for liver transplant evaluation. Median ejection fraction was 55%. Heart catheterizations were done in 79.1%, 35.3% of whom had high Fontan pressures. Over half (53.9%) required repeat catheterization and 16.3% got additional heart surgery. 1 patient was referred for heart transplant. None developed chronic kidney disease (CKD). Conclusion: Our results show that fibrosis evaluation via TEG screening and laboratory/imaging surveillance may be confounded by congestive hepatopathy, commonly necessitating liver biopsy. Frequent heart catheterizations are crucial for surveillance in those with advanced fibrosis or congestion. Risk of liver or heart transplant as well as CKD remains low. An interdisciplinary protocol is imperative to establish clearer guidelines on surveillance techniques/intervals to reduce morbidity. (Table Presented).

Internal Medicine

Ali SA, **Ahmad Adil S**, **Harris K**, **Kamran W**, **Elatrache M**, **Zuchelli T**, and **Piraka C**. Navigating Obstacles: A Case Report on Endoluminal Treatment of Afferent Limb Syndrome Post-Whipple Procedure for Cholangiocarcinoma. *Am J Gastroenterol* 2024; 119(10):S2596. Full Text

S.A. Ali, Henry Ford Hospital, Detroit, MI, United States

Introduction: Afferent limb syndrome (ALS) is a rare complication of the Whipple pancreaticoduodenectomy (0.3%-1%). While optimal treatment is not established, surgical revision is a traditional approach for malignant ALS. Recently, endoscopic or radiologic interventions, such as stenting or percutaneous biliary drainage, have emerged as palliative alternatives. Case Description/Methods: This is a 74-year-old man with history of metastatic cholangiocarcinoma stage IIB status post neoadjuvant therapy followed by Whipple procedure. Course was complicated by obstructive jaundice due to partially obstructing afferent limb jejunal mass seen on enteroscopy, biopsy-proven to be recurrent cholangiocarcinoma. The resultant severe stricture could not be traversed endoscopically hence an internal-external percutaneous transhepatic cholangiography (PTC) drain was inserted, complicated by persistent leak around the insertion site requiring several tube exchanges. He was later admitted for jaundice & poor oral intake. Abdominal imaging re-demonstrated the mass with an abrupt transition point (Figure 1). A cholangiogram revealed dilated small bowel loop in the afferent limb concerning for ALS. Based on imaging, there was no good window for an endoscopic ultrasound-guided jejuno- or gastrojejunostomy to bypass the obstruction. Therefore, a 22 mm x 6 cm uncovered metal Wallflex stent (Boston Scientific, Marlborough, MA) was inserted across the site (Figure 1B), which improved his symptoms & oral intake without further PTC leaks. Discussion: Malignant ALS post-Whipple negatively impacts outcomes & quality of life in a population with already limited life expectancy. Diagnosis can be a challenge as it may not present with typical gastrointestinal (GI) obstruction symptoms, requiring clinical suspicion & imaging (commonly computerized tomography as upper GI series may not detect its presence). Management requires a multidisciplinary approach with surgeons, therapeutic endoscopists, &/or interventional radiologists. Our case underscores the importance of prompt recognition to allow for an early intervention. Palliative surgical revision is limited by low success rates given overall poor patient condition or from tumor burden causing kinks. Percutaneous approaches introduce risk of retrograde biliary infection, & in this case failed due to downstream obstruction. Endoluminal interventions, despite

technical difficulty, emerge as promising alternatives which warrant further prospective trials comparing outcomes with other modalities. (Figure Presented).

Internal Medicine
Ali SA, **Khadra M**, **Sitto M**, **Graifman M**, and **Gietzen J**. Semaglutide's Hidden Perils: A Rare Case of Malnutrition and Wernicke Encephalopathy. *Am J Gastroenterol* 2024; 119(10):S2964. Full Text

S.A. Ali, Henry Ford Hospital, Detroit, MI, United States

Introduction: With increasing use, concerns about semaglutide's long-term effects have been raised due to its potential to cause extended malnutrition, which can lead to vitamin deficiencies such as thiamine even without a history of alcohol use. We report a rare case of semaglutide-associated Wernicke Encephalopathy (WE) in an older adult with numerous comorbidities. Case Description/Methods: A 74-year-old woman with history of ischemic stroke, coronary artery disease, hypertension, hypothyroidism, depression, & class 2 obesity (body mass index 35 kg/m2) presented to the emergency department with generalized weakness after 3 days of low oral intake & decreased appetite. She was adherent to her medications, including semaglutide initiated 6 months & subsequently stopped 2 months prior (following 47 pounds weight loss) due to nausea, vomiting, abdominal pain, fatigue, lightheadedness, generalized weakness, & decreased bowel movements with the 0.5 mg dose, resulting in 3 hospitalizations. She exhibited changes in mental status, oriented to person & place but not to time or situation. Notable findings included incidental COVID-19 infection, vertical & horizontal nystagmus, & diffuse areflexia. Diagnostic imaging revealed right frontal lobe encephalomalacia & chronic micro-idiopathic alterations, while electroencephalogram indicated mild cerebral dysfunction. Thyroid stimulating hormone, vitamin B12, ammonia, & infectious/paraneoplastic/autoimmune workup were negative. She was treated with IV immunoglobulin for possible COVID-19-induced encephalopathy without improvement. Ultimately, her symptoms were attributed to WE & axonal neuropathy due to protein-calorie malnutrition & multiple vitamin/mineral deficiencies (zinc & vitamins B6, C, D, A). Treatment with IV thiamine was empirically initiated & continued despite a normal serum thiamine level, but her cognitive condition remained poor, leading to a diagnosis of WE possibly complicated by Korsakoff syndrome. She was ultimately discharged to hospice care. Discussion: This case underscores the need for awareness of the risks associated with semaglutide, along with the diagnostic challenges in recognizing WE as a complication of semaglutide-induced nutritional deficiency. While traditionally linked to alcohol use, WE should be considered when patients present with prolonged dietary deficiencies, altered mental status, & oculomotor abnormalities even in the setting of normal serum thiamine. Diagnosis should be made promptly & treatment given empirically to reduce the risk of lasting complications.

Internal Medicine
Ali SA, **Kostecki P**, **Khan MZ**, and **Bhan A**. A Rare Case of Primary Gastrointestinal Mantle Cell Lymphoma Hiding in Plain Sight as Colon Polyps. *Am J Gastroenterol* 2024; 119(10):S1917-S1918. Full Text

S.A. Ali, Henry Ford Hospital, Detroit, MI, United States

Introduction: Mantle cell lymphoma (MCL) is an aggressive subtype of B cell non-Hodgkin lymphoma that constitutes only a small fraction (0.4%) of all primary gastrointestinal lymphomas. Patients with MCL have a high relapse rate and poor prognosis. Case Description/Methods: A 71-year-old man presented with 6 months of non-specific symptoms including abdominal discomfort, altered bowel habits, and weight loss. Although he had a normal colonoscopy 4 years prior, a repeat endoscopic examination revealed significant lymphomatous polyposis, with hundreds of non-bleeding polyps localized from the rectum to the distal ascending colon. Histopathological assessment of the polyps revealed a lymphoid infiltrate consistent with MCL. Cytogenetic analysis of bone marrow aspirate along with imaging revealing extensive mesenteric and retroperitoneal adenopathy and a mildly enlarged spleen confirmed the MCL diagnosis. The patient underwent 6 cycles of bendamustine and rituximab followed by maintenance rituximab therapy every 2 months. Throughout and after treatment, serial imaging showed markedly reduced adenopathy, and colonoscopy performed 2 months post-treatment (prior to maintenance therapy) demonstrated completely normal colon without evidence of any residual polyps. One month after

completing initial chemotherapy, an incidental complex renal lesion was diagnosed as clear-cell renal cell carcinoma (World Health Organization / International Society of Urologic Pathologists grade 1, 4 cm, limited to the kidney), and the patient underwent successful partial nephrectomy after completion of chemotherapy. Discussion: Our case underscores the imperativeness of thorough endoscopic evaluation in patients with non-specific gastrointestinal symptoms to ensure early detection and effective management of rare colonic cancers. This is particularly important with classic “red-flag” symptoms and features suggesting malignancy and despite normal recent colonoscopies (as in our patient who had a normal colonoscopy 4 years prior). The case further highlights how quickly the rare condition of gastrointestinal MCL can arise, necessitating swift immunohistochemical, imaging, and cytogenetic analysis to identify this aggressive condition. Even with a delayed presentation and diagnosis, diligent and timely treatment can still result in significant disease remission. The co-occurrence of gastrointestinal MCL with renal cell carcinoma introduces additional complexity to the case and suggests a potential association warranting further study (see Figure 1).

Internal Medicine

Ali SA, **Shamaa O**, **Omeish H**, **Mullins K**, and **Heidemann D**. Open Access Colonoscopy: Assessing the Outcomes of a Novel Electronic Medical Record Best Practice Alert (BPA) in Reducing Inappropriate Colonoscopy Referrals. *Am J Gastroenterol* 2024; 119(10):S281-S282. Full Text

S.A. Ali, Henry Ford Hospital, Detroit, MI, United States

Introduction: In our prior study, we established that open access colonoscopy (OAC) for colon cancer screening is burdened by high inappropriate referral rates, leading to delayed patient care, increased resource use, & lower colonoscopy completion rates for rejected patients. Our group initiated a quality improvement project involving an electronic medical record (EMR) best practice alert (BPA) that notifies providers if specific criteria prohibiting OAC are met. This study assesses the BPA's outcomes after implementation. Methods: Starting April 2023, an EMR BPA was launched at our primary care clinic. Upon ordering OAC, if a patient meets prohibitive criteria, the BPA (seen in Figure 1) notifies the provider to cancel the order & either refer to gastroenterology (GI) or order stool testing. If the order remains, a text box appears for an optional explanation. High-risk patients have only the GI referral option. Concurrently, we liberalized OAC guidelines, raising hemoglobin A1c (HbA1C) & body mass index (BMI) thresholds. Data from January to March 2024 was collected post-BPA refinement, & a random sample of 200 patients was chart reviewed to assess outcomes. Results: From January to March 2024, the BPA was triggered 508 times. Mean age was 61.1 years. Common BPA triggers were hypokalemia ≤3.3 mmol/L (18.5%), HbA1C ≥9.5% (18.5%), hemoglobin ≤10 g/ dL (15.5%), age ≥80 years (15.5%), BMI ≥50 kg/m2 (13.5%), & blood pressure ≥180/110 (8%). Most common alternatives were referral to GI (53%), stool testing (2%), or neither (45%). Those who ordered neither mostly proceeded with the order without any reason/changes (54.4%), or canceled it (24.4%). For “high risk” patients where the BPA triggered (n=51), only 52.9% were referred to GI. There were 5 cases where the BPA inaccurately fired, 19 cases where OAC referral was still accepted by GI despite BPA accuracy, & 20 cases where referral was rejected for another individualized reason. Only 11% of the sample completed any colon cancer screening & 9% completed a colonoscopy; mean time from referral to colonoscopy was 77.1 days. Conclusion: The BPA appears to reduce inappropriate referrals but effectiveness is limited by provider awareness & inability to factor in personalized patient factors. Low completion rates may be due to demographic challenges like missed appointments or socioeconomic barriers, as well as the recent nature of the data. This suggests a need for longer BPA implementation to fully assess its impact on referral appropriateness & completion rates. (Table Presented).

Internal Medicine

Alluri S, **Lloyd J**, and **Caines AN**. The Dark Side of Slimming: Weight Loss Supplement Induced Liver Injury. *Am J Gastroenterol* 2024; 119(10):S2885. Full Text

S. Alluri, Henry Ford Health, West Bloomfield, MI, United States

Introduction: Drug-induced liver injury (DILI) is a significant and underrecognized cause of acute liver failure, with weight loss supplements being a notable culprit due to unregulated ingredients and

widespread use. Diversity of causative agents in DILI results in a sundry of clinical presentations that often mimic other liver diseases, making diagnosis complex. This case report delves into the diagnostic challenges and clinical implications of DILI. Case Description/Methods: A young African American woman with history of hypertension and obesity, presented with 1 week of new-onset jaundice, pruritus, and vomiting. She denied alcohol use, personal or family history of liver disease, or new medications apart from weight loss supplements purchased online 2 months prior. Initial lab work revealed ALT 1593, AST 1309, Tbili 12.5, ALP 191, and INR 1.65. Infectious, metabolic workup was negative, with positive antimitochondrial antibody (AMA) of 86 U/mL, and negative Anti- smooth muscle antibody (16 U/mL) . Subsequent imaging with US and MRCP showed no structural abnormality. Liver biopsy done to differentiate drug induced liver injury (DILI), drug induced autoimmune liver disease, and autoimmune related liver disease and/or overlap syndrome. Biopsy showed diffuse mixed inflammation typical of acute hepatocellular injury rather than the focal lymphocytic biliary injury characteristic of PBC. Patient was diagnosed with DILI secondary to herbal/ dietary supplements (HDS) based on the drug exposure timeline, histologic findings, and the negative workup for alternative etiologies. Supplement was discontinued, however due to prolonged jaundice and lack of spontaneous recovery, glucocorticoids were initiated in Hepatology clinic 2 months later . Subsequent labs at 4 month follow up, showed significant improvement to ALT 36, AST 52, ALP 61 , Tbili 0.9, and INR 1.3. Discussion: This case highlights the need for awareness of DILI, which is often underreported and can lead to severe outcomes. With the rise in access to weight loss supplements, coupled with minimal patient education on associated risks, providers must be thorough in history taking and workup. The patient's positive AMA titer, though an uncommon finding in DILI, is important to recognize as it may indicate a predisposition to autoimmune liver disease, guiding future monitoring. Although histopathology is not a standard diagnostic criterion for DILI, it proved imperative in establishing diagnosis in our case, emphasizing its value in clinical practice.

Internal Medicine

Alluri S, and **Matin T**. Isolated Colonic Polypoid Ganglioneuromas in Patient With Neurofibromatosis Type 1. *Am J Gastroenterol* 2024; 119(10):S2058. Full Text

S. Alluri, Henry Ford Health, West Bloomfield, MI, United States

Introduction: Ganglioneuromas are rare, benign neurogenic tumors arising from the peripheral nervous system, which can occur in the mediastinum, retroperitoneum, adrenal gland, and uncommonly, the GI tract. Intestinal ganglioneuromas are typically diagnosed in adolescents and young adults and can manifest as polypoid, multifocal, or diffuse involvement of the intestinal tract. While patients are often asymptomatic, large lesions can cause significant downstream effects such as Gastrointestinal bleeding, motility issues and obstruction, making recognition imperative. Diffuse ganglioneuromatosis has been associated with syndromic conditions such as MEN2B and Cowden, however association with Neurofibromatosis 1 (NF1) remains largely undocumented. Case Description/Methods: We report the case of a 60-year-old African American woman with history of neurofibromatosis type 1 (NF1), who presents for colonoscopy after reporting several months of intermittent constipation. She was diagnosed with NF1 at the age of 22 with disease manifestations including Lisch nodules, and cutaneous and cervical neurofibromas. Colonoscopy unexpectedly revealed an 11 mm sessile polyp in the cecum, and 2 sessile polyps in the sigmoid colon, which were removed via cold snare polypectomy. Histopathology revealed Ganglioneuroma and lipomas with immunostaining positive for s100 protein supporting diagnosis of ganglioneuroma (GN). Discussion: Intestinal ganglioneuromas can be categorized as polypoid, multifocal, or diffuse with the latter 2 having had documented association with NFI. However, association with NF1 and solitary lesions has been sparsely documented in literature. In our peculiar case, an older woman with history of NF1 presented with 3 isolated polypoid ganglioneuromas in sigmoid colon and cecum. While the incidence and risk of malignant transformation of ganglioneuromas is low, it is important to be mindful of this pathology in order to provide definitive management with surgical removal. Recognition can be delayed due to non-specific presenting symptoms and lack of screening guidelines in patients with NF1. While association is more well established with MEN2B and Cowden, testing for these conditions along with NF1 should be considered based on concomitant clinical findings in patient's without history of systemic syndromes.

Internal Medicine

Alluri S, **Singh B**, **Sarowar A**, **Ramanan S**, **Rehman S**, and **Jafri SM**. Patterns and Predictors of Outcomes in Total Parenteral Nutrition Associated Liver Disease. *Am J Gastroenterol* 2024; 119(10):S1386. Full Text

S. Alluri, Henry Ford Health, West Bloomfield, MI, United States

Introduction: Total parenteral nutrition (TPN) is used as a life-saving intervention in patients who are unable to tolerate alternative nutrition. However, elevated liver enzymes in patients requiring TPN are a significant predictor of morbidity and have been associated with increased mortality rates as well. Given the complexity and clinical implications of TPN associated liver disease, bridging the gap in understanding and management of this phenomenon is pivotal. Our study aims to elucidate patterns and predictors of liver enzyme elevation in this patient population, with a focus on clinical management and outcomes. Methods: A retrospective chart review was conducted of all adults (18 years or older) at our center (2014-2024) with history of elevated liver enzymes (Alanine transaminase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), and Total Bilirubin) while on TPN. Data on basic patient demographics, indication for TPN, Duration of TPN therapy and Liver enzyme elevation, changes in TPN formulation, and mortality were collected. Results: A total of 111 patients with history of elevated liver enzymes (ALT, AST, ALP, and Total Bilirubin) while on TPN were included, 48 (43.2%) were male, 63 (56.8 %) were females, and 87 (78.4%) were White. Most common indications for TPN initiation were prolonged malnutrition in 41 (36.9) patients, and short gut syndrome in 39 (35.1) patients. Mortality occurred in 52 (46.8%) of patients. Indication for TPN (P=0.82) and Duration of TPN therapy (P5 0.516) did not show statistically significant differences in risk of mortality. However, there was a significantly higher incidence of mortality in patients who underwent change in TPN therapy in comparison with those who did not (16.3%, 83.7%, P=0.007). Additionally, those with change in TPN had significantly shorter duration of time from peak Liver enzyme value to death (P5 0.028). Conclusion: This study observed a link between TPN modification and higher mortality rates despite not having a correlation between duration on TPN therapy and mortality. In considering the simultaneous findings of significantly reduced time from peak Liver enzymes to death, this suggests that alterations in TPN therapy may be critically delayed till severe progression of liver disease. Our study highlights the need for early consideration of TPN adjustment and further clinical studies to promote better outcomes in patients with TPN associated liver disease.

Internal Medicine

Alluri S, **Todd S**, **Lloyd J**, and **Jafri SM**. Lynch Syndrome and Liver Disease - Connecting the Dots. *Am J Gastroenterol* 2024; 119(10):S2885. Full Text

S. Alluri, Henry Ford Health, West Bloomfield, MI, United States

Introduction: Lynch syndrome (LS) is an autosomal-dominant disorder that increases risk of carcinogenesis via defects in DNA mismatch repair genes. Typically, it has been associated with colorectal and gynecological cancers, but has been more rarely been connected to biliary cancers as well. The intricate relationship between LS and liver disease is highlighted by the increased incidence of hepatobiliary manifestations, making vigilant screening and management imperative. Case Description/Methods: We report the case of an elderly White woman with hypothyroidism, who presented with a long history of persistently elevated Alkaline phosphatase, with presenting values of ALT 24, AST 30, ALP 305, and total bilirubin 0.50. She was asymptomatic without toxometabolic risk factors. The patient has an interesting family history of 2 sisters with PMS2 positive LS, one of whom also had autoimmune hepatitis (AIH) and intrahepatic cholangiocarcinoma, and a brother who underwent liver transplantation for cirrhosis of unknown etiology. Serologies positive for antimitochondrial antibody (AMA) of 17 U/mL, antinuclear antibody (ANA) ratio >1:55, SSA/SSB antibodies >240 and 167 U/mL, and positive smooth muscle antibody (SMA). Liver biopsy showed chronic cholestasis and patchy portal inflammation without bile duct inflammation or granulomas. She was initiated on Ursodiol and MRCP was ordered, with repeat bloodwork after 2 months showing near normalization of ALP to 144. Discussion: This case observes an elderly women with newly diagnosed PBC without cirrhosis, who prompted extensive hepatobiliary workup due to personal and family history of LS and liver disease. Mutations in

PMS2 genes carry a lower risk for malignancy compared to other mismatch repair genes, which has led some experts to suggest less rigorous screening approach. However, as this case highlights, assessing for hepatobiliary manifestations of LS is extremely important. This case also demonstrates the importance of both laboratory and pathologic screening for various pathologies in liver disease. While family history, serologies and clinical presentation suggested LS and PBC, biopsy introduced new suspicion for PSC. Family history of idiopathic cirrhosis and cholangiocarcinoma further complicates the clinical picture, raising questions about the interplay between autoimmune liver disease and LS. This case advocates for a comprehensive and thorough evaluation for liver disease in patients with history of Lynch Syndrome.

Internal Medicine

Alomari A, **Abusuliman M**, **Saleem A**, **Malick AN**, **Jomaa D**, Althunibat I, and **Gueorguieva I**. Paradoxical Psoriasis and Alopecia Areata After the Use of Anti-TNF in a Patient With Crohn's Cisease. *Am J Gastroenterol* 2024; 119(10):S2546-S2547. Full Text

A. Alomari, Henry Ford Hospital, Detroit, MI, United States

Introduction: Autoimmune reactions to anti-tumor necrosis factor (TNF) therapy present a clinical challenge while managing inflammatory bowel disease (IBD). Among these reactions, psoriasis and alopecia can occur as extraintestinal manifestation and due to immunosuppressive medication. We aim to highlight the complexity of autoimmune responses triggered by anti-TNF therapy in a patient with Crohn's disease who developed alopecia and psoriasis of the scalp. Case Description/Methods: A 20-year-old man patient was diagnosed with Crohn's disease after experiencing abdominal cramps, rectal pain, and bleeding. Colonoscopy showed aphthous ulcerations and severe inflammation in the terminal ileum. He was started on infliximab, which improved his symptoms. A year and a half later, his symptoms started to recur, requiring increased dosages. Four months later, the patient reported hair loss. Dermatologists saw the patient and noticed psoriasiform changes on the scalp and ears, and a biopsy showed psoriatic alopecia and alopecia areata features suggestive of anti-TNF alpha related alopecia. Treatments including Triamcinolone injections, clobetasol, and calcipotriene failed to alleviate symptoms. Ultimately, medication was changed to Ustekinumab, which improved his hair loss and Crohn's symptoms, further supporting the diagnosis of anti-TNF alpha-related alopecia. Discussion: The association between anti-TNF-α agents and onset of psoriasiform skin eruptions, and the paradoxical nature of these reactions are well described in the literature. The proposed mechanism relies on the role of IFNγ in the pathogenesis of psoriasis, as blocking TNFa leads to uncontrolled production of IFNγ contributing to the skin eruption. One Meta-Analysis described 134 patients who developed alopecia with IBD therapy. Of those, 78 were on anti-TNF-α therapy. Psoriatic Alopecia was the most reported (n = 41), followed by Alopecia Areata (n = 19), and psoriatic alopecia with alopecia areata features. (n = 3). Diagnosis criteria include absence of psoriasis history, alopecia plaque(s) on the scalp, and psoriasiform rash elsewhere after starting treatment. Our patient met the criteria, with hair regrowth after stopping infliximab. Differentiating these reactions from primary psoriatic alopecia/alopecia areata is important as it affects our management. Lastly, it is important to collaborate in a multidisciplinary approach involving gastroenterology and dermatology when caring for our IBD patient community.

Internal Medicine

Alomari A, Al Smadi K, Sqour H, Althunibat I, and Hushki A. A Rare Case of Extramedullary Plasmacytoma of the Stomach. *Am J Gastroenterol* 2024; 119(10):S3200. Full Text

A. Alomari, Henry Ford Hospital, Detroit, MI, United States

Introduction: Plasma cell neoplasms (PCNs) are a group of disorders including multiple myeloma (MM), solitary plasmacytoma of bone (SPB) and primary extramedullary plasmacytoma (EMP). These disorders are characterized by monoclonal secretion of immunoglobulins from differentiated B lymphocytic cells. Most EMP cases occur in the head and neck with relatively rare presentation in other parts of the body. Herein, we introduce a case of EMP with a gastric mass presenting with upper gastrointestinal tract bleeding. Case Description/Methods: A 55-year-old man with a history of multiple myeloma in clinical remission after 4 cycles of bortezomib, thalidomide, and dexamethasone (VTD) and autologous stem cell transplantation. The patient was presented with 2 weeks of melena and hemoglobin drop. Endoscopic

gastroduodenoscopy (EGD) showed a 4 x 4 cm mass with deep necrotic central ulceration at the anterior wall of the proximal corpus without active bleeding (Figure 1). Accordingly, a biopsy was collected, and pathology report showed involvement by CD138 positive poorly differentiated plasma cells, that are restricted for Lambda light chain and is consistent with the diagnosis of extramedullary gastric plasmacytoma for which he received chemotherapy, unfortunately the patient developed sepsis and multiorgan failure, after his first cycle and his admission ended up by death. Discussion: MM with EMP is a rare variant of PCNs where tumors composed of plasma cells arise outside the bone marrow. The most common sites for EMP include the respiratory tract, urinary bladder, brain, thyroid, and skin. EMP involvement of the gastrointestinal tract is indeed a rare occurrence representing < 1% of MM cases. Intraabdominal EMPs usually have a relatively slow-growing and indolent course with nonspecific symptoms like abdominal pain, melena, hematochezia, intussusception or localized perforation. The specific anatomical location of the EMP plays a role in determining the method used for obtaining a formal tissue diagnosis such as gastroscopic biopsy for gastric EMPs. Multiple myeloma with EMP presents a unique and challenging scenario lacking an established treatment consensus and requiring individualized therapy based on each patient's circumstances. It is important to keep a wide differential diagnosis for gastroenterology bleed especially in patients with complex medical history. This case illustrates the importance of histopathological examination in establishing a definitive diagnosis and guiding management. (Figure Presented).

Internal Medicine

Alomari A, **Nimri F**, **Shamaa O**, **Abusuliman M**, **Saleem A**, Nimri R, **Omeish H**, **Malick AN**, and **Zuchelli T**. Factors Associated With Worsening Ascites Following ERCP in Cirrhotic Patients: A Retrospective Analysis. *Am J Gastroenterol* 2024; 119(10):S1147. Full Text

A. Alomari, Henry Ford Hospital, Detroit, MI, United States

Introduction: Even in patients with liver cirrhosis, ERCP remains the gold standard treatment for pancreatic and biliary diseases. These patients are more likely to have adverse outcomes. We investigated the worsening of ascites as a complication of ERCP in cirrhosis patients. Methods: A retrospective chart review was carried out on all cirrhosis patients aged 18 years and above who had an ERCP at our center between January 2015, and November 2023. Our analysis did not include any patients with liver transplants. Basic patient demographics, ERCP indications, liver function markers, ERCP indications, and morbidity were among the collected data. Results: In patients with cirrhosis who underwent ERCP (n=277), 181 (65.3%) were males, 183 (66.1%) were white. The most common etiology of cirrhosis was alcohol in 108 (38.9%) patients. Jaundice was the most common indication for ERCP in 99 (35.7%) patients. The course of 22 (8%) patients was complicated by worsening ascites post procedural. Comparing those whose ERCP course was complicated by worse ascites to those who did not, patients with worsening ascites were more likely to have a higher MELD score at the time of ERCP (25.6 ± 8.0 vs. 18.6 ± 8.2, P< 0.001), higher INR (1.6 ± 0.5 vs. 1.4 ± 0.4, P = 0.049), and performed inpatient vs. outpatient (81.8% vs. 58.0%, P=0.029). Additionally, they had a higher incidence of ascites (90.9% vs. 59.1%, P=0.003) HRS (38.1% vs. 17.3%, P=0.019), and hyponatremia (63.6% vs. 36.4%, P=0.012) at presentation. Conclusion: While ERCP continues to be an invaluable procedure for therapeutic and diagnostic interventions in pancreatic and biliary disorders, patients with liver cirrhosis have more risks for post-ERCP complications including ascites. Patients who have ascites at presentation have a higher risk for worsening ascites after ERCP. Patients with higher MELD score, higher INR, HRS, hyponatremia at the time of ERCP and those who are getting the procedure as inpatient have a higher risk of developing worsening ascites post ERCP. Understanding the specific risk factors associated with post-ERCP complications in patients with liver cirrhosis is crucial for optimal patient care and to lower rates of complications.

Internal Medicine

Alomari A, **Nimri F**, **Shamaa O**, **Saleem A**, **Abusuliman M**, Nimri R, Althunibat I, and **Zuchelli T**. Risk Factors and Predictors of Hepatic Encephalopathy Following ERCP in Cirrhotic Patients: A Retrospective Analysis. *Am J Gastroenterol* 2024; 119(10):S1355. Full Text

A. Alomari, Henry Ford Hospital, Detroit, MI, United States

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) poses unique challenges in patients with liver cirrhosis, a population prone to heightened post-procedural complications. We investigated hepatic encephalopathy (HE) as a complication of ERCP in patients with liver cirrhosis. Methods: A retrospective chart review was carried out on all cirrhosis patients aged 18 years and above who had an ERCP at our center between January 2015, and November 2023. Our analysis did not include any patients with liver transplants. Basic patient demographics, ERCP indications, liver function markers, ERCP indications, and morbidity were among the collected data. Results: In patients with cirrhosis who underwent ERCP (n=277), 181 (65.3%) were males, 183 (66.1%) were White. The most common etiology of cirrhosis was alcohol in 108 (38.9%) patients. Jaundice was the most common indication for ERCP in 99 (35.7%) patients. The course of 24 (8.6%) patients were complicated by HE. Comparing those whose ERCP course was complicated by HE to those who did not, patients with HE were likely to have a higher MELD score at the time of ERCP (26.7±9.4 versus 18.4±7.9, P<0.001), higher INR (1.9±0.6 versus 1.4±0.6, P<0.001), ascites (95.8% versus 58.3%, P<0.001), undergone balloon dilatation (75% versus 54%, P=0.047) , and had higher incidence of HE at presentation (62.5% versus 37.7%, P=0.018). Interestingly, cirrhotic patients with hypertension were less likely to develop HE post-ERCP (37.5% versus 59.3%, P=0.039). Conclusion: Our study highlighted the risk of hepatic encephalopathy (HE) in liver cirrhosis patients undergoing ERCP. Those who developed HE had higher MELD scores, INR levels, and were more likely to have ascites. Surprisingly, hypertension seemed to lower the risk of post-ERCP HE. Patients undergoing balloon dilatation during ERCP had a higher risk of HE. This emphasizes the importance of careful patient selection and procedural considerations to minimize HE risk in cirrhotic patients undergoing ERCP, especially if performed as an outpatient.

Internal Medicine

Alomari A, **Saleem A**, **Abusuliman M**, **Omeish H**, **Dababneh YJN**, Althunibat I, and **Ginnebaugh B**. Gastric Lap Band as a Cause of Pseudoachalasia. *Am J Gastroenterol* 2024; 119(10):S2259. Full Text

A. Alomari, Henry Ford Hospital, Detroit, MI, United States

Introduction: Achalasia is a rare esophageal motility disorder characterized by impaired relaxation of the lower esophageal sphincter and loss of esophageal peristalsis. Pseudoachalasia, often caused by malignancy or mechanical obstruction, mimics the clinical presentation of achalasia. [1] This case report highlights an unusual presentation of pseudoachalasia caused by a gastric lap band. Case Description/Methods: We present the case of an 80-year-old woman with a surgical history of laparoscopic gastric banding for obesity who was diagnosed with achalasia in 2013. Management was initially conservative following a comprehensive diagnostic workup including EGD, VFSS, esophageal manometry, and a barium study. The patient did not wish to undergo myotomy. She was lost to follow up for over 10 years and re-presented due to progressive solid and liquid dysphagia with accompanied regurgitation. After further chart review, it was found that her laparoscopic gastric band had not been assessed for 2 decades. Taking into account her surgical history, pseudoachalasia due to lap band migration or hyperinflation was considered. A repeat barium swallow study demonstrated delayed passage of contrast through a narrow lumen at the level of the gastric band suggestive of obstruction. The patient was then referred to bariatric surgery for deflation of the gastric lap band. Discussion: Pseudoachalasia is a condition that mimics the clinical features of primary achalasia. It can be caused by a variety of etiologies including malignancy, particularly those involving the gastroesophageal junction, as well as anatomical abnormalities or previous surgical interventions. Identifying pseudoachalasia is imperative for effective treatment initiation. While primary achalasia may be managed with interventions such as Heller myotomy or POEM, pseudoachalasia requires addressing the underlying cause. For our patient, this meant deflation of the gastric lap band. Routine achalasia work-up sometimes fails to distinguish between pseudo and primary achalasia, thus a high clinical suspicion and proper history is paramount in initiating diagnostic work-up. This case highlights the importance of considering pseudoachalasia in patients with a history of gastric surgeries due to their altered anatomy.

Internal Medicine

Aloum K, Forlemu AN, Garzon-Siatoya WT, Panjwani A, Ciobanu C, Dokmak A, **Abusuliman M**, Kumar V, Bandaru P, Mbakop RNS, Ginjupalli M, Gayam VR, Sharma AR, Etienne D, Reddy M, and Narendra N. Intersecting Paths of Osteoarthritis and Metabolic-Associated Steatotic Liver Disease. *Am J Gastroenterol* 2024; 119(10):S1255-S1257. Full Text

K. Aloum, St. Barnabas Hospital, Bronx, NY, United States

Introduction: Metabolic-associated steatotic liver disease (MASLD) is characterized by hepatic fat accumulation in individuals with metabolic risk factors such as obesity, insulin resistance, dyslipidemia, and hypertension. Osteoarthritis (OA) is the predominant form of arthritis and involves progressive joint cartilage degeneration. A recent national study reported a significant association between the 2 diseases. MASLD and OA share metabolic etiologies. Whether both conditions are related still needs elucidating. Methods: Patients with a diagnosis of OA and patients with a diagnosis of MASLD were identified utilizing the National Inpatient Sample (NIS) data from 2016 to 2020. Primary outcome was the association of the 2 diseases in the general population tested by multivariable logistic regression analysis. Secondary outcomes were the differences in the characteristics and outcomes between a cohort of MASLD with OA and a control cohort of MASLD without OA. Unweighted data from NIS were multiplied with appropriate discharge and hospital-level weights to represent the population across the USA. Results: OA was significantly associated with MASLD (Odds Ratio=1.226; P=0.00; Confidence Interval 1.21-1.24) with adjusting for sex, age, race, Charlson Comorbidity Index, obesity, smoking, location and hospital characteristics (Table 1). Out of a total of 2,982,525 with MASLD, 10.78% of those patients had osteoarthritis. Patients with MASLD that had OA were older in age than MASLD who did not have OA (63 years vs 54 years), had higher percentage of females (64% vs 52%), had a higher component of White ethnicity (77% vs 66%) and had a higher percentage of Medicare insured patients (58% vs 38%). Interestingly, MASLD with OA were noted to have a lower mortality rate, shorter length of stay, and fewer total charges. All the aforementioned results were statistically significant with a P<0.0001. The rest of the results of the comparison between the 2 cohorts are in the attached table. Conclusion: This study establishes a positive association between OA and MASLD. Shared risk factors such as obesity, dyslipidemia, and insulin resistance, alongside chronic low-grade inflammation, likely contribute to their co-occurrence through shared metabolic and inflammatory pathways. The findings in this study highlight the importance of understanding the relationship between OA and MASLD, and warrant further investigation into the causal pathways, therapeutic interventions, and comprehensive management approaches to improve outcomes for affected individuals.

Internal Medicine

Althunibat I, Qirem M, **Alomari A**, Atiyat R, Bains Y, DaCosta T, Jagirdhar GSK, and Hussain M. Rectal Xanthoma: A Case Report of a 56-Year-Old Female Patient. *Am J Gastroenterol* 2024; 119(10):S1978. Full Text

I. Althunibat, Saint Michael's Medical Center, Newark, NJ, United States

Introduction: Xanthomas are raised, waxy-looking, yellowish lesions resulting from accumulation of cholesterol and fats. Their most common location is the skin. However, though rare, they can occur in the gastrointestinal (GI) tract. Typically, they are usually found incidentally on colonoscopic examinations, appearing as red polyps or occasionally as yellowish- white in formations with a size of 1-3 mm. They can be misdiagnosed for lipomas. Although most commonly they are completely asymptomatic, some cases were reported with obstructive symptoms such as pain, abdominal distension and vomiting. Histologically, rectal xanthomas consist of aggregates of foamy macrophages in the lamina propria, which are negative for mucin and cytokeratin but positive for CD68 immunostain. Case Description/Methods: We present a case of a 55-year-old gentleman with past medical history of diabetes type 2, hypertension, hyperlipidemia, and obesity, who presented to undergo screening colonoscopy. At the time of presentation, the patient exhibited no GI symptoms or complaints, and laboratory test results were within normal limits. Colonoscopy was done and it showed diverticulosis throughout the colon, and multiple diminutive polyps, along with an 8 mm polyp that was found in the rectum. Biopsy was taken and histopathological evaluation of the 8mm polyp showed collections of foamy cells in the lamina propria

suggestive of mucosal xanthoma, without dysplastic changes. The patient was evaluated 2 weeks after the colonoscopy and was doing well with no complaints or symptoms, and will be followed based on the regular colonoscopy surveys. Discussion: Some studies were focusing on the relationship between dyslipidaemia and the development of rectosigmoid xanthomas.one study highlighted the role of lipid metabolism abnormalities as the underlying cause of xanthomas with evidence suggesting that treating hyperlipidaemia can lead to the resolution of gastric xanthomas in some cases. Conversely, other studies found no significant association between gastric xanthomas and diabetes mellitus, hypercholesterolemia, or skin lesions. Further research is needed to explore the intricate relationship between xanthomas and lipid metabolism, shedding light on potential therapeutic avenues and management strategies (see Figure 1).

Internal Medicine

Althunibat I, Qirem M, **Alomari A**, Jagirdhar GSK, Hussain M, Bains Y, Atiyat R, and DaCosta T. A Rare Case of Hepatic Perivascular Epithelioid Cell Tumor (PEComa) in a 73-Year-Old Female Patient. *Am J Gastroenterol* 2024; 119(10):S2792-S2793. Full Text

I. Althunibat, Saint Michael's Medical Center, Newark, NJ, United States

Introduction: Perivascular epithelioid cell tumors (PEComas) are a rare group of mesenchymal neoplasms composed of perivascular epithelioid cells. While commonly found in the kidney, uterus, and soft tissues, PEComas of the liver are exceedingly rare. Here we present a rare case of incidentally found PEComa of the liver which is an extremely rare case as few similar cases have been reported in the litreture Case Description/Methods: A 73-year-old woman patient presented with asymptomatic hepatic mass while being evaluated for lower abdominal pain. Computed tomography (CT) without contrast was done initially as the patient had pre-renal acute kidney injury at the time of evaluation, it showed features of diverticulitis. No lesions were detected in the liver. The patient also had an ultrasonographic (US) imaging of the abdomen as part of her evaluation. The imaging showed a left hepatic lobe hypovascular complex lesion measuring 1.2 x 1.2 x 1.8 cm in size (Figure 1). The patient was discharged after her diverticulitis have been managed and planned to be followed for further evaluation of the mass. A CT-guided biopsy was performed following localization of the lesion site based on ultrasound findings, as the lesion was not visualized on initial CT imaging. Histopathological evaluation showed a well circumscribed epithelioid and spindle cells. Smooth muscle differentiation was confirmed after staining with (SMA) and Melan A (Figure 1). the mass also showed positivity on immunohistochemical staining with (HMB-45) which confirms melanocytic differentiation as well, consistent with PEComa (Figure 1) Discussion: PEComa comprises a spectrum of infrequent mesenchymal tumors. Clinical presentation is non-specific and mostly being asymptomatic. In our case we present a challenge in diagnosis of such tumors. Diagnosis is based on histopathological evaluation, and although most of the cases reported in the literature were evaluated after surgical resection, some of them were diagnosed after image-guided biopsies as we did in our case. This entity of tumors needs further studies on their natural behaviour as some malignant cases were reported. In addition, a clearer approach for diagnosis and treatment needs to be established with more prognostication tools and patient categorization are needed.

Internal Medicine

Bai S, **Singh B**, **Ethakota J**, **Tariq H**, and **Rahman A**. Unmasking the Silent Invader: Tuberculosis Colitis. *Am J Gastroenterol* 2024; 119(10):S1928-S1929. Full Text

S. Bai, Henry Ford Jackson Hospital, Jackson, MI, United States

Introduction: Gastrointestinal tuberculosis (TB) is a prominent form of extrapulmonary TB that presents diagnostic challenges due to symptom overlap with other gastrointestinal conditions and the limited accuracy of current diagnostic tests. There is a critical need for increased awareness of this disease, particularly in regions with low disease prevalence such as developed countries. Left untreated, gastrointestinal TB can result in considerable morbidity, requiring prolonged hospital stays and sometimes surgical intervention. Early and accurate diagnosis followed by prompt initiation of therapy is crucial in preventing these complications. This detailed case study focuses on TB colitis, highlighting its clinical features, diagnostic approaches, and management protocol of extended drug resistant

tuberculosis. Case Description/Methods: We present the case of a 36-year-old immigrant from Honduras who initially presented with rectal bleeding, night sweats, and a notable weight loss of 30 pounds over 8 weeks. Colonoscopy identified Acid-fast bacilli (AFB)-positive granulomatous colitis, prompting a multidisciplinary diagnostic approach that included imaging studies, colonoscopy and microbiological confirmation. Discussion: This case underscores the importance of considering tuberculosis (TB) in the differential diagnosis of gastrointestinal symptoms. TB can affect the digestive tract, presenting similarly to conditions like Crohn's disease. Colonoscopy with deep biopsy is crucial for tissue diagnosis, revealing characteristic ulcerative and hypertrophic lesions. Polymerase chain reaction (polymerase chain reaction) significantly enhances diagnostic sensitivity and specificity compared to traditional methods. Treatment involves anti-TB medication, with follow-up colonoscopy showing gut response within 3-4 weeks. Surgical intervention may be necessary for complications such as stricture formation. Timely recognition and management are essential to prevent morbidity associated with TB colitis, especially in atypical presentations. Increasing clinician awareness is critical for improving diagnostic accuracy and ensuring prompt initiation of appropriate therapy (see Figure 1).

Internal Medicine

Bai S, **Singh B**, **Kisule A**, and **Ranjan N**. Splenic infarct and SMA thrombosis as a manifestation of Seronegative Antiphospholipid Syndrome. *Am J Gastroenterol* 2024; 119(10):S3004-S3005. Full Text

S. Bai, Henry Ford Jackson Hospital, Jackson, MI, United States

Introduction: Antiphospholipid Syndrome (APS) presents with a wide spectrum of clinical manifestations, ranging from asymptomatic cases to life-threatening catastrophic APS. Thrombosis in large or microvessels can affect virtually any organ system. Diagnostic criteria for APS have evolved, typically requiring the presence of 1 clinical criterion and 1 laboratory criterion. However, emerging research highlights cases where patients exhibit clinical features of APS despite transiently positive or persistently negative antiphospholipid antibody (aPL) titers, a condition termed seronegative APS (SN-APS). This diagnosis, often 1 of exclusion, is considered only after ruling out other inherited and acquired thrombophilic conditions Case Description/Methods: A 45-year-old man with a history of recurrent pulmonary emboli, pancreatitis with pseudocyst, and retinal artery occlusion presented with generalized abdominal pain. Laboratory findings revealed elevated white blood cell count of 25k and lipase 60, with other parameters within normal limits. Computed tomography abdomen showed a splenic abscess, and computed tomography angiography identified thrombosis in the splenic artery and superior mesenteric artery (SMA). Seronegative anti-phospholipid syndrome (SN-APS) was suspected due to recurrent thrombotic events despite initial negative aPL tests. He underwent abscess drainage and received empirical treatment with ceftriaxone and metronidazole. Management involved transitioning from direct oral anticoagulants to Vitamin K Antagonists for SN-APS, highlighting the importance of personalized therapy and ongoing research for optimal patient care. Discussion: The initial clinical diagnosis in this patient was based on a history of multiple thrombotic events, starting with pulmonary emboli, followed by ophthalmological complications, and subsequently a splenic abscess and infarct. Differential diagnoses included thrombophilia, malignancy, and disseminated intravascular coagulation. During hospitalization, aPL testing was initially negative, possibly due to consumption. Over a 6-month follow-up post-discharge, laboratory results remained negative for autoimmune diseases, thrombophilia, and infectious diseases. This case highlights the complexity of diagnosing SN-APS, characterized by recurrent thrombosis including involvement of the splenic and superior mesenteric arteries, and challenges in treatment with direct oral anticoagulants, emphasizing the importance of personalized therapeutic strategies and ongoing clinical monitoring (see Figure 1).

Internal Medicine

Chaudhary A, Shahzil M, Hasan F, Muhammad A, **Jomaa D**, Ejaz A, **Faisal MS**, **Dababneh Y**, **Rodrigues PP**, Khaqan MA, and **Jafri SM**. IMPACT OF CLOSTRIDIOIDES DIFFICILE INFECTION ON OUTCOMES IN LIVER TRANSPLANT RECIPIENTS: A COMPREHENSIVE META-ANALYSIS. *Hepatology* 2024; 80:S1072-S1073. Full Text

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Background: Clostridioides difficile (C. difficile) is a Gram-positive, anaerobic, spore-producing bacillus common in the human gastrointestinal tract. Gastrointestinal dysbiosis, often due to antibiotic use, can lead to severe CDI, a frequent healthcare-associated complication, especially in liver transplant (LT) recipients. LT recipients are at higher risk due to compromised immune defenses and other factors. This meta-analysis aims to understand CDI mortality rates, hospital length of stay, MELD scores, PPI use, and CDI recurrence in LT recipients. Methods: This meta-analysis adhered to Cochrane guidelines and PRISMA standards. A comprehensive search was conducted across PubMed, MEDLINE, Embase, Scopus, and CENTRAL databases until October 2023. Inclusion criteria targeted RCTs and observational studies with LT patients. Data extraction followed PICOS criteria using Excel. Statistical analyses utilized RevMan with a random-effects model, considering results significant at $p < 0.05$. Risk of bias was assessed with the Newcastle- Ottawa Scale, and GRADE considerations determined evidence certainty. Results: Of 2144 screened studies, 10 studies with 1,216,500 LT patients were included: 39,309 with CDI and 1,177,191 without CDI. Primary outcomes assessed were mortality and hospital length of stay (LOS). Mortality showed no significant difference (RR: 1.34; 95% CI: 0.38, 4.72). LOS was significantly longer in CDI patients (mean difference: 6.00 days; 95% CI: 2.83, 9.17). Secondary outcomes included PPI use and MELD scores. PPI use showed no significant association with CDI risk (RR: 2.18; 95% CI: 0.29, 16.27). MELD scores were significantly higher in CDI patients (mean difference: 2.77; 95% CI: 1.34, 4.20). CDI recurrence rate was 14.7%. Risk of bias was assessed with the Newcastle-Ottawa Scale, and evidence quality was evaluated using GRADE, showing moderate quality for most outcomes due to confounding bias and non-randomization. Conclusion: This meta-analysis shows that CDI significantly impacts morbidity and length of hospital stay in liver transplant recipients but does not affect mortality. Patients with CDI had longer hospital stays and higher preoperative MELD scores, highlighting the importance of vigilant postoperative monitoring. Further research is needed to identify specific risk factors and optimize patient outcomes through targeted interventions and preventive measures.

Internal Medicine

Chaudhary AJ, Al-Nabolsi A, Naveed M, Ali A, Iqbal R, Azeem B, Rehan MO, Asim R, Shafique N, **Jafri SM**, and Ashfaque F. Trends in Mortality Due to Pancreatitis Among Patients Aged 55 and Older in the United States: Insights from the CDC WONDER Database. *Am J Gastroenterol* 2024; 119(10):S60-S61. Full Text

A. Al-Nabolsi, Corewell Health Farmington Hills, Dearborn, MI, United States

Introduction: Pancreatitis remains one of the leading causes of death in the elderly in the United States. This study intents to analyze trends and demographic differences in mortality due to pancreatitis among patients aged 55 and older from 1999 to 2020. Methods: We employed a retrospective analysis to calculate age-adjusted mortality rates (AAMRs) per 100,000 persons using data from the CDC WONDER database. Average Annual Percentage Change (AAPC) and Annual Percentage Change (APC) were used to estimate the trends by calendar year, sex, race/ethnicity and geographic region. Results: Between 1999 and 2020, pancreatitis caused 129,208 deaths among older U.S. adults (55+). Most fatalities occurred in medical facilities (68.1%). The overall AAMR for pancreatitis-related deaths decreased from 9.1 in 1999 to 8.2 in 2020, with an AAPC of -0.92 (95% CI: -1.41 to -0.61, P< 0.000001). A moderate decline was seen from 1999 to 2016 (APC: -1.93, P = 0.003199), followed by a sharper increase from 2016 to 2020 (APC: 3.52, P = 0.047590). Stratified by sex, older men had higher AAMRs compared to older women (men: 9.5; women: 6.7). Both genders saw decreased AAMRs, with a slightly more pronounced decrease in women (men: AAPC: -0.91, P< 0.000001; women: AAPC: -1.01, P< 0.000001). Racial disparities were evident, with the highest number of deaths among Whites (78.90%). AAMRs were highest among Black or African Americans, followed by American Indians or Alaska Natives, Whites, Hispanics, and Asians. All racial groups saw variable decreases in AAMRs from 1999 to 2020, with the most pronounced decline in Asians (AAPC: -3.36, P< 0.000001). Geographically, AAMRs varied, highest in West Virginia (12) and lowest in New York (5.9). The Southern region had the highest average mortality (8.5). Nonmetropolitan areas had higher AAMRs than metropolitan areas (9.4 vs 7.6). Both areas saw decreases in AAMRs from 1999 to 2020. Conclusion: This study identifies trends and disparities in pancreatitis mortality among older adults in the US. Despite declining overall rates, differences persist across sex, race/ethnicity, and regions. Targeted interventions and equitable

healthcare access are crucial to reduce mortality and enhance outcomes. Further research is needed to understand and address these disparities effectively. (Figure Presented).

Internal Medicine
Chaudhary AJ, **Khan MZ**, Jaan A, Sohail A, **Jomaa D**, Shahzil M, **Manivannan A**, Asif H, **Saleem A**, **Faisal MS**, **Jamali T**, **Faisal MS**, and **Schairer J**. Outcomes of Needle Knife Stricturotomy (NKSt) and NKSt With Balloon Dilation (NKSt-BD) in Patients With IBD Strictures: A Single Center Experience. *Am J Gastroenterol* 2024; 119(10):S1056. Full Text

A.J. Chaudhary, Henry Ford Health, Detroit, MI, United States

Introduction: In recent years, endoscopic balloon dilatation (BD), and needle knife stricturotomy have emerged as safe and effective options for managing strictures associated with inflammatory bowel disease (IBD). These bowel sparing techniques, individually, have gained popularity and served as an alternative to surgical interventions. In this study, we delve into our tertiary care center's experience with using these techniques simultaneously, to treat IBD related strictures. Methods: A retrospective chart review was performed on patients with Crohn's disease that underwent NKSt alone and NSKt with BD at our tertiary care center between 2018 to 2023. Retrospective demographic, clinical, and procedure-specific information was extracted from the electronic medical record. Patients with strictures related to a disease other than IBD were excluded from the study. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC). Results: In this study involving 50 patients with IBD related fibrotic strictures, 39 (78%) patients underwent NKSt intervention, while 11 (22%) underwent simultaneous NKSt with balloon dilation (NKSt-BD). Patients who underwent NKSt-BD were younger (43.0 ± 10.9 vs 51.2 ± 15.8) and predominantly male (72.7%). (Table 1) NKSt alone was the most common intervention in IBD patients with anastomotic strictures (61.5%) while NKSt-BD was used in 6 patients with anastomotic strictures and 5 patients with non-anastomotic strictures. NKSt-BD was usedmostly for longer strictures (2.76 1.3 cm) and NKSt without BD was used for relatively shorter strictures (1.2 6 1 cm). Bleeding was the most common peri-procedural complication (7.7%) followed by abdominal pain (2.5%) in NKSt group. No complications were observed in the NKSt-BD group. Only 4 patients in the NKSt group developed complications within 10 days of procedure. (Table 1) Symptoms recurred in 9 (23%) patients in NKSt group and 2 (18.1%) patients who underwent NKSt-BD. 15 (38.4%) patients in NKSt group and 7 (63.6%) patients in NKSt-BD had to undergo repeat endoscopy; 1 patient in the NKSt group underwent surgery. Conclusion: Our study demonstrates the clinical and technical success of using NSKt in conjunction with BD compared to NSKt alone. The NSKt-BD group was effective and safer in longer fibrotic strictures, however statistical significance was not achieved likely due to the sample size. More multi-centre studies with larger population size need to be conducted to improve generalizability (see Figure 1).

Internal Medicine
Chaudhary AJ, **Khan MZ**, Naveed M, Jaan A, Iqbal R, Rehan MO, Azeem B, Ali A, Ansari H, Ahmed F, Ullah H, and **Jafri SM**. Trends in Mortality Due to Non-Alcoholic Fatty Liver Disease Among Patients Aged 25 and Older in the United States: Insights from the CDC WONDER Database. *Am J Gastroenterol* 2024; 119(10):S1450-S1451. Full Text

A.J. Chaudhary, Henry Ford Health, Detroit, MI, United States

Introduction: Non-Alcoholic Fatty Liver Disease (NAFLD) is an emerging health concern with increasing mortality rates. This study examines trends and demographic disparities in mortality due to NAFLD among adults aged 25 and older in the United States from 1999 to 2020. Methods: A retrospective analysis was conducted using death data from the CDC WONDER database spanning 1999-2020. Age-adjusted mortality rates (AAMRs) per 100,000 persons were calculated, and trends assessed using Average Annual Percentage Change (AAPC) and Annual Percent Change (APC). Data were stratified by year, sex, race/ethnicity, and geographical regions. Results: Between 1999 and 2020, NAFLD accounted for 71,623 deaths among adults aged 251 in the US Deaths primarily occurred in medical facilities (37.8%) and at decedents' homes (40.9%). The overall AAMR for NAFLD-related deaths increased from 1.1 in 1999 to 3.1 in 2020, with an AAPC of 5.29 (95% CI: 4.80 to 6.04, P < 0.000001). AAMR showed a minor increase from 1999 to 2012 (APC: 1.32, P = 0.150), followed by a striking rise from 2012 to 2020

(APC: 12.07, P < 0.000001). Men exhibited slightly higher AAMRs compared to women (men: 1.6; women: 1.4). The AAMR of women showed a significant increase than men. Racial disparities were evident, with Americans having the highest AAMR (3.7), followed by Hispanics (1.7), Whites (1.6), Blacks (0.9), and Asians (0.6). All racial groups experienced increased AAMRs except Black individuals, who saw a decrease. The increase was most pronounced in Americans (AAPC: 6.08, P < 0.000001).Geographically, AAMRs ranged from 0.8 in Alabama to 2.5 in Oklahoma. The Western region had the highest average AAMR (2.1). Nonmetropolitan areas exhibited higher AAMRs than metropolitan areas (nonmetropolitan: 1.6; metropolitan: 1.5). Conclusion: This study reveals the notable increase in mortality rates due to NAFLD in past 2 decades. Our target population was adult liver disease patients aged 25 and above in the United States. Interestingly, the AAMR has nearly tripled from 1999 to 2020. The results highlights the disparities in race trends and geographic regions. Thus, there is an urgent need for focused interventions which would improve overall health outcomes (Figure 1). .

Internal Medicine

Chaudhary AJ, **Samad M**, **Khan MZ**, Naveed M, Azeem B, Iqbal R, Ali A, Rehan MO, Mohammad T, Ansari H, and Muhibullah F. Trends in Mortality Due to Disorders of Peptic Ulcer Among Patients Aged 55 and Older in the United States: Insights from the CDC WONDER Database. *Am J Gastroenterol* 2024; 119(10):S1660-S1661. Full Text

M. Samad, Henry Ford Hospital, Rochester Hills, MI, United States

Introduction: Peptic ulcer disease remains a significant cause of morbidity and mortality among older adults. This study aims to analyze trends and demographic disparities in mortality due to peptic ulcers among patients aged 55 and older in the United States from 1999 to 2020. Methods: Utilizing data from the Centers for Disease Control and Prevention (CDC) WONDER database, a retrospective analysis was conducted to determine age-adjusted mortality rates (AAMRs) per 100,000 persons. Trends were assessed using average annual percentage change (AAPC) and annual percent change (APC), stratified by year, sex, race/ethnicity, and geographical regions. Results: Between 1999 and 2020, peptic ulcers caused 150,717 deaths among adults aged 55 and older in the US, mostly in medical facilities (66.3%). The overall AAMR decreased significantly from 18.4 in 1999 to 7.7 in 2020, with an AAPC of -4.60 (95% confidence interval [CI]: -5.0 to -4.23, P< 0.000001). Notably, a sharp decline was seen from 1999 to 2009 (APC: -8.53, P< 0.000001), followed by a slower decrease from 2009 to 2020 (APC: -0.86, P5 0.129). Men had slightly higher AAMRs than women (men: 11.3; women: 8.1), with both experiencing decreased rates (men: AAPC: -4.76, P< 0.000001; women: AAPC: -4.16, P< 0.000001). Racially, Whites had the highest AAMR (9.6), followed by Black or African Americans (9.4), Asian or Pacific Islanders (8.9), American Indian or Alaska Natives (8.8), and Hispanic or Latino populations (7.1). All racial groups saw significant declines in AAMRs from 1999 to 2020, with the most substantial decrease in Asian individuals (AAPC: -5.51, P< 0.000001).Geographically, AAMRs varied by state, highest in Vermont (AAMR: 13.6) and lowest in Massachusetts (AAMR: 6.7). The Western region had the highest average AAMR (11.7). Nonmetropolitan areas had slightly higher AAMRs than metropolitan areas throughout, both seeing significant decreases from 1999 to 2020 (Figure 1). Conclusion: This study reveals significant declines in mortality rates due to peptic ulcers among older adults in the United States from 1999 to 2020. However, demographic disparities persist, underscoring the need for targeted interventions and equitable healthcare access to further reduce mortality and improve health outcomes in affected populations. Further research is warranted to explore underlying factors contributing to these disparities and to inform effective public health strategies.

Internal Medicine

Chaudhary AJ, Tepe G, Hafeez N, **Jamali T**, **Khan MZ**, **Adil SA**, and **Ginnebaugh B**. A Rare Case of Colorectal Cancer With Delayed Duodenal Metastasis: A Case Report. *Am J Gastroenterol* 2024; 119(10):S2146-S2147. Full Text

A.J. Chaudhary, Henry Ford Health, Detroit, MI, United States

Introduction: The liver is the most common site of colorectal cancer (CRC) metastasis, followed by the lung, regional lymph nodes, and peritoneum. We present an exceptionally rare case of CRC

metastasizing to the duodenum in a patient with a history of resolved stage IV-A ileocecal adenocarcinoma and previous liver metastasis, who had been adherent to post-surgical surveillance. Case Description/Methods: A 42-year-old woman presented with a 2-week history of persistent fatigue, shortness of breath, presyncope, and hematochezia. Her medical history was notable for stage IV-A ileocecal adenocarcinoma with liver metastasis, for which she had undergone a right hemicolectomy and partial hepatectomy, both with negative margins for dysplasia and adenocarcinoma. Subsequent surveillance, including annual carcinoembryonic antigen (CEA) levels and computed tomography (CT) scans, consistently showed no evidence of disease recurrence. However, during the current presentation, the patient exhibited a hemoglobin level of 5.9 g/dL, necessitating a transfusion of 2 units of blood. A CT scan of the abdomen and pelvis with intravenous contrast revealed a central mesenteric mass, measuring up to 3 cm in long axis dimension. This mass invaded the duodenum, encased the superior mesenteric artery, abutted the superior mesenteric vein, and displayed a new 8 mm lesion in the peripheral hepatic segment 5/8. Notably, CEA levels were elevated at 11.1 ng/mL, down from 13.1 ng/mL a year prior. An esophagogastroduodenoscopy revealed a 3 cm fungating mass in the second part of the duodenum, raising concerns for carcinoma. Biopsies confirmed the presence of invasive adenocarcinoma originating from the colon and metastasizing to the duodenum. Subsequent colonoscopy identified diverticulosis, non bleeding hemorrhoids, and ulcers in the colon. The case was presented to the tumor board, which collectively determined that the patient was not a candidate for surgical resection due to vascular involvement, and palliative care was consulted given the poor prognosis. Discussion: Among CRC patients, the most common cause of death is disease recurrence and metastasis. Despite adhering to current guidelines, our patient developed recurrent metastatic disease in both the colon and duodenum. Further evaluation and possible modification in the guidelines for perioperative surveillance of high-risk patients can help to anticipate disease recurrence and improve health outcomes, particularly as it relates to less common CRC metastatic sites.

Internal Medicine

Chaudhary AJ, Tepe G, **Jamali T**, **Zarrar Khan M**, Shahzil M, **Saleem A**, **Faisal MS**, and **Russell S**. Unique Endoscopic Variations of Asymptomatic Segmental Colitis Associated with Diverticulosis (SCAD): A Case Report. *Am J Gastroenterol* 2024; 119(10):S2388-S2389. Full Text

A.J. Chaudhary, Henry Ford Health, Detroit, MI, United States

Introduction: Segmental colitis associated with diverticulosis (SCAD) is a rare condition characterized by segmental circumferential thickening of the colonic wall, particularly in the sigmoid region, alongside colonic diverticulosis. We present a unique case of asymptomatic SCAD in a 69-year-old man with a significant history of peripheral artery disease (PAD), who exhibited distinctive SCAD findings on colonoscopy. Case Description/Methods: A 69-year-old man patient with an extensive history of PAD requiring multiple vascular stents and right femoral endarterectomy presented with acute right-sided leg pain. Computed tomography angiography was obtained which revealed bilateral superficial femoral artery occlusion and an incidental diffuse sigmoid wall thickening. On review of systems the patient denied any diarrhea, constipation, nausea, vomiting, or hematochezia. Physical exam findings were unremarkable, with no abdominal pain, tenderness, or distension. Despite the patient's benign presentation, given his significant vascular history and concurrent Computed tomography findings colonoscopy was performed to explore potential etiologies such as ischemia or malignancy. Colonoscopy identified multiple diverticula and polypoid lesions, without significant ulceration or inflammation in the sigmoid colon, located between 25 and 30 cm proximal to the anus. This unique endoscopic variation of SCAD has not been reported in existing literature (Figure 1A, B, C, D). Notably, the patient was asymptomatic, differing from typical SCAD presentations. Histopathology was further obtained 30 cm proximal to the anus which revealed colonic mucosa with reactive changes and no evidence of active inflammation, dysplasia, or carcinoma. Ultimately, given the patient's asymptomatic nature, active treatment was deferred and follow-up colonoscopy was scheduled in 3 years. Discussion: The presentation of SCAD is diverse; in this case, our patient was asymptomatic and exhibited atypical findings on endoscopy. Most SCAD cases follow 1 of 4 patterns-A, B, C, or D-but our patient presented outside these typical endoscopic patterns. In addition, our patient denied any history of typical SCAD symptoms including chronic intermittent abdominal pain, non-bloody diarrhea, and hematochezia. By sharing this case, we contribute to the collective knowledge base, enhancing our understanding of atypical presentations in gastrointestinal pathology, particularly SCAD.

Internal Medicine
Dawod S, **Ali SA**, **Khalil N**, **Betcher S**, **Xiong T**, and **Mullins K**. Unexpected Visitors: A Primary Esophageal Melanoma. *Am J Gastroenterol* 2024; 119(10):S2274-S2275. Full Text

S. Dawod, Henry Ford Health, Detroit, MI, United States

Introduction: Melanoma, a malignancy arising from melanocytes, is predominantly associated with the skin, yet its occurrence in extracutaneous sites such as the esophagus is rare, constituting less than 1% of esophageal malignancies. As of 2021, only 347 cases have been reported in the literature. Endoscopically, esophageal melanoma presents with varied appearances, from pigmented spots and patches to amelanotic masses, posing challenges in differentiation from other esophageal tumors. We present a case of primary esophageal melanoma in an 81-year old patient. Case Description/Methods: Our patient is an 81-year-old man with history of metabolic syndrome, esophagitis, and cryptogenic cirrhosis. He presented to the office for evaluation of difficulty swallowing of 3 weeks duration. He denied heartburn, regurgitation, or weight loss. He endorsed preceding cough and fatigue for months prior as well. He was not on any acid suppression therapy. His last esophagogastroduodenoscopy (EGD) was 2 years prior, and was only remarkable for grade I esophageal varices, as well LA grade A esophagitis. His physical exam was unremarkable. He underwent an esophagogastroduodenoscopy (EGD) which showed a large fungating mass that was partially obstructing and partially circumferential, at the level of the middle esophagus. (Figure 1) The mass was sampled, and was consistent with a malignant melanoma. He subsequently underwent full body imaging with PET-CT which was remarkable for paraesophageal lymphadenopathy. (Figure 1) Dermatologic exam was normal. Brain MRI ruled out intracranial metastasis. The patient was referred to oncology and was initiated on immunotherapy. Discussion: Our case highlights a rare instance of esophageal melanoma. Presenting symptoms, such as difficulty swallowing in our 81-year-old patient, often mimic more common esophageal conditions, emphasizing the diagnostic challenges. Esophageal melanomas tend to be aggressive, as evident by his normal EGD 2 years prior, with a high risk for metastasis. Therapeutic options for esophageal melanoma remain challenging due to its rarity, with surgery being a cornerstone, often complemented by immunotherapies. However, the absence of standardized treatment guidelines accentuates the need for ongoing research to establish optimal therapeutic strategies. Its rarity calls for a multidisciplinary approach involving gastroenterologists, oncologists, surgeons, dermatologists and pathologists in forming personalized treatment plans for optimal patient outcomes.

Internal Medicine
Dawod S, Dawod Q, Smith E, Crawford CV, and Zarnegar R. A Life-Threatening GI Bleed Secondary to Duodenal GIST Requiring Urgent Surgical Resection. *Am J Gastroenterol* 2024; 119(10):S3082-S3083. Full Text

S. Dawod, Henry Ford Health, Detroit, MI, United States

Introduction: Gastrointestinal stromal tumors (GISTs) are rare primary gastrointestinal neoplasms that can develop anywhere along the gastrointestinal (GI) tract. Presentation varies by location but can range from asymptomatic, to local obstructive symptoms and bleeding. They can form anywhere along the GI tract. Duodenal GIST is relatively rare when compared to other sites. We showcase a patient presenting with a life-threatening bleed secondary to duodenal GIST requiring surgical resection. Case Description/Methods: A 64-year-old woman patient with a past medical history of type 2 diabetes mellitus and gastro-esophageal reflux disease presented with 3 days of melenic stools, bilious emesis and left-sided abdominal pain. On exam, she was tachycardic and normotensive with tenderness to palpation in the left lower quadrant. Initial investigations revealed a hemoglobin 5.5 g/dl. She was resuscitated and a Computed tomography angiography revealed active contrast intraluminal extravasation within the 3rd portion of duodenum with a mass-like collection of hyperattenuating material suggesting a intraluminal hematoma (Figure 1). The patient thereafter underwent an esophagoduodenoscopy which showed a large, superficially ulcerated submucosal mass with a visible vessel in the third portion of the duodenum not actively bleeding. No intervention was performed due to close proximity to the ampulla. The endoscopic appearance was consistent with GIST. Surgery was consulted due to inability to biopsy the

lesion and ensure adequate control of bleeding, and the patient underwent an open duodenal resection. The mass was measured at 3.9 x 2.1 x 1.7 cm. No lymphadenopathy was noted intra-operatively. Pathology confirmed a low-grade GIST with clean margins. Discussion: Duodenal GISTs comprise up to 5% of all GIST occurrences, with the literature suggesting that bleeding as initial presentation carries a non-favorable prognosis. Our case highlights a rare cause of life-threatening upper GI bleeding secondary to duodenal GIST requiring urgent surgical resection for definitive management. While GI bleeding is a common presentation among patients with GIST, our patient had profound bleeding with severe anemia and an initial computed tomography with concerns for hematoma. This proves the value of early endoscopic evaluation in order to both achieve hemostasis and identify the etiology of the suspected bleed. In addition, the importance of a systematic and multi-disciplinary decision making among patients with GIST is imperative.

Internal Medicine

Dunn W, Alkhouri N, Yip TCF, Castera L, Takawy M, Adams L, Verma N, Arab JP, **Jafri SM**, Zhong B, Dubourg J, Chen V, Singal A, Díaz LA, Dunn N, Nadeem R, Wong V, Abdelmalek M, Wang Z, Duseja A, Almahanna Y, **Omeish H**, Ye J, Harrison S, Arrese M, Robert S, Wong GLH, Bajunayd B, and Shao C. ENHANCING PREDICTION OF MODERATE FIBROSIS OR HIGHER IN MASLD PATIENTS FOR RESMETIROM TREATMENT VIA MACHINE LEARNING. *Hepatology* 2024; 80:S553-S555. Full Text

W. Dunn, University of Kansas Medical Center, Rochester, United States

Background: The recent FDA approval of Resmetirom for treating Metabolic Dysfunction-Associated Steatohepatitis (MASLD) in patients with moderate to advanced fibrosis necessitates precise patient selection for liver biopsy. Currently, a Vibration-controlled Transient Elastography (VCTE) based algorithm FAST is utilized to diagnose at-risk MASH (≥ F2 + NAS 4). However, no existing VCTE-based algorithm effectively targets moderate fibrosis or higher (≥F2) alone. The mAchine Learning ADvanceD fibrosis and at-risk mash Novel predictor (ALADDIN) study addresses this gap by introducing a novel machine learning-based web calculator that estimates the likelihood of moderate fibrosis using routine laboratory parameters with and without VCTE measurements. Methods: A total of 3708 patients with biopsy-confirmed MASLD from six centers worldwide were divided into Training and Test Set on a 1:1 basis, supplemented by 1289 patients from nine centers for External Validation. ALADDIN models, employing Random Forest, Gradient Boosting Machines, and XGBoost enhanced by Bayesian updates, were developed to evaluate moderate fibrosis (stage ≥ F2). Results: In the Test Set, the ALADDINF2-VCTE model demonstrated an Area Under the Curve (AUC) of 0.789 (95% CI 0.767-0.810), significantly outperforming the FAST model (AUC: 0.663, 95% CI 0.637-0.689, p <0.0001). In the External Validation Set, this model maintained an AUC of 0.796 (95% CI 0.769-0.823), again outperforming FAST (AUC: 0.705, 95% CI 0.673-0.737, p < 0.0001). The ALADDIN-F2-Lab model, which employs routine laboratory parameters without VCTE, achieved an AUC of 0.762 (95% CI 0.741-0.784) in the Test Set and 0.735 (95% CI 0.708-0.762) in the External Validation Set. The 95% CI for the difference in AUCs was 0.075 to 0.129 in the Test Set and -0.014 to 0.061 in the External Validation Set. It did not exceed the preset noninferiority margin Δ of -0.1. Furthermore, the ALADDIN-F2-VCTE model demonstrated superior calibration, decision curve analysis, and classification accuracy using a dual cut-off approach compared to the FAST model. Conclusion: The VCTE-based ALADDIN-F2-VCTE model, accessible through ALADDIN1, has demonstrated superior performance compared to established VCTEbased indices, FAST, for diagnosing moderate fibrosis or higher. As the only model specifically developed to target moderate fibrosis or higher using VCTE, ALADDIN-F2-VCTE uniquely supports the refined selection of patients, potentially reducing the necessity for liver biopsies and allowing more patients to receive appropriate treatment with Resmetirom. Additionally, the ALADDIN-F2-Lab model, employing routine laboratory parameters without VCTE, accessible through https://aihepatology.shinyapps.io/ ALADDIN2/, offers an effective alternative when VCTE is unavailable, facilitating broader application in clinical practice. (Figure Presented).

Internal Medicine

Elfert K, Ismail A, **Abusuliman M**, Abosheaishaa H, Nassar M, Salem AE, Aloum K, and Elhanafi SE. Safety of Esophageal Dilation Procedures in Patients on Antithrombotic Therapy: A US Collaborative Network Cohort Study. *Am J Gastroenterol* 2024; 119(10):S433. Full Text

K. Elfert, West Virginia University, Morgantown, WV, United States

Introduction: Esophageal dilation procedures, such as balloon dilation, pneumatic dilation, and Savary dilation, are frequently performed on patients prescribed antithrombotic medications. This study aimed to assess the safety of these procedures in patients on anticoagulation (AC) and dual antiplatelet medications (DAPT) using a US-based multi-institutional database. Methods: The study cohorts were identified using the TriNetX US Collaborative Network database based on the CPT codes for esophageal balloon, pneumatic, and Savary dilation. Patients undergoing these procedures on uninterrupted AC were compared to those who did not receive any AC for at least one week prior to the procedure. Furthermore, patients undergoing these procedures on uninterrupted DAPT were compared to a control group of patients who did not receive any anti-platelets for at least one week prior to the procedure and also to patients on aspirin only. Propensity score matching (1:1) was conducted based on demographics and comorbidities. The primary outcome was post-procedural gastrointestinal bleeding within 30 days of the procedure. Results: A total of 1,465 patients were identified in AC group and a total of 538 patients in DAPT group. After propensity score matching, the incidence of post-procedural bleeding in the esophageal balloon dilation procedures with AC was higher compared to patients who were not on AC one week before the procedure (3.55% vs. 1.67%, RR (95%CI): 2.1(1.3-3.4), P 0.0016). Similar results were observed with subgroups analysis of balloon, pneumatic, and Savary dilation (Table 1). The incidence of post-procedural bleeding in the esophageal dilation group on DAPT was not significantly different from the incidence in the no antiplatelet control group (3.41% vs. 2.46%, RR (95% CI): 1.4 (0.7-2.8), P 0.36). Additionally, there was no significant difference in the risk of post-procedural bleeding between DAPT and the aspirin group (3.43% vs. 2.29%, RR (95%CI): 1.5 (0.7-3.0), P 0.27). Further subgroup analysis based on dilation modality showed no significant difference in rate of post-dilation bleeding (Table 2). Conclusion: In this multi-institutional cohort study, the incidence of post-esophageal dilation bleeding was significantly higher in patients on anticoagulants. However, this was not noted in patients on DAPT compared to control groups regardless of the dilation modality.

Internal Medicine

Faisal MS, **Chaudhary AJ**, **Saleem A**, **Abusuliman M**, **Kostecki P**, **Ahmad Adil S**, **Faisal MS**, **Yudovich A**, and **Entz A**. Esophagitis and Melena: A Rare Presentation of Stevens-Johnson Syndrome. *Am J Gastroenterol* 2024; 119(10):S2463-S2464. Full Text

M.S. Faisal, Henry Ford Health, Detroit, MI, United States

Introduction: Esophageal involvement in Stevens-Johnson syndrome (SJS) is relatively rare but can occur. It may manifest as focal ulcerations or diffuse esophagitis, potentially leading to bleeding and melena in severe cases. We present a case of a patient who presented with severe esophagitis and gastrointestinal bleeding as the presenting symptom of SJS. Case Description/Methods: A 67-Year-old-man presented to the emergency department with confusion, agitation and productive cough. These symptoms had progressively worsened over a week. He had no relevant past medical history. On initial presentation, he was found to be febrile, tachypneic and tachycardic. Chest X-Ray was concerning for lobar pneumonia and the patient was started on Vancomycin and Cefepime for hospital-acquired-pneumonia. On day 7 of admission, the patient had 3 melenic stools with a Hemoglobin drop from 8.4 g/dl to 6.7 g/dl within 24 hours. The patient was transfused with 2 units of packed RBCs and underwent an Esophagogastroduodenoscopy (EGD) for evaluation. EGD findings included severe esophagitis with stigmata of recent bleeding, 1 gastric ulcer with mild oozing and 2 duodenal ulcers. Patient was started on Intravenous Pantoprazole and Carafate. Over the next 2 days, the patient had continued melena and drops in Hemoglobin requiring frequent blood transfusions, along with sloughing of skin in the groin and oral mucosa. SJS with oral and esophageal involvement was suspected and the patient was started on IV steroids. Antibiotics were discontinued considering they could be the offending agent. A cutaneous biopsy confirmed SJS. The patient passed away 3 days after the EGD due to complications of the disease Discussion: Esophagitis and Gastrointestinal bleeding have a wide range of differential diagnosis, including Gastroesophageal reflux disease, Peptic ulcer disease and esophageal varices. Although typically recognized for its cutaneous manifestations, SJS can also present with gastrointestinal complications which can precede cutaneous symptoms. Esophageal manifestations of SJS include

ulceration, esophagitis, strictures and potentially melena. Management focuses on supportive care and withdrawal of causative agents. Early recognition of SJS in such presentations is crucial for improved outcomes. This case highlights the need for heightened awareness among clinicians to consider SJS in differential diagnoses of unexplained melena, despite its rarity in causing gastrointestinal bleeding. (Figure Presented).

Internal Medicine
Faisal MS, Fatima M, **Saleem A**, **Chaudhary AJ**, Shahzil M, **Abusuliman M**, **Faisal MS**, and **Jafri SM**. Association of Glucagon-Like Peptide-1 Therapies and Risk of Cancer in Liver Transplant Patients. *Am J Gastroenterol* 2024; 119(10):S1368. Full Text

M.S. Faisal, Henry Ford Health, Detroit, MI, United States

Introduction: Patients who undergo liver transplantation are at higher risk of complications from diabetes and obesity. Glucagon-like peptide-1(GLP-1) analogues have revolutionized management of these conditions and are increasingly being used in post-transplant patients. However, the safety of these agents in this population, particularly their association with cancer risk, is controversial. We aimed to assess the association of semaglutide and tirzepatide with cancer in patients who undergo liver transplant. Methods: All patients who underwent liver transplant at our institution were included from 2018-2023. We did a retrospective cohort study to assess whether they received GLP-1 analogues, including semaglutide and tirzepatide, before and after liver transplant. Data including patient demographics, comorbidities and exposure was collected. Primary outcome was development of malignancy. Secondary outcomes were 1-and 3-year mortality. Results: Overall, 366 patients underwent liver transplant from 2018-2023. Of these, 42(13%) were exposed to semaglutide or tirzepatide while 324(88%) had no such exposure after transplant. No patients were exposed before transplant. The mean age was 58.12 +/- 7.6 in the exposed group and 58.44 +/- 11.5 in the control group. 14(33.6%) were female in the exposed group while (119) 36.7% were female in the control group. 37(88.1%) in the exposed group had diabetes while 111(34.2%) in the control group had diabetes(P<0.001). Similarly, 28(66.7%) patients in the exposed group had BMI >30 while 111(34.5%) patients in the control group had BMI >30(P<0.001). Follow up period was 3.74 +/-1.3 years 4.01 +/-1.5 years in the exposed and control groups respectively. In this period, 2(4.8%) patients in the exposed group were diagnosed with cancer versus 26(8.1%) in the control group (P=0.76). There was no cancer related mortality at 1 year while at 3 years, it was similar in both groups. For malignancies, 1(50%) patient in the exposed group had HCC, while 5(18%) patients in the control group had either HCC or CCA. No patient in the exposed group was diagnosed with skin malignancies, while 13(46%) patients in the control group were diagnosed with such malignancies. 11 in the control group were diagnosed with other malignancies including lymphoma, follicular thyroid cancer, and leukemia. Conclusion: The use of semaglutide and tirzepatide was not associated with cancer in patients who undergo liver transplantation. We were limited by single center and smaller number of patients (see Table 1).

Internal Medicine
Faisal MS, **Obri M**, **Faisal MS**, **Nimri F**, **Dawod S**, **Youssef RM**, **Chaudhary AJ**, **Alluri S**, **Dang D**, **Watson A**, **Elatrache M**, **Singla S**, **Piraka C**, **Pompa R**, and **Zuchelli T**. Utility of Imaging in Predicting Biliary Strictures Post Liver Transplant. *Am J Gastroenterol* 2024; 119(10):S107-S108. Full Text

M.S. Faisal, Henry Ford Health, Detroit, MI, United States

Introduction: Post liver transplant biliary strictures are a common complication following orthotropic liver transplantation. ERCP with stenting is the standard of care for management of these strictures. However, ERCP carries risks of infection, bleeding and pancreatitis. Therefore, confirming strictures on imaging can prevent unnecessary procedures. We aimed to assess the accuracy of MRI/MRCP and CT prior to ERCP in predicting biliary strictures. Methods: All patients who had ERCP post-transplant for biliary strictures were included in the study from 2015-2022. We then retrospectively assessed whether they had MRI/MRCP or CT prior to ERCP to look for a biliary stricture. If imaging was obtained, we assessed whether it was suspicious for biliary stricture as characterized by focal narrowing and upstream biliary dilation. We assessed the factors that were associated with either a positive or a negative image prior to

ERCP. Results: Eighty-nine patients were confirmed to have a post-transplant anastomotic biliary stricture on ERCP during this time. The mean age of the population was 59.74 +/- 10.8 years. Thirty-3 (37.1%) were female and 73% were White 73%. Median days post-transplant for initial ERCP was 68 (IQR 30-175). Stenting was done for 98.9% of the patients. Initial stenting was done by plastic stents in 91.0%. There was documented removal of stone and sludge in 64.0% of the cases. Main complications encountered were post ERCP pancreatitis in 5.6% and cholangitis 4.5%. MRCP was done prior to ERCP in 44 (49.4%) of cases and it was definitive for a stricture in 33 cases (75%). CT was done prior to ERCP in 27 (30.3%) of cases. It was definitive for a stricture in 9 patients (33.3%). 83 (93.3) had recurrent strictures after initial ERCP requiring further stenting. Median number of procedures following initial stenting was 1 (Range 1-7). Patients who had MRCP diagnostic for stricture had the test done further from transplant median 110 (IQR 47-221) days, compared median 64 (IQR 30-200) days post transplant in patients who had MRCP negative for a stricture (P=0.09) possibly indicating improved accuracy of MRCP further away from transplant. Conclusion: ERCP with stenting is the standard of care for post-transplant biliary strictures. While CT does not appear to be accurate in diagnosing post-transplant biliary strictures, MRCP prior to ERCP can be a safe and effective noninvasive test to define anatomy and confirm a stricture (Figure Presented).

Internal Medicine

Faisal MS, **Saleem A**, **Chaudhary A**, Fatima M, Shahzil M, **Abusuliman M**, **Faisal MS**, and **Jafri SM**. NO INITIAL INCREASE IN CANCER RISK WITH GLUCAGON LIKE PEPTIDE-1 THERAPIES FOLLOWING LIVER TRANSPLANTATION. *Hepatology* 2024; 80:S1050-S1051. Full Text

M.S. Faisal, Henry Ford Hospital, Detroit, MI, United States

Background: Patients who undergo liver transplantation are at higher risk of complications from diabetes and obesity. Recently, Glucagon-like peptide-1(GLP-1) analogues have revolutionized management of these conditions and are increasingly being used in post-transplant patients. However, the safety of these agents in this population, particularly their association with cancer risk, is controversial. We aimed to assess the association of semaglutide and tirzepatide with cancer in patients who undergo liver transplant. Methods: All patients who underwent liver transplant at our institution were included from 1/2018-12/2023. We did a retrospective cohort study to assess whether they received GLP-1 analogues, including semaglutide and tirzepatide, after the liver transplant. Data including patient demographics, comorbidities and exposure to semaglutide or tirzepatide were collected. Primary outcome was development of malignancy. Secondary outcomes were 1-and 3-year mortality. Results: 366 patients were included who underwent liver transplant from 01/2018-12/2023. Of these, 42 (13%) were exposed to semaglutide or tirzepatide while 324 (88%) had no such exposure. The mean age of the population was 58.12 +/- 7.6 in the exposed group and 58.44 +/- 11.5 in the control group. 14(33.6%) were female in the exposed group while (119) 36.7% were female in the control group. Comorbidities, including HTN, stroke and ESRD were comparable in both groups. 37(88.1%) in the exposed group had diabetes while 111(34.2%) in the control group had diabetes($p<0.001$). Similarly, 28(66.7%) patients in the exposed group had BMI>30 while 111(34.5%) patients in the control group had BMI>30($p<0.001$). The follow up period was 3.74 +/-1.3 years for the exposed group and 4.01 +/-1.5 years in the control group. For outcomes, 2(4.8%) patients in the exposed group were diagnosed with cancer in the follow up period versus 26(8.1%) in the control group ($p=0.76$). There was no cancer related mortality at one year while at 3 years, it was similar in both groups. For malignancies, 1(50%) patient in the exposed group had HCC, while 5(18%) patients in the control group had either HCC or cholangiocarcinoma. No patients in the exposed group were diagnosed with skin related malignancies including BCC, SCC and Malignant Melanoma, while 13 (46%) patients in the control group were diagnosed with such malignancies. 1 patient in the exposed group was diagnosed with Post Transplant Lymphoproliferative Disorder. 11 patients in the control group were diagnosed with other malignancies including prostate cancer, lymphoma, follicular thyroid cancer, and leukemia. Conclusion: In our cohort, the use of semaglutide and tirzepatide was not associated with cancer in patients who undergo liver transplantation. We were limited by single center and smaller number of patients. Further large scale, multicenter studies are needed to confirm the safety of these medications.

Internal Medicine

Fatima M, Shahzil M, **Faisal MS**, Khalid A, Munir L, Qureshi AA, Rehmani M, **Javaid Chaudhary A**, Ali Khaqan M, and **Faisal MS**. Trends and Disparities in Chronic Hepatitis-Related Mortality in the United States, 1999-2020: An Epidemiological Analysis. *Am J Gastroenterol* 2024; 119(10):S1227. Full Text

M. Fatima, King Edward Medical University, Punjab, Lahore, Pakistan

Introduction: Chronic hepatitis caused 1.1 million deaths in 2019 and 1.3 million in 2022 according to World Health Organization. These results underline the impact of behavioral, environmental and cultural factors despite available testing and treatment. This study analyzes trends in chronic hepatitis-related mortality from 1999 to 2020, using age-adjusted mortality rates (AAMR) to identify patterns across demographic and regional populations. Methods: Data from Centers for Disease Control Wonder database, examining chronic hepatitis-related death trends from 01/1999 to 12/2020, using International Classification of Diseases-10 code K73.0., was collected. AAMRs per 100,000 population and average annual percentage change (AAPC) were calculated. Annual percentage change (APC) with 95% Confidence Interval (CI) was assessed to understand AAMR trends. Mortality rates were standardized to the 2000 United States Population and Joinpoint was used for regression analysis across various demographics. Age trends were studied in pediatric, young adults, middle adults, and older adults groups. The Monte Carlo Permutation Procedure (MCPP) analyzed mortality trends. Statistically significant results were determined with a P-value < 0.05. Results: From 1999 to 2020, there were 8,862 chronic hepatitis B related deaths. Mortality declined, with age-adjusted rates (AAR) showing a consistent decrease. The APC was -2.46 from 1999-2002, -31.0 from 2002-2005, and -2.86 from 2005-2020. A significant decrease was seen in Northeast and Midwest. Females experienced a steeper decline from 2002-2005 (APC: -41.39, P=0.003883, CI [-57.94, -18.32]), while males declined from 2001-2007 (APC: -13.23, P=0.000405, CI [-17.99, -8.20]). Black individuals had higher mortality with a significant decrease until 2007 (APC: -17.90, P=0.000019, CI [-23.53, -11.85]), while White individuals saw declines from 2002-2005 (APC: -31.16, P=0.006319, CI [-46.37, -11.64]). Urban areas showed significant drops from 2002-2005 (APC: -31.10, P=0.009090, CI [-47.09, -10.27]). High mortality was seen in the 65-74-year group before 2002 but evened out across age groups afterward (Figure 1). Conclusion: This study reveals a decline in chronic hepatitis-related mortality from 1999 to 2020 with disparities across gender, race, and regions. Females and Black individuals experienced higher but decreasing mortality rates and urban areas saw substantial drops, especially from 2002 to 2005. Even then, high mortality persisted in the 65-74 age group before 2002. Targeted public health interventions are essential to address these disparities and disease burden. (Table Presented).

Internal Medicine

Jaan A, **Chaudhary AJ**, Dhawan A, Farooq U, Fatima Sheikh L, and Thor S. Superiority of Frailty Over Age in Predicting Outcomes Among Clostridium difficile Patients: Evidence From National Data. *Am J Gastroenterol* 2024; 119(10):S180-S181. Full Text

A. Jaan, Rochester General Hospital, Rochester, NY, United States

Introduction: Clostridioides difficile infection (CDI) is a growing healthcare concern characterized by rising trends in morbidity and mortality in the United States and Europe. Consequently, there is a growing imperative to prioritize prevention and control measures. While frailty has been linked to poor outcomes in general, its implications in patients with CDI are yet to be comprehensively investigated. This study aims to bridge this gap by conducting a nationwide analysis. Methods: Using the National Readmission Database from 2016 to 2020, we employed the International Classification of Diseases, 10th revision, Clinical Modifications (ICD-10-CM) codes to identify adult patients (age >18 years) admitted with CDI. We further stratified CDI hospitalizations based on the presence of frailty. Utilizing a multivariate regression model, we assessed the impact of frailty on CDI outcomes. STATA 14.2 was utilized for statistical analysis. Results: We included 144,611 adult patients with CDI, of whom 98,167 (67.88%) were frail (Table 1). After adjusting for confounding variables, in-hospital mortality due to CDI was significantly higher in frail patients (adjusted odds ratio [aOR] 4.87). Additionally, frail patients had higher odds of AKI requiring dialysis (aOR 9.50), septic shock (aOR 14.23), and intensive care unit admission (aOR 6.80). Complications specific to CDI were also found to have elevated odds in frail patients, such as paralytic

ileus (aOR 1.64), toxic megacolon (aOR 10.22), intestinal perforation (aOR 2.30), and severe disease requiring colectomy (aOR 3.90). CDI recurrence also had higher odds in frail patients (aOR 3.65). Finally, resource utilization estimated by total parenteral nutrition requirement, total hospitalization charges, length of stay, rehabilitation discharge, and 30-day readmission rates was also higher among frail patients (Table 1, Figure 1). When adjusted for frailty, age (cut-off ≥65) was minimally predictive of mortality and did not predict intensive care unit admission, toxic megacolon, colectomy or CDI recurrence. Conclusion: Our study underscores the significant association between frailty and various critical endpoints of CDI, including its incidence, inpatient mortality, severity and CDI recurrence. Additionally, frailty emerged as an independent predictor of resource utilization. Recognizing frailty as a determinant of CDI outcomes can aid clinicians in risk stratification for this population. (Table Presented).

Internal Medicine

Jaan A, Dhawan A, **Chaudhary AJ**, Hafeez N, Nepal M, Fatima Sheikh L, McFarland M, and Dunnigan K. Morbidity of Clostridioides difficile in Necrotizing Pancreatitis: Insights from National Data. *Am J Gastroenterol* 2024; 119(10):S39-S40. Full Text

A. Jaan, Rochester General Hospital, Rochester, NY, United States

Introduction: Necrotizing pancreatitis (NP) is a severe and life-threatening form of acute pancreatitis and is frequently associated with organ dysfunction, necessitating intensive care management. The presence of Clostridioides difficile infection (CDI), a common nosocomial infection, can further complicate the clinical course of NP by exacerbating gastrointestinal symptoms and increasing the risk of sepsis. This study aims to analyze the prevalence and outcomes in NP patients with a concurrent CDI. Methods: Using the National Readmission Database 2016-2020, we employed the International Classification of Diseases, 10th revision, Clinical Modifications (ICD-10-CM) codes to identify adult patients (age >18 years) admitted with NP. We further stratified NP hospitalizations based on the presence of CDI. Utilizing a multivariate regression model, we compared the outcomes of NP in patients with CDI. STATA 14.2 was utilized for statistical analysis. Results: We included 68,839 NP patients, of whom 1,217 (1.77%) had CDI. Adjusted analysis showed significantly higher odds of mortality (adjusted odds ratio [aOR]:2.99, P< 0.001), septic shock (aOR:4.94, P< 0.01), acute kidney injury requiring dialysis (AKId) (aOR:2.31, P< 0.001) and ICU admission (aOR:3.53, P< 0.001) in NP patients with CDI (Table 1). Pancreatitis-specific complications such as pancreatic pseudocyst, portal vein thrombosis, and infection of necrosis requiring necrosectomy were also higher in patients with a CDI. Moreover, NP patients with CDI also had higher odds of developing abdominal compartment syndrome, a rare life-threatening complication. Conclusion: The presence of CDI in patients with NP is associated with higher rates of pancreatitis-specific complications and significantly worse hospitalization outcomes. These findings underscore the importance of vigilant monitoring and proactive management of CDI in NP patients to improve outcomes and reduce the healthcare burden. (Table Presented).

Internal Medicine

Jaan A, Dhawan A, **Chaudhary AJ**, Shahnoor S, Hafeez N, Sheikh LF, and Ahlawat S. Abdominal Compartment Syndrome in Decompensated Cirrhosis: Findings from a National Cohort. *Am J Gastroenterol* 2024; 119(10):S1259. Full Text

A. Jaan, Rochester General Hospital, Rochester, NY, United States

Introduction: Abdominal compartment syndrome (ACS), caused by increased intra-abdominal pressure resulting in compromised organ function, is a serious complication in critically ill patients and is associated with increased morbidity and mortality. This study aims to analyze the prevalence, outcomes and predictors of ACS in hospitalizations for decompensated cirrhosis. Methods: Using the National Readmission Database 2016-2020, we employed the International Classification of Diseases, 10th revision, Clinical Modifications (ICD-10-CM) codes to identify adult patients (age .18 years) admitted with decompensated cirrhosis (DC). We further stratified DC hospitalizations based on the presence of ACS. Utilizing a multivariate regression model, we compared the outcomes of DC in patients with ACS and determined predictors of ACS. STATA 14.2 was utilized for statistical analysis. Results: We included 618,696 DC patients, of whom 838 (0.14%) patients had ACS. After adjusting for confounding variables,

we found significantly higher odds of mortality (adjusted odds ratio [aOR]:18.62, P<0.001), septic shock (aOR: 9.28, P<0.001), vasopressor requirement (aOR:10.03, P<0.001), mechanical ventilation (aOR:14.20, P<0.001) in cirrhotic patients with ACS (Table 1). Additionally, liver-specific complications such as upper gastrointestinal bleeding (aOR: 2.34, P<0.001), hepatorenal syndrome (aOR: 5.16, P<0.001), and spontaneous bacterial peritonitis (aOR: 2.58, P<0.001) had elevated odds in the ACS group. Further, using multivariate logistic regression analysis, we determined predictors of ACS in DC patients. North American Consortium for the Study of End-Stage Liver Disease (NACSELD)-ACLF score ≥2 (aOR: 12.06), malignancy (aOR: 1.86), chronic kidney disease (aOR: 1.71), blood transfusion (aOR: 1.68), active infection (aOR: 1.56), hyponatremia (aOR: 1.51), and coagulopathy (aOR: 1.37) were predictive of ACS development in DC patients (Figure 1). Conclusion: ACS in cirrhotic patients is associated with significantly worse hospitalization outcomes as well as higher rates of liver-specific complications. Early identification and prompt management of this vulnerable patient cohort are imperative to enhance clinical outcomes. Further research is warranted to better understand the underlying mechanisms and refine clinical approaches for optimal care.

Internal Medicine

Jaan A, Dhawan A, Hafeez N, **Chaudhary AJ**, Sheikh LF, Fredua S, Gopep N, Bkhet A, Shahnoor S, and Farooq U. Palliative Care in Alcoholic Hepatitis: A Nationwide Study of Predictors, Readmission, and Overtime Trends. *Am J Gastroenterol* 2024; 119(10):S1257-S1258. Full Text

A. Jaan, Rochester General Hospital, Rochester, NY, United States

Introduction: Alcoholic hepatitis (AH), a clinical syndrome precipitated by alcohol abuse, can manifest as acute liver failure (ALF) and thus carries a poor prognosis. AH-related hospitalizations constitute about 0.9% of the total admissions nationwide. Palliative care (PC) is gaining increasing recognition in the management of chronic diseases including end-stage liver disease. However, despite the growing recognition of PC across various medical domains, there remains a dearth of data exploring its utilization patterns in AH hospitalizations. Our study aims to explore patterns of PC utilization among AH patients and its impact on readmission. Methods: Using the National Readmission Database 2015-2020, we employed the International Classification of Diseases, 10th revision, Clinical Modifications (ICD-10-CM) codes to identify adult patients admitted with AH. The patients were categorized into 2 groups based on whether they had a palliative care encounter (PCE) during the same hospitalization. Using a multivariate regression model, we assessed predictors of PCE and its impact on 90-day readmission. Statistical analysis was performed using STATA version 14.2. Results: We identified 68,062 hospitalizations for AH, of whom 3,784 (5.56%) had PCE in index hospitalization. Analysis showed that North American Consortium for the Study of End-Stage Liver Disease -Acute on Chronic Liver Failure (NACSELD-ACLF) score ≥ 2 was associated with the highest odds of receiving PCE (adjusted odds ratio [aOR] 8.54, P<0.01), followed by metastatic malignancy (aOR 3.72, P=0.04), dementia (aOR 2.69, P=0.04), CKD (aOR 2.50, P<0.01) and admission to large-sized hospitals (aOR 1.66, P=0.03). Readmission analysis of patients discharged alive showed that adjusted 90-day readmission was significantly lower in patients who received index admission PCE (aOR 0.45, P<0.01) (Table 1, Figure 1). The total hospitalization days in case of readmissions within 90 days were 19,655 days, costing $152,000,000 USD. Longitudinal analysis of PCE in AH hospitalizations showed a non-significant change from 5.39% in 2016 to 5.69% in 2020 (trend P-value: 0.07). Conclusion: Our study highlights that PCE is associated with more than 50 % reduction in 90-day readmission rates in AH patients. Despite these promising outcomes, our analysis revealed a static trend in PC utilization over the study period, indicating potential areas for improvement in integrating PC into the comprehensive management of AH patients.

Internal Medicine

Jaan A, Farooq U, Dhawan A, **Chaudhary AJ**, Fatima Sheikh L, Hafeez N, and Shah TU. The Impact of Frailty on the Clinical Outcomes of Acute Cholangitis: A Retrospective Study. *Am J Gastroenterol* 2024; 119(10):S39. Full Text

A. Jaan, Rochester General Hospital, Rochester, NY, United States

Introduction: Acute cholangitis (AC) is a lethal infection of the biliary tract with varying degrees of severity. While endoscopic retrograde cholangiopancreatography (ERCP) remains the mainstay drainage modality, the timing of drainage is contingent on the severity of AC. Though frailty is linked to poor outcomes in general, its implications for AC patients remain unexplored. This study aims to bridge this research gap by conducting a nationwide analysis. Methods: Using the National Inpatient Sample Database (NIS) from 2017 to 2020, we employed the International Classification of Diseases, 10th revision, Clinical Modifications (ICD-10-CM) codes to identify adult patients (age >18 years) admitted with AC. We further stratified AC hospitalizations based on the presence of frailty. Utilizing a multivariate regression model, we compared the impact of frailty on the outcomes and procedural performance of AC patients. STATA 14.2 was utilized for statistical analysis. Results: We included 32,310 AC patients, out of whom 11,230 (34.76%) patients were frail. After adjusting for confounding variables, in-hospital mortality of AC was significantly higher in frail patients (adjusted odds ratio [aOR] 3.95; P< 0.01) (Table 1). Additionally, frail patients were found to have significantly higher odds of septic shock (aOR 16.26, P< 0.01), acute renal failure (aOR =.71, P< 0.01), acute respiratory failure (aOR 10.51, P< 0.01), vasopressor requirement (aOR =.02, P< 0.01), and mechanical ventilation (aOR 11.61, P< 0.01). From a procedural viewpoint, frail patients had higher odds of undergoing percutaneous biliary drainage (PBD) but lower odds of undergoing “early” ERCP (ERCP within 24 hours of admission). We also found that frail patients, when compared to their non-frail counterparts, were more likely to undergo PBD as opposed to early ERCP (aOR 1.46, P= 0.01). Age, after adjusting for frailty, was not seen as a predictor of outcomes. Finally, resource utilization was also significantly higher among frail patients. Conclusion: Frailty independently predicts poor AC outcomes and has a notable impact on the choice of biliary drainage procedure. Recognizing frailty instead of age alone as a determinant of AC outcomes can aid clinicians in risk stratification and guide tailored interventions in this population (Table Presented).

Internal Medicine

Jaan A, Maryyum A, **Chaudhary AJ**, Hafeez N, Dhawan A, Sheikh LF, and Ahlawat S. Bacterial Infections in Variceal Hemorrhage: A National Study of Clinical Impact. *Am J Gastroenterol* 2024; 119(10):S679-S680. Full Text

A. Jaan, Rochester General Hospital, Rochester, NY, United States

Introduction: Variceal upper gastrointestinal bleeding (VUGIB) presents a critical challenge in clinical settings, often complicated by the development of concurrent infections. This study seeks to determine the incidence and clinical implications of VUGIB hospitalizations complicated with infections. Methods: Using the National Readmission Database 2019, we employed the International Classification of Diseases, 10th revision, Clinical Modifications (ICD-10-CM) codes to identify adult patients (age .18 years) admitted with VUGIB. We further stratified VUGIB hospitalizations based on the presence of a concurrent same-admission infection (i.e., pneumonia, spontaneous bacterial peritonitis (SBP), urinary tract infection (UTI), or bacteremia). Utilizing a multivariate regression model, we compared the impact of secondary infection on the outcomes and procedural performance of VUGIB patients. STATA 14.2 was utilized for statistical analysis. Results: Among the 9,565 VUGIB patients, 750 (8.5%) developed infections (Table 1). Of these, 43.2 % had a urinary tract infection (UTI), 35.89% had bacterial pneumonia, while bacteremia was present in 7.70%. Adjusted analyses revealed that VUGIB patients who developed concurrent infections exhibited significantly higher odds of mortality (adjusted odds ratio [aOR]: 2.36, P < 0.001), alongside an increased likelihood of complications such as hemorrhagic shock (aOR: 1.84), hepatorenal syndrome (aOR: 3.32), need for vasopressors (aOR: 2.13) and mechanical ventilation (aOR: 3.47) (Table 1). Moreover, those who developed infections had higher odds of requiring repeat esophagogastroduodenoscopy (EGD) (aOR: 1.52) and transjugular intrahepatic portosystemic shunt (TIPS) (aOR: 1.54). Finally, resource utilization, as estimated by total parenteral nutrition requirement, rehabilitation discharge, length of hospital stay, and hospitalization charges, was substantially higher in patients who developed infection (P< 0.001). Longitudinal analysis over 2016-2020 did not show a statistically significant change in rates of infection (Figure 1). Conclusion: Our study revealed that infections among VUGIB patients are associated with markedly worse clinical outcomes, including higher mortality, hemorrhagic shock, rebleeding requiring repeat EGD and need for TIPS. These findings underscore the need for vigilant infection prevention and management strategies to improve patient prognosis and alleviate the burden on the healthcare system.

Internal Medicine

Jaan A, Sarfraz Z, Dhawan A, Farooq U, **Chaudhary AJ**, Nepal M, Sheikh LF, and Thor S. Frailty Predicts Mortality and Procedural Performance in Patients With Non-Variceal Upper Gastrointestinal Bleed: Results From Nationwide Analysis. *Am J Gastroenterol* 2024; 119(10):S678-S679. Full Text

A. Jaan, Rochester General Hospital, Rochester, NY, United States

Introduction: Nonvariceal upper gastrointestinal bleeding (NVUGIB) is a common cause of hospitalization in the United States. With approximately 400,000 admissions annually and a mortality rate of 5-10%, it has a substantial burden on the U.S. healthcare system. Frailty, a multifaceted syndrome characterized by a decline in the function of organ systems, is generally linked to worse outcomes. However, its specific implications on NVUGIB are yet to be comprehensively analyzed. This study aims to bridge this research gap by conducting a nationwide analysis. Methods: Using the National Readmission Database (NRD) from 2019, we employed the International Classification of Diseases, 10th revision, Clinical Modifications (ICD-10-CM) codes to identify adult patients (aged ≥18 years) admitted with a principal diagnosis of NVUGIB. We further stratified NVUGIB hospitalizations based on the presence of frailty. Utilizing a multivariate regression model, we assessed the impact of frailty on outcomes and procedural performance in NVUGIB hospitalizations. STATA 14.2 was utilized for statistical analysis. Results: We included 218,647 adult patients admitted with NVUGIB, of whom 99,892 (45.69%) patients were frail (Table 1). After adjusting for confounding variables, in-hospital mortality due to NVUGIB was significantly higher in frail patients (adjusted odds ratio [aOR] 5.64; P< 0.01). Additionally, frail patients had elevated odds of acute kidney injury (AKI), hemorrhagic shock, vasopressor requirement and respiratory failure requiring mechanical ventilation (P< 0.01). Procedural analysis revealed lower odds of overall esophagogastroduodenoscopy (EGD) and EGD within 24 hours but higher odds of rebleeding requiring repeat EGD and radioembolization (P< 0.01) (Figure 1). Finally, resource utilization estimated by total hospitalization charges (THC), length of stay (LOS), discharge to rehabilitation facilities, and 30- day readmission rates were also significantly higher among patients with malnutrition (P< 0.01). Conclusion: Our study underscores the significant association between frailty and various critical endpoints of NVUGIB, including AKI, shock and respiratory failure, in-hospital mortality and costs. Additionally, frailty emerged as an independent predictor of procedural intervention performed as well as resource utilization. Recognizing frailty as a determinant of NVUGIB outcomes can aid clinicians in risk stratification for this population.

Internal Medicine

Khadra M, **Ali SA**, **Omeish H**, Alsakarneh S, Haddadin F, Haddadin S, and **Dahhan W**. Clinical Outcomes Among Patients With Gastroparesis Undergoing Gastric Peroral Endoscopic Myotomy (G-POEM) Versus Surgical Pyloroplasty. *Am J Gastroenterol* 2024; 119(10):S1629-S1630. Full Text

M. Khadra, Detroit Medical Center, Detroit, MI, United States

Introduction: Gastroparesis is a common disease with severity ranging from mild to refractory, which can pose challenges to both the patient and the provider. The available interventions directed at the pylorus are gastric peroral endoscopic myotomy (G-POEM) and surgical pyloroplasty. We aimed to investigate the peri-operative outcomes and complications in patients with gastroparesis undergoing G-POEM versus surgical pyloroplasty using a national database. Methods: Using the combined releases of the year 2016 of the National Inpatient Sample (NIS) database, we identified primary gastroparesis hospitalizations who were treated with G-POEM versus surgical pyloroplasty, using the International Classification of Diseases, Tenth Revision (ICD-10) codes. Univariable and multivariable regression analyses were performed to examine outcomes, including mortality, length of stay, and total healthcare charges. Baseline patient characteristics were evaluated using t-test and chi-square tests. STATA (IC-16.1 version; STATA Corp, College Station, TX) was used for the statistical analyses. Results: Among a total of 9,951 patients with gastroparesis, 8,966 underwent G-POEM and 985 underwent surgical pyloroplasty. Patients who underwent G-POEM were more likely to be younger (mean age 45.3 61.3 vs 61.5 60.88, P< 0.001) and were less likely to have hypertension (33.5% vs 47.9%, P< 0.001) and coronary artery disease (8.01% vs 19.1%, P< 0.001) (Figure 1). In regards to peri-operative outcomes, patients who underwent G-

POEM had a significantly shorter length of stay (8.1 vs 13.1 days, Coef. -3.22 [-5.24 to -1.19], P=0.002), lower incidence of post-operative respiratory failure (adjusted odds ratio [aOR] 0.07 [0.01 to 0.47], P=0.007), were less likely to be discharged to a skilled nursing facility (aOR 0.44 [0.27 to 0.71], P< 0.001) and had a significantly lower total hospital charge (Coef. -65,175.71 [-102,172 to -28,179.39], P< 0.001). There was no significant difference in all-cause mortality, post-operative gastrointestinal bleeding, operative injury to the gastrointestinal tract and the need for blood transfusion (Table 1). Conclusion: Our analysis suggests that while there is no difference in mortality between patients with gastroparesis who underwent G-POEM versus surgical pyloroplasty, G-POEM was associated with significantly reduced healthcare resource utilization. Further prospective studies are warranted to evaluate the efficacy and safety of G-POEM versus surgical pyloroplasty in patients with gastroparesis.

Internal Medicine

Khan MZ, **Chaudhary AJ**, Shahzil M, Jaan A, Sohail A, **Manivannan A**, Asif H, **Saleem A**, **Faisal MS**, **Adil SA**, **Alluri S**, **Faisal MS**, and **Schairer J**. Needle-Knife Stricturotomy (NKSt) for IBD-Related Strictures: A Single-Center Experience. *Am J Gastroenterol* 2024; 119(10):S971-S972. Full Text

M.Z. Khan, Henry Ford Health, Detroit, MI, United States

Introduction: In recent years, various endoscopic treatment options have emerged for managing strictures associated with inflammatory bowel disease (IBD) and non-IBD conditions. Among these, needle knife stricturotomy (NKSt) has gained attention as a novel approach. By avoiding or delaying surgery, NKSt offers a potential alternative for patients with fibrotic strictures. In this study, we delve into our tertiary care centre's experience with NKSt, exploring its efficacy and role in treating strictures. Methods: A retrospective chart review was performed on patients with Crohn's disease who underwent NKSt at our tertiary care center between 2018 to 2023. Retrospective demographic, clinical, and procedure-specific information was extracted from the electronic medical record. Patients with strictures related to a disease other than IBD were excluded from the study. Results: In this study involving 48 patients, 30 (62.5%) had anastomotic strictures (AS), while 18 (37.5%) exhibited non-anastomotic strictures (NAS). Demographically, both populations were comparable across all variables assessed. Treatment approaches varied; anti-TNF agents were predominantly used in the AS cohort. (Table 1) At the time of NKSt, steroids were being used by 4 (22.2%) NAS patients and 7 (23.3) AS patients. Abdominal pain was the chief symptom for both groups (NAS: 61%; AS 56.7%) The colon was identified as the most frequent stricture location in both subgroups (AS: 33.3%, NAS: 27.7%). Non-anastomotic strictures had a marginally greater mean length (1.58 ± 0.36 cm) compared to AS (0.9 ± 0.5 cm). In addition to the NSKt, balloon dilatation was performed concurrently on 5 NAS patients (28%) and 6 AS patients (20%). No peri-procedural complication was observed in either group. Symptom recurrence was observed in 22% of NAS cases and 23% of AS cases post-procedure. Subsequent endoscopic intervention was necessary for half of the participants; however, surgical intervention was not required for any patient within either group. Conclusion: In recent times endoscopic stricturotomy has emerged as a safe and effective way of treating AS, and non-AS. The rates of complications in our study were low and the patients had an uneventful procedural course. Previous case series have demonstrated the efficacy of this intervention in strictures , 3 cm such as in our study. With a small sample size being a limitation of this study, we aim to gather more data to increase generalizability and compare NKSt with other endoscopic methods (Figure 1).

Internal Medicine

Manas F, **Nakdali R**, **Almajali DA**, **Bhan A**, and **Simon R**. Exploring the Clinical Landscape of Papillary Thyroid Microcarcinoma with Lymph Node Metastasis: A Single-Institution Case Series and Implications for Treatment Decisions. *J Endocr Soc* 2024; 8:A1024-A1025. Full Text

F. Manas, Henry Ford Hospital, Detroit, MI, United States

Introduction: Papillary thyroid microcarcinomas (PTMC) refer to papillary thyroid carcinomas with primary tumor size ≤ 1cm. Characterized by their indolent nature, PTMCs boast a mortality rate of less than 1%. Loco-regional spread occurs in approximately 2-6% of cases, while distant metastasis is observed in about 1-2%. Notably, the rate of recurrence after lymph node (LN) metastasis can reach up to 20%. The optimal management of PTMC remains controversial with some studies suggesting no discernible

difference in clinical outcomes between patients undergoing active surveillance and those opting for surgical removal. There is limited research on thyroid cancer oncogenes that can predict the progression of PTMC outside of the thyroid gland. We report the clinical outcomes of a series of patients with PTMC who presented with LN metastasis at our institution.Case Series: We describe five patients diagnosed with papillary thyroid microcarcinoma with LN metastasis. All patients presented with a neck mass and evaluation by fine needle aspiration (FNA), showed papillary thyroid cancer. The tumor sizes ranged from 0.15 cm to 1 cm and all cases had extensive LN involvement, with sizes ranging from 0.7 to 4.5 cm. All patients received adjuvant RAI according to ATA guidelines. Molecular testing was not available for any of these patients.Discussion: Our case series offers valuable insight into the clinical outcomes of individuals with PTMC who underwent total thyroidectomy with LN dissection. We postulate that there are two separate groups of patients with PTMC. One group with indolent disease, which lends itself to careful follow-up, even without surgery, and the other group with aggressive disease at presentation. The challenge lies in the correct classification of the patient at baseline so that therapy is tailored to the type of cancer. We need better predictors of disease severity so that patients can be risk-stratified appropriately. The absence of clear guidelines regarding the optimal extent of surgery for PTMC adds complexity to treatment decisions. Nevertheless, our case series sheds light on the infrequent occurrence of PTMC with LN metastasis. It is noteworthy that despite the absence of a mutational profile for these patients, consistent with prior small-scale studies, no genetic alterations have been identified as reliable predictors of LN metastasis in PTMC. Our findings underscore the imperative for further investigative studies to enhance our ability to predict more aggressive cases of PTMC. By addressing the gap in knowledge, future research endeavors may contribute to the refinement of treatment strategies for individuals with PTMC.

Internal Medicine

Meribout S, Meribout AL, Salem AE, Barberan Parraga C, Hassan K, Mujtaba Baqir S, **Abusuliman M**, Mohamed IB, Tokayer AZ, and Kalloo A. Predictors of Inpatient Hospital Pancreatitis in CKD Patients Undergoing ERCP: A Comprehensive National Analysis. *Am J Gastroenterol* 2024; 119(10):S1149-S1150. Full Text

S. Meribout, Maimonides Medical Center, Brooklyn, NY, United States

Introduction: Despite advancements in endoscopic technology, post-ERCP complications persist as significant concerns. Identifying the risk factors associated with ERCP-related complications is crucial for judicious patient selection and targeted strategies to mitigate adverse events. Conducting endoscopic procedures in individuals with renal dysfunction carries a heightened susceptibility to complications. However, scant literature exists elucidating the adverse event profile of ERCP in CKD and ESRD populations. Methods: We conducted a comprehensive national dataset analysis to evaluate the clinical outcomes and safety parameters associated with ERCP in CKD and ESRD patients. This study compared the incidence of pancreatitis among different CKD stages (n=9,764). A secondary aim was to delineate the risk factors contributing to postprocedural adverse events in this patient cohort. Results: Post-ERCP pancreatitis (PEP) was significantly higher in the ESRD group (4.57%) compared to Stage 1 CKD (1.33%) with adjusted OR (aOR) = 1.03 (97.5% CI: 1.0002-1.06, $P < 0.048$). Pancreatic procedures carried a higher risk for PEP than biliary procedures (OR = 1.0299, 97.5% CI: 1.0172-1.0429, $P < 0.0001$). PEP was not associated with age, sex, type of hospital, or most comorbidities (COPD, PUD, DM, HTN, PVD, CVA) ($P > 0.05$). However, a higher incidence of PEP was associated with AMI (OR = 1.0322, 97.5% CI 1.005-1.060, P = 0.022), CHF (OR = 1.0118, 97.5% CI 1.0028-1.021, P = 0.0104), and malignancy (OR = 1.0218, 97.5% CI 1.0105-1.0331, P = 0.0001). Conclusion: The incidence of PEP is significantly higher in patients with ESRD compared to patients with stage 1 CKD. Pancreatic procedures pose a higher risk for PEP than biliary procedures. PEP was not associated with age, sex, type of hospital, or most comorbidities, but was higher in patients with AMI, CHF, and malignancy. The increasing correlation between ESRD and PEP could be explained by fluid overload-induced papillary edema, making biliary cannulation difficult. Another mechanism is the higher occurrence of gallstones caused by elevated bile cholesterol levels and disruptions in the autonomic nervous system due to uremia, leading to cholestasis. These findings underscore the importance of careful patient selection and risk stratification in CKD and ESRD patients undergoing ERCP to mitigate the risk of PEP. (Table Presented).

Internal Medicine

Meribout S, Meribout AL, Salem AE, Barberan Parraga C, Jana K, Hassan K, **Abusuliman M**, Mohamed IB, Tokayer AZ, and Kalloo A. The Risk of Bleeding Complications in Patients Undergoing ERCP is Impacted by the Degree of Renal Impairment. *Am J Gastroenterol* 2024; 119(10):S1150-S1151. Full Text

S. Meribout, Maimonides Medical Center, Brooklyn, NY, United States

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) has advanced into a critical therapeutic intervention for various biliary and pancreatic conditions, including tumors, choledocholithiasis, pancreatic pseudocysts, and postoperative biliary complications. Despite technological advancements, ERCP-related complications, particularly bleeding, remain significant concerns. It is well-established that CKD and ESRD patients have an increased risk of bleeding after procedures due to coagulation abnormalities, platelet dysfunction, and heightened fibrinolytic activity. While a few studies have shown increased bleeding risks in CKD and ESRD patients undergoing ERCP, no study has compared the bleeding incidence among different CKD stages. This study aims to evaluate the risk of bleeding associated with ERCP across different CKD stages and identify factors contributing to this risk. Methods: We conducted a retrospective analysis using the National Inpatient Sample (NIS) database from 2016 to 2019, including 9,764 patients with impaired renal function who underwent inpatient ERCP. Patients with underlying haematological diseases and cirrhosis were excluded to minimize confounding factors related to bleeding tendencies. We analyzed demographic information, health insurance status, hospital type, and procedural details to determine bleeding risks. Results: Bleeding risk was found to be proportional to the stage of renal impairment. ESRD patients had significantly higher ERCP-related bleeding compared to Stage 1 CKD patients (OR = 1.016, 97.5% CI: 1.0092-1.0226, P < 0.0001). Urban teaching hospitals exhibited an increased bleeding risk compared to rural hospitals (OR = 1.01, 97.5% CI = 1.0029-1.0171, P = 0.0057), whereas urban non-teaching hospitals did not show a significant difference (P = 0.1). Pancreatic procedures, age, and sex were not associated with increased bleeding risk (P > 0.05). Conclusion: The risk of bleeding after ERCP is proportional to the severity of renal impairment. The experience of endoscopists in urban teaching hospitals might explain the higher bleeding risk observed in these settings. Although pancreatic procedures, age, and sex did not influence bleeding risk, the findings suggest the need for careful patient selection and consideration of endoscopic techniques to mitigate bleeding complications. Further research is required to establish optimal strategies for managing ERCP-related bleeding in CKD patients, particularly those with ESRD. (Table Presented).

Internal Medicine

Meribout S, Meribout AL, Salem AE, Mujtaba Baqir S, Jana K, **Abusuliman M**, Hassan K, Koubeissy A, Tokayer AZ, and Kalloo A. Asian Patients Have Higher Post-ERCP Complications: A Nationwide Analysis of ERCP Safety. *Am J Gastroenterol* 2024; 119(10):S1148-S1149. Full Text

S. Meribout, Maimonides Medical Center, Brooklyn, NY, United States

Introduction: In recent years, endoscopic retrograde cholangiopancreatography (ERCP) has evolved into a sophisticated therapeutic intervention. Despite technological advancements, post-procedure complications remain a concern. ERCP entails risks such as bleeding, pancreatitis, perforation, and biliary infections. Identifying risk factors associated with ERCP-related complications is crucial for patient selection and mitigating adverse events. Methods: We utilized the Nationwide Inpatient Sample (NIS) database from 2016 to 2019, including 9764 CKD patients undergoing ERCP. Demographic details and complication incidence were analyzed. Patients were categorized into 5 CKD stages. Those with hematological diseases and cirrhosis were excluded. Results: Patients with Stage 5 CKD were relatively younger, with a mean age of 65.1±13.4 years. End-stage renal disease (ESRD) patients exhibited the highest complication incidence (17.54%), surpassing those with CKD Stages 1, 2, 3, and 4 (14.67%, 12.66%, 12.69%, 13.19%, respectively; P < 0.01). Caucasians constituted the predominant racial group across all CKD stages, accounting for 49.33% in Stage 1, 65.93% in Stage 2, 72.20% in Stage 3, 67.96% in Stage 4, and 46.55% in Stage 5. Compared to Caucasians, Asian patients exhibited the highest risk of post-ERCP complications, with an odds ratio (OR) of 1.0±37 (97.5% confidence interval [CI] = 1.0256-1.1031, P = 0.0009) (Table 1). This group also faced increased risks of death (OR = 1.0203, 97.5% CI =

1.0102-1.0412, P = 0.0415) and cholecystitis (OR = 1.0307, 97.5% CI = 1.0026-1.0596, P = 0.0321). However, no statistically significant differences were observed for infection, bleeding, and pancreatitis (P > 0.05). African Americans exhibited a higher risk of cholecystitis (OR = 1.018) but lower risks of pancreatitis (OR = 0.9862) and bleeding (OR = 0.993). Native Americans had a lower incidence of infection (OR = 0.9895). Conclusion: Asians exhibited elevated post-ERCP complications possibly due to higher biliary tract pathology incidences. Variations in complications among racial groups may be related to genetic or environmental factors. The NIS database's overrepresentation of Caucasians warrants caution in generalizing findings. Increased communication with ethnic minority patients and further studies are crucial for better understanding these differences. (Table Presented).

Internal Medicine

Mohamed I, **Abusuliman M**, Hassan N, Naeem A, Abosheaishaa H, Gaur R, Abdalla M, Mahmoud M, El Telbany A, Jaber F, Abboud Y, Dahiya DS, and Ghoz H. Comparative Efficacy and Safety of Insufflation Methods in Enteroscopy: A Systematic Review and Network Meta-Analysis. *Am J Gastroenterol* 2024; 119(10):S612. Full Text

M. Abusuliman, Henry Ford Health, Detroit, MI, United States

Introduction: Device-associated enteroscopy, including double and single balloon enteroscopy , has transformed small bowel diagnostics and therapy. Optimal bowel insufflation is crucial for clear visualization. Traditional air insufflation causes bowel distension and discomfort. Alternatives like CO2, which is absorbed quickly, and water-exchange techniques, which reduce bowel loop formation, are explored for better outcomes. Our review evaluates the efficacy and safety of CO2, water, and air insufflation. Methods: Our systematic review and network meta-analysis covered 4 databases: Embase, Medline, Cochrane, and Scopus, evaluating insufflation methods in enteroscopy. Using Covidence, results were screened via PICO criteria, identifying 6 randomized trials. Data extraction included study and patient characteristics, and outcomes. Bias was assessed with RoB 2. Statistical analysis in R language software used the 'netmeta' package, calculating mean differences and risk ratios with 95% CIs, creating network plots, and ranking techniques via SUCRA curves and P-scores. Results: This analysis involves 6 studies with a total of 615 patients and 617 enteroscopies. No significant differences in oral intubation depth were found between Air and Water insufflation compared to CO2 (Air: MD -51.44, P = 0.138; Water: MD 48.3, P = 0.34). Similarly, in anal intubation, no significant differences were observed (Air: MD -31.47, P = 0.57; Water: MD -8.80, P = 0.91). In the combined oral and anal intubation, neither Air nor Water showed statistically significant differences compared to CO2 (Air: MD -58.31, P = 0.33. Water: MD -12.73, P = 0.81). Air led to a significantly longer anal procedure time compared to CO2 (MD 42.1, P < 0.0001), while Water did not differ (MD 10.3, P = 0.76). Water had a longer oral procedure time compared to CO2 (MD 14.40, P = 0.001), while whereas Air showed no statistically significant difference (MD 1.20, P = 0.12). Regarding the total endoscopy rate, Water was associated with a significantly higher rate of successful endoscopy compared to CO2, while Air showed a significantly lower rate. No significant differences in adverse events were found. Conclusion: Our analysis found no significant differences in intubation depth among CO2, Air, and Water insufflation. CO2 resulted in shorter procedure times, while Water showed a higher success rate for endoscopy. No significant disparities in adverse events were observed among the techniques.

Internal Medicine

Morse P, **Chouman A**, **Tamr A**, **Saleem A**, **Cunningham C**, and **Umanath K**. CMV Colitis in Immunocompetent Host. *Am J Gastroenterol* 2024; 119(10):S2432-S2433. Full Text

P. Morse, Wayne State School of Medicine, Detroit, MI, United States

Introduction: Cytomegalovirus (CMV) is a double-stranded DNA virus which causes disease in humans based on their immune status. Despite being a common infection in immunocompromised hosts, CMV colitis rarely occurs in the immunocompetent. Symptoms of CMV colitis are nonspecific, including diarrhea, abdominal pain, fever, and rectal bleeding. We present an immunocompetent patient who was identified as having biopsy proven CMV colitis. Case Description/Methods: A 55-year-old woman with a history of well-controlled type 2 diabetes and end-stage renal disease (ESRD) on dialysis presented to

the hospital with painless hematochezia and diarrhea for two months with acute worsening in the last week. Imaging several weeks before presentation to the ED was suggestive of ischemic colitis, but no further studies were completed at that time. Her hemoglobin on presentation was 8.4 g/dL. The next day, her hemoglobin dropped to 6.5 g/dL requiring blood transfusion. The patient's white blood cell count was mildly decreased at 3.6 K/mL with a normal differential. She underwent esophagogastroduodenoscopy, which was normal, and colonoscopy, which showed diffuse inflammation and a colonic ulcer which was biopsied. Pathology showed features of ischemic colitis and stained positive for CMV. Serum CMV quantitation at this time was 1474 IU/mL. She started intravenous ganiciclovir, which was transitioned to oral valganciclovir at discharge. Upon outpatient follow up two weeks later, the patient reported compliance with the valganciclovir and resolution of her symptoms. Serum CMV quantitation was undetectable at this visit. Discussion: Here we present a patient with well-controlled diabetes and ESRD on dialysis who presented with CMV colitis. Despite multiple comorbidities, she was immunocompetent. Given the patient's positive biopsy staining for CMV, elevated serum CMV quantitation, and complete resolution of symptoms on valganciclovir, CMV colitis is the most likely diagnosis. Diabetes and ESRD on dialysis are known to be comorbid conditions with CMV colitis in immunocompetent hosts. Additionally, prior research indicates that being age 55 or over is also a risk factor. It is hypothesized that these comorbidities contribute to a weakening of the immune system, facilitating CMV colitis to develop in patients traditionally considered immunocompetent. Clinicians should consider CMV colitis in otherwise unexplained abdominal symptoms, particularly in patients with multiple comorbidities like diabetes, ESRD, and age 55 or greater.

Internal Medicine

Nabaty RM, **Agha YH**, and **Suresh S**. Unmasking Intestinal Plasmablastic Lymphoma in an Immunocompetent Crohn's Disease Patient. *Am J Gastroenterol* 2024; 119(10):S2567. Full Text

R.M. Nabaty, Henry Ford Health, Detroit, MI, United States

Introduction: Plasmablastic lymphoma (PBL) is a rare and aggressive subtype of diffuse large B-cell lymphoma. Originally reported in the oral cavity of immunocompromised Human immunodeficiency virus (HIV) patients, it has also been associated with immunosuppression and Epstein-Barr virus (EBV) infection. It commonly manifests in extranodal sites like the GI tract, especially in patients with inflammatory bowel disease (IBD). Diagnosis is challenging due to histological similarities with plasmablastic myeloma, but factors like EBV status and myeloma-defining signs aid in differentiation. We present a rare case of an HIV-negative, immunocompetent, patient with Crohn's disease post proctocolectomy and end-ileostomy who presented with acute blood loss anemia and was found to have small bowel PBL. Case Description/Methods: A 75-year-old man with a history of Crohn's disease and adenocarcinoma of the colon, status post total proctocolectomy with abdominoperineal resection and end-ileostomy, presented with ileostomy bleeding and a significant hemoglobin decrease. He underwent bi-directional endoscopy. Upper endoscopy was unremarkable. Ileoscopy was notable for an obstructing and circumferential ulcerated mass in the distal ileum and severe luminal stenosis. Biopsies of the mass revealed high-grade neoplasm with plasmocytic phenotype, consistent with PBL. CT enterography revealed a long segment of small bowel wall thickening in the right abdomen and numerous distant abdominal lymph nodes, and no evidence of metastasis. Upon follow-up with oncology, he began chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone. Discussion: PBL, while primarily associated with HIV patients, has been reported in HIV-negative patients with IBD, and more frequently in Crohn's disease. This has been hypothesized to be attributed to immunosuppressive therapy or an immunocompromised state. While rare in presentation, reported cases of primary GI-PBL have presented with progressive odynophagia, melena, obstruction, hematochezia, and B symptoms commonly seen in malignancy. There is a paucity of literature on GI-PBL, limited to case series and reports. Our case highlights a primary GI-PBL associated with Crohn's disease in an immunocompetent patient with no history of HIV or EBV. To date, a treatment regimen has not been well defined. Despite treatment advancements, PBL patients have an average survival of 19 months. Thus, it is vital to consider GI-PBL on the differential and continue research on this rare and diagnostically challenging malignancy.

Internal Medicine

Nakdali R, and **Athimulam S**. Leydig Cell Tumor: A Rare Cause of Post-menopausal Hyperandrogenism. *J Endocr Soc* 2024; 8:A851. Full Text

R. Nakdali, Henry Ford Health, Detroit, MI, United States

Introduction: Ovarian steroid cell tumors are a rare subtype of sex-cord stromal tumors. Leydig cell tumors is a subtype of sex-stromal tumors that is found in < 1% of all ovarian tumors. They are typically benign, unilateral, and secrete androgens which causes virilization. Below we present the case of a postmenopausal woman who presented with signs of virilization and was diagnosed with an ovarian Leydig cell tumor. Case: A 62-year-old postmenopausal woman, with a history of partial hysterectomy with right oophorectomy presented to Endocrinology clinic for evaluation of thyroid nodules. However, clinically she had signs of virilization noted by the provider on examination. She reported progressive androgenic alopecia, cystic acne, oily skin, hoarseness of voice and hirsutism, with increase hair growth over upper lip, chin and jaw line requiring daily shaving. She denied taking any supplements. She reported embarrassment of these physical changes and prior providers had attributed this to aging, therefore not prompting further testing. This caused significant emotional distress to the patient, leading to isolation. Biochemical testing confirmed elevated bioavailable testosterone (193.1 ng/dL) and total testosterone levels (579 ng/dL), with no evidence of hypercortisolemia. Magnetic resonance imaging (MRI) revealed a heterogenous soft tissue mass (2.9 x 2.1 x 2.1 cm) in the left ovary. She underwent a left salpingo-oophorectomy and pathology confirmed a welldifferentiated 2.4 cm Leydig cell tumor. Post-operatively, she reported improvement in facial and body hirsutism, reduced shaving frequency decrease in androgenic hair loss, with noticeable hair growth in her frontal scalp, and her skin became less oily with reduced acne. Post-operative labs confirmed cure of hyperandrogenism (Bioavailable testosterone < 2.6 ng/dL; Total testosterone: < 10ng/dL; and Free androgen index < 0.5%). She has been referred to genetics for evaluation. Discussion: Post-menopausal hyperandrogenism poses a diagnostic challenge as it can be mistaken for hormonal imbalances seen with aging. Often times, patients do not report symptoms due to embarrassment unless specifically addressed by provider. Initial testing consists of total and free testosterone and dehydroepiandrosterone sulfate (DHEAS) levels to assess the source of hyperandrogenism. Ruling out hypercortisolemia and assessment for ingestion of testosterone or DHEA supplements is vital. Pelvic ultrasound or cross-sectional imaging (CT or MRI) of abdomen and pelvis can identify structural abnormalities in the ovaries or adrenal glands. Prompt evaluation and management can alleviate significant distress to the patient. Leydig cell tumors represent a rare but important consideration in the differential diagnosis of postmenopausal hyperandrogenism, such as in our patient.

Internal Medicine

Nakdali R, **Faber A**, and **Simon R**. From Chronic Inflammation to Metastatic Challenge: A Complex Intersection of Hidradenitis Suppurativa, Hypercalcemia, and Squamous Cell Carcinoma. *J Bone Miner Res* 2024; 39:80. Full Text

R. Nakdali, Henry Ford Hospital, United States

Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition that impacts hair follicles and often involves apocrine-rich, intertriginous skin regions. HS presents with relapsing, recurrent inflamed skin lesions that develop into draining abscesses, fibrosis, and disfiguration. Squamous cell carcinoma occurs in 4.6% of HS. Hypercalcemia associated with cutaneous carcinomas is rare in association with HS. We report a patient with parathyroid hormone-related protein (PTH-RP) driven hypercalcemia and squamous cell carcinoma arising from HS. A 66-year-old male presented to the hospital with decreased oral intake and confusion. His medical history was significant for atrial fibrillation and HS of the groin and perineum complicated by previous admissions for sepsis. He was admitted one month prior for sepsis due to an HS flare where he was incidentally noted to have new-onset hypercalcemia of 13.1 mg/dL. He was treated with IV fluids, calcitonin, and Zoledronic acid. The etiology of his hypercalcemia was not evaluated at that time. Workup this admission revealed leukocytosis of 40.8 k/UL, hypercalcemia of 15.1 mg/dL, ionized calcium of 1.94 mmol/L, low PTH of 2.0 pg/mL, elevated PTH-RP of 27 pg/mL, normal vitamin D and angiotensin converting enzyme. CT of the abdomen revealed irregular thickened skin with soft tissue gas within the perineum, scrotum and gluteal soft tissue, concerning for Fournier's gangrene. CT of the chest

showed diffuse metastatic disease involving the right sixth and tenth ribs, para-aortic lymph nodes, pulmonary nodules, and likely malignant bilateral pleural effusions with incidental pulmonary emboli. He was admitted to ICU with septic shock and promptly started on broad spectrum antibiotics. Dermatology was concerned for potential transformation of his known HS into metastatic squamous cell carcinoma (SCC). This was confirmed on biopsy of perineal skin which revealed moderately to well-differentiated squamous cell carcinoma. His hypercalcemia was managed with IV fluids and Zoledronic acid. Unfortunately, the patient passed due to cardiac arrest one month later. This case demonstrates the significance of early recognition of hypercalcemia as a potential harbinger of cancer and the importance of considering transformation of chronic skin conditions into SCC in the setting of newly diagnosed hypercalcemia. In this case, humoral hypercalcemia of malignancy due to PTH-RP production from transformed HS into metastatic SCC was identified.

Internal Medicine

Omeish H, Bader H, Maghnam R, Barham H, Maghnam J, Al-Thunaibat A, and Abu-Sulb A. Primary Care Physicians' Experiences of Obesity Counseling and Management in Culturally and Linguistically Diverse Populations. *Am J Gastroenterol* 2024; 119(10):S1537-S1538. Full Text

H. Omeish, Henry Ford Health, Detroit, MI, United States

Introduction: The purpose of the study was to explore Primary care physicians' experiences and perspectives of obesity counseling and management of culturally and linguistically diverse populations. Particularly in reference to Spanish speaking patients with low English proficiency. Methods: Semi-structured interviews were employed to achieve the aim of this study. 27 interviews were conducted. Participants were recruited from medical practices in Bernalillo county, New Mexico and Monmouth county, New Jersey. All participants provided primary care in clinics with a large proportion of LEP individuals. Of the 27 physicians, 17 were males and 10 were female. 23 physicians were trained in Internal Medicine and 4 were trained in Family medicine. All providers were either American board certified or board eligible. All interviews were conducted in English while encounters were audio taped. All transcripts were de-identified, followed by inductive thematic analysis. Results: On average, interviews lasted 14 minutes. Thematic analysis of the interview transcripts identified 5 key themes: time constraints, chief complaint prioritization, lack of knowledge of access pathways, limited health literacy, and physician bias. Conclusion: Few studies have investigated physicians' perspectives on delivering primary and secondary prevention to non-English speaking individuals. Primary care doctors are the first point of contact for healthcare, and understanding their views on managing obesity in non-English speaking patients is crucial for ensuring equitable care for minority groups. Physicians perceive obesity counseling and management in culturally and linguistically diverse patients to be more challenging. Identified barriers include time constraints, chief complaint prioritization, and physician bias. This study aims to propose practical strategies to address this disparity and promote fair treatment across all patient populations. Strategies include cultural competence training, dedicated follow-up appointments to focus on obesity counseling, referral to specialized clinics, education on billing and reimbursement to help navigate the system more effectively and ensure comprehensive care. .

Internal Medicine

Omeish H, Berg A, Von Hohenberg M, and Bader H. Abdominal Imaging Versus Tissue Biopsy: A Challenging Case of Abdominal TB. *Am J Gastroenterol* 2024; 119(10):S3078-S3079. Full Text

H. Omeish, Henry Ford Health, Detroit, MI, United States

Introduction: Tuberculosis, caused by Mycobacterium tuberculosis, remains 1 of the leading infectious causes of death worldwide. It is classified as either pulmonary or extrapulmonary. The gastrointestinal system involvement in tuberculosis is rare. Case Description/Methods: A 22-year-old man, with no significant past medical history who recently immigrated from Yemen, presented with a 3-month history of abdominal pain, nausea/vomiting, 20-pound weight loss, intermittent fevers, and night sweats. Laboratory tests showed mild microcytic anemia (hemoglobin 11.2 g/L, mean corpuscular volume 67mm3), elevated ferritin, and low iron and total iron binding capacity levels. Computed tomography scan showed extensive soft tissue involvement in the mesentery, enlarged porta hepatis lymph node, mass on bowel loops and

liver metastases suggesting peritoneal malignancy spread such as lymphoma (Figure 1). Biopsy revealed necrotizing granulomatous inflammation. Further workup included negative fungal culture, AFB sputum culture smear and MTB polymerase chain rection, AFB blood culture. An abdominal tissue culture was positive for M. tuberculosis, and a positive Quantiferon tuberculosis (TB) test confirmed the diagnosis of tuberculosis. Discussion: Tuberculosis can affect the gastrointestinal system most commonly the leocaecal region and is the sixth most common site of extrapulmonary TB. Bacteria reach the gastrointestinal tract via hematogenous spread, ingestion of infected sputum, or direct spread from adjacent areas. Pathological features include ulcers, fibrosis, bowel wall and omental thickening, enlarged lymph nodes and peritoneal tubercles. Peritoneal TB presents in 3 forms: wet with ascites, dry with adhesions, and fibrotic with omental thickening. Usually presenting with a lower abdominal pain, palpable mass or complications like perianal fistulae, obstruction, perforation, or malabsorption. Only 25% of cases show pulmonary lesions. Ascitic fluid analysis shows high protein, low SAAG, lymphocytic cells, and elevated ADA. Treatment involves at least 6 months of antitubercular therapy. This case highlights the diagnostic complexities associated with extrapulmonary abdominal tuberculosis, emphasizing the necessity for heightened clinical suspicion in high risk populations such as immigrants, immunocompromised individuals, and travelers to endemic regions. It also emphasizes the potential discordance between radiological findings and definitive diagnosis, highlighting the risk of anchoring bias. Maintaining a broad differential diagnosis early in the evaluation process can help minimize anchoring bias.

Internal Medicine

Omeish H, **Chaudhary AJ**, **Jamali T**, **Saleem A**, and **Khan MZ**. A Rare Case of Pancreatic Cancer Causing Secondary Achalasia. *Am J Gastroenterol* 2024; 119(10):S2272. Full Text

H. Omeish, Henry Ford Health, Detroit, MI, United States

Introduction: Secondary achalasia or pseudoachalasia is a rare esophageal motility disorder resembling idiopathic achalasia. Most pseudoachalasia cases involve neoplasia at or near the esophagogastric (EG) junction. Pancreatic cancer rarely causes pseudoachalasia. This disorder may result from circumferential obstruction of the distal esophagus or malignant infiltration destroying inhibitory neurons. We present a rare case of pseudoachalasia caused by pancreatic cancer highlights the need to consider malignancies beyond the EG junction in diagnosis. Case Description/Methods: A 77-year-old woman with a history of pancreatic adenocarcinoma presented with a 6-month history of dysphagia, abdominal pain, and a 30 lb weight loss over 3 months. Laboratory findings revealed leukocytosis, high anion gap metabolic acidosis due to starvation ketosis, and elevated liver enzymes (AST 299 U/L, ALT 384 U/L, alkaline phosphatase 942 IU/L). A CT scan of the abdomen showed progression of the pancreatic head mass, encasing vascular structures, worsening biliary duct dilation, centrally necrotic mesenteric lymph nodes, and new small ascites. An esophagogram revealed significant narrowing of the distal esophagus, gastroesophageal junction, and proximal stomach. An EGD with ERCP demonstrated type 3 achalasia and a single moderate localized malignant biliary stricture treated with biliary sphincterotomy and stent placement. The patient received 5 cycles of radiation therapy followed by resumption of chemotherapy. Due to declining health and comorbidities, further pancreatic cancer treatment was considered inappropriate. After discussion with the patient and family, they opted for hospice care, and the patient passed away 5 months later. Discussion: This case underscores the critical need to broaden the differential diagnosis when evaluating patients with unexplained dysphagia. While rare, pseudoachalasia, which has been associated with pancreatic cancer in only 4 reported cases, should be considered in such patients. When standard treatments fail to alleviate symptoms in typical achalasia cases, secondary achalasia may be suspected (see Figure 1).

Internal Medicine

Omeish H, Haddadin F, Omeish R, and Haddadin S. UNLOCKING THE HEARTLIVER CONNECTION: EXPLORING DIASTOLIC HEART FAILURE RISK IN MASLD PATIENTS DEVOID OF CARDIOVASCULAR HISTORY. *Hepatology* 2024; 80:S470. Full Text

H. Omeish, Henry Ford health

Background: MASLD, ranging from nonalcoholic fatty liver to MASH, shares metabolic risk factors with CVD, which is the leading cause of death in MASLD patients. While the association between MAFLD and heart failure with reduced ejection fraction (HFrEF) is established, the link with HFpEF is emerging, yet evidence remains scarce. This study aims to explore the risk and predictors of new-onset heart failure with preserved ejection fraction (HFpEF) in patients with a history of MASH but without prior CVD. Methods: This study analyzed data from 81,309 MASH patients from the 2016 National Inpatient Sample (NIS) to examine adult patients (> 18 years) diagnosed with MASH. Patients with prior coronary artery disease and heart failure were excluded. Using ICD-10 codes, new-onset heart failure with preserved ejection fraction (HFpEF) was identified as the primary disease leading to hospitalization in MASLD patients without prior CVD. Demographics, baseline characteristics, and comorbidities were compared between MASH patients with and without new-onset HFpEF. The study also investigated predictors of new-onset HFpEF in MASH patients without prior CVD, utilizing multivariate analysis to adjust for various factors including age, gender, race, comorbidities, and hospital characteristics. STATA software was employed for statistical analyses. Results: In this retrospective study, 71.1% of patients lacked prior CVD and were analyzed. New-onset HFpEF occurred in 1.1% (n = 645) of these patients (OR 1.2 [1.01 to 1.44], P = 0.042). Comparatively, those with newonset HFpEF were older (65.7 ± 0.9 vs 58 ± 0.2, P < 0.001), predominantly female (75.9% vs 64.2%, P = 0.008), and had a higher percentage of white race (P = 0.016). They were also more likely to have dyslipidemia (39.5% vs 28.6%, P = 0.005), CKD (38.7% vs 18.5%, P < 0.001), OSA (34.9% vs 15.5%, P = 0.001), and AF (20.7% vs 4.6%, P < 0.001) as seen in Table-1. Multivariate analysis revealed older age (Coef. 1.03 per year [1.01 to 1.05], P < 0.001), female gender (OR 2.1 [1.34 to 3.24], P = 0.001), Native American race (OR 3.0 [1.22 to 7.48], P = 0.017), OSA (OR 3.1 [2.01 to 4.63], P < 0.001), AF (OR 3.7 [2.31 to 5.94], P < 0.001), and CKD (OR 1.9 [1.16 to 3.21], P < 0.001) as predictors of newonset HFpEF in MASH patients without prior CVD as seen in Table-2. Conclusion: The current study demonstrated an association between MASH and new-onset HFpEF in patients without a prior history of CVD. Predictors of developing HFpEF in patients with MASH include older age, female gender, Native American race, history of AF, OSA, and CKD. Such findings highlight the importance of risk factor recognition and identification of susceptible groups in patients with MASH who are at risk of developing HFpEF. The growing body of evidence demonstrating the association between both diseases calls for further investigations to well establish the mechanism, risk factors, and morbidity of HFpEF in patients with MASH.

Internal Medicine

Omeish H, **Khan MZ**, **Chaudhary AJ**, **Salgia R**, and **Jafri SM**. A Case of Acute Budd Chiari Syndrome Treated With Portosystemic Shunting. *Am J Gastroenterol* 2024; 119(10):S2882. Full Text

H. Omeish, Henry Ford Health, Detroit, MI, United States

Introduction: Budd-Chiari syndrome (BCS) is a rare condition involving hepatic venous outflow obstruction. While it typically progresses slowly, it can cause acute decompensation of liver disease creating significant management challenges. Here we present a case of acute BCS leading to severe decompensation of liver disease managed by Transjugular intrahepatic portosystemic shunt (TIPS). Case Description/Methods: A32-year-oldwomanwith a history of iron deficiency anemia, presented with sudden right upper quadrant abdominal pain. Labs showed ALT of 255 U/L and AST 196 U/L, bilirubin 1.7 mg/dL, hemoglobin 6.8 mg/dL, platelets 140 x 10∧9/L, and INR 1.35. CT abdomen revealed thrombi in the hepatic and portal veins, suggestive of BCS, and signs of portal hypertension. Serological workup including autoimmune, Wilson's disease, viral hepatitis, etc, were negative. Liver biopsy showed centrilobular hepatocellular necrosis, sinusoidal dilatation, and mild portal fibrosis consistent with hepatic venous outflow obstruction. Hypercoagulable workup revealed Paraoxysmal nocturnal hemoglobinuria. Multi-disciplinary discussion with hematology and hepatobiliary surgeons was ensued and the patient was started on continuous heparin. Despite anticoagulation therapy, the patient's condition did not improve, leading to consideration for liver transplant. Due to extent of the clot, limited experience with management of PNH, and the patient's hesitance, dTIPS was performed. Her proceeding hospital course was complicated by gastrointestinal bleeding from hepatic artery aneurysms, managed with coil embolization. Otherwise she did well and was discharged in stable condition. Discussion: BCS, a rare hepatic venous outflow obstruction disorder, predominantly affects women in their third or fourth decade, presenting with abdominal pain, ascites, and hepatomegaly. Most cases of BCS entail an underlying thrombophilia

disorder, with PNH contributing to 19% of cases. In PNH patients, management is often complicated as morbidity and mortality with thrombosis is high. In recent times Eculizumab has proven to mitigate thromboembolism risk. Symptoms onset can range from acute presentation, such as our case, to chronic TIPS typically has been used to manage chronic decompensation of liver disease caused by BCS but has seldom been used as a rescue therapy for sequealae of portal hypertension, such as in our case. Therefore, multidisciplinary decision-making is important when encountering rare causes and presentation of BCS.

Internal Medicine

Omeish H, **Mueller A**, **Jafri SM**, and **Moonka D**. NOVEL INSIGHTS INTO THE ACCURACY OF FIB-4 AND FIBROSCAN SCORES COMPARED TO LIVER BIOPSY IN THE ASSESSMENT OF LIVER FIBROSIS IN PATIENTS WITH MASLD. *Hepatology* 2024; 80:S452. Full Text

H. Omeish, Henry Ford health

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is prevalent, with fibrosis stage being a critical predicting prognosis. Liver biopsy is the gold standard for staging but is invasive and costly. Non-invasive tests like FibroScan and FIB4 aid in pre-selecting patients for biopsy. This study compares FibroScan and FIB4 accuracy in predicting fibrosis staging in patients with MASLD. Methods: A cross-sectional study on 116 MASLD patients undergoing both FibroScan and liver biopsy within one year was conducted. Demographic, biochemical data, and FIB4 levels were collected. Patients were categorized by fibrosis levels: minimal/no (F0-F1), moderate (F2- F3), and severe (F4), using FibroScan kPa scores, FIB4 levels, and biopsy results. Results: Of 116 patients (55 males, 61 females; 82 < 65 years, 34 older; 89 white, 25 non-white; 26 BMI < 30, 89 BMI > 30), 37.07% were F0-1 by FIB4, with 64.71% agreement by FibroScan. For F2-3, 58.62% were identified by FIB4, with 60% agreement by FibroScan. In F4, 4.31% were classified by FIB4, with 60% agreement by FibroScan. Kappa statistic (0.1253) indicates slight agreement beyond chance, emphasizing caution when using these methods interchangeably. Table-1 compares FIB4 values and biopsy stages, showing moderate agreement, particularly for F4. Among 43 F0-1 cases by FIB4, 52.17% matched F0-1 biopsy, 38.24% were F2-3, and 11.63% were F4. For 68 F2-3 cases by FIB4, 16.18% were F0-1, 58.82% were F2-3, and 25.00% were F4. Among 5 F4 cases by FIB4, none were F0-1, 40.00% were F2-3, and 60.00% confirmed F4 by biopsy. Table-1 also correlates FibroScan and biopsy stages. Of 17 F0-1 cases by FibroScan, 64.71% matched biopsy, 35.29% were F2-3, none F4. Among 55 F2-3 cases by FibroScan, 16.36% were F0-1, 74.55% F2-3, 9.09% F4. Of 44 F4 cases by FibroScan, 6.82% were F0-1, 47.73% F2-3, and 45.45% confirmed F4 by biopsy. Significant F2-3 agreement, some F0-1 and F4 discrepancies were observed. Conclusion: Both FIB-4 and FibroScan showed a correlation with liver fibrosis, particularly in moderate fibrosis. However, discrepancies exist across different stages, with better performance in moderate fibrosis. Caution is advised when using non-invasive tests interchangeably with biopsy for fibrosis assessment in MASLD patients.

Internal Medicine

Omeish H, **Mueller A**, **Jafri SM**, and **Moonka D**. How Accurate Is FIB-4 vs Fibroscan in Clinical Practice: Comparing Methodology of Liver Fibrosis Assessment. *Am J Gastroenterol* 2024; 119(10):S1385. Full Text

H. Omeish, Henry Ford Health, Detroit, MI, United States

Introduction: The associated risks of liver biopsy for assessing fibrosis in patients with Metabolic dysfunction-associated steatotic liver disease (MASLD) have heightened the need to validate non-invasive fibrosis scores for accuracy and efficacy. This study aims to compare the accuracy of the FIB-4 (Fibrosis-4) and Fibroscan scores in diagnosing fibrosis in MASLD patients. Methods: A total of 116 patients were categorized into 3 groups based on their Fibroscan kPa (kilopascal) scores: Group I with mild fibrosis (MF), comprising F0 to F1, and Group II with moderate fibrosis (AF), comprising F2-F3, with group 3 with advanced fibrosis classified as F4. Results: The study evaluated the correlations between Fibroscan, FIB-4 values and liver biopsy stage in various subgroups of patients. In the overall cohort (N=116), significant positive correlations were found between Fibroscan and liver biopsy stage (R=0.246,

P=0.008), and liver biopsy stage and FIB-4 value (R=0.537, P<0.001). Among males (N=55), a strong significant correlation was observed between liver biopsy stage and FIB-4 value (R=0.727, P<0.001), though correlations involving Fibroscan were not significant. In females (N=61), significant positive correlations existed between all pairs of measures, with the strongest being between liver biopsy stage and FIB-4 value (R=0.349, P=0.006). Age-related analysis showed that in patients younger than 65 (N=82), significant correlations were found between Fibroscan and liver biopsy stage (R=0.332, P=0.002), and liver biopsy stage and FIB-4 value (R=0.602, P<0.001). For those aged 65 or older (N=34), only the correlation between liver biopsy stage and FIB-4 value was significant (R=0.390, P=0.023). Racial analysis revealed that in the White race group (N=89), significant correlations were found across all measures, while in the non-White group (N=25), only the correlation between liver biopsy stage and FIB-4 value was significant (R=0.706, P<0.001; Table 1). Conclusion: Both FIB-4 and Fibroscan can be used to rule out advanced fibrosis in MASLD patients. However, a stronger relationship between liver biopsy stage and FIB-4 value was noted compared to their individual associations with Fibroscan.

Internal Medicine

Omeish H, **Nimri F**, **Alomari A**, **Saleem A**, and **Tang J**. A Mysterious Case of Abdominal Pain and Distention Revealing Eosinophilic Enteritis. *Am J Gastroenterol* 2024; 119(10):S2054-S2055. Full Text

H. Omeish, Henry Ford Health, Detroit, MI, United States

Introduction: Eosinophilic Gastroenteritis (EGE) is a rare disorder marked by eosinophilic infiltration and peripheral eosinophilia. It can occur anywhere in the gastrointestinal tract without specific causes of eosinophilia. While its exact cause is unknown, hypersensitivity is significant. Symptoms include nausea, vomiting, abdominal pain, and weight loss. Diagnosis involves endoscopic biopsies, and prevalence is increasing with more endoscopic procedures. First-line treatment is steroids. We describe a case of diffuse abdominal pain leading to EGE diagnosis. Case Description/Methods: A 25-year-old woman presented with a month-long history of diffuse abdominal pain, fatigue, bloating, nausea, vomiting, poor appetite, and decreased oral intake. She denied fever, weight loss, rash, or allergic disease history and reported recent travel to the Bahamas and Jamaica. Physical exam was unremarkable except for mild tachycardia. Labs showed leukocytosis with hypereosinophilia. Extensive workup ruled out secondary causes (Table 1). Computed tomography revealed small bowel thickening, ascites, and pleural effusions. Paracentesis removed 900 cc, showing a Total Nucleated Cell Count of 1,637 and 87% eosinophils. Esophagogastroduodenoscopy showed gastropathy (Figure 1), and duodenal biopsies revealed extensive eosinophilic infiltration, suggesting eosinophilic enteritis. Treatment included IV ceftriaxone, Flagyl, and Ivermectin, later switching to pantoprazole and high-dose prednisone. Follow-up showed complete resolution of symptoms after 3 weeks. Discussion: EGE is a rare condition with peripheral eosinophilia and gastrointestinal eosinophilic infiltration. Early suspicion is crucial, and secondary causes must be ruled out. EGE often affects men over 30 with allergy history and high serum IgE. It can impact any part of the digestive system, especially the stomach's antrum. Diagnosis involves gastrointestinal symptoms and eosinophilic infiltration. The incidence is rising, but true prevalence is unknown. Treatment, primarily steroids, shows up to 90% improvement. Alternatives include antihistamines, mast cell stabilizers, leukotriene antagonists, and PPIs. Early diagnosis is key. (Figure Presented).

Internal Medicine

Rashi F, and **Peleman R**. When Food Makes You Skip a Beat: Esophageal Cancer Presents as Supraventricular Tachycardia. *Am J Gastroenterol* 2024; 119(10):S2262-S2263. Full Text

F. Rashi, Henry Ford Macomb Hospital, Clinton Township, MI, United States

Introduction: Esophageal cancer (EC) has a poor prognosis with a high mortality rate and usually presents with progressive dysphagia with unintentional weight loss, often being asymptomatic in the initial stages. (1) Moreover, tachycardia has been associated with increased mortality risk in cancer patients. Radiation and esophagectomy have been associated with tachyarrhythmias (TA). (2,3) However, our case of EC presented as supraventricular tachycardia (SVT). Case Description/Methods: A 71-year-old man with a history of hyperlipidemia, hypertension, and tobacco use presented to the hospital with chest pain and palpitations. Initial electrocardiogram revealed SVT; vagal maneuver and adenosine improved

his heart rate and rhythm. Of note, the patient also reported slight difficulty in swallowing for 6 months and had noticed some weight loss. Computed tomography pulmonary angiography was done initially to rule out pulmonary embolism however, revealed a large esophageal mass with extraluminal extension. Subsequently, he underwent a barium swallow study which showed a 7.5 cm segment apple core lesion causing severe luminal narrowing at mid-esophagus, with severe dilation of the cervical esophagus concerning for malignancy. This was followed by an esophagogastroduodenoscopy (EGD) demonstrating esophageal mass at 27 cm with a small amount of oozing blood. Biopsy was remarkable for squamous cell carcinoma of the esophagus, moderate to poorly differentiated. The patient had a feeding jejunostomy inserted and further imaging revealed evidence of metastatic disease to the skull and distal right femur. Patient was initially started on palliative radiation therapy, followed by chemotherapy including- 5-Fluorouracil, Oxaliplatin, and Nivolumab based regimen, and has received 6 cycles so far. Discussion: Cases with esophageal masses and large hiatal hernias have been known to present as TA. (4,5,6,7) The likely mechanism is the external compression of the left atrium by the mass and subsequent stimulation of the vagus nerve. To the best of our knowledge, no reports of EC presenting as SVT have been reported. Our case demonstrates the need for clinical vigilance regarding EC and masses when dealing with SVT or TA to ensure accurate diagnosis and treatment (see Figure 1).

Internal Medicine

Rashi F, **Shams S**, **Zeilenga C**, and **Peleman R**. An Adventurous Tract - Double Pylorus in Chronic Liver Disease. *Am J Gastroenterol* 2024; 119(10):S3205-S3206. Full Text

F. Rashi, Henry Ford Macomb Hospital, Clinton Township, MI, United States

Introduction: Double pylorus (DP) is a rare entity, with an incidence ranging from 0.02%-0.01% in all endoscopies. DP with cirrhosis is very sparse. DP exists in congenital and acquired forms. Research suggests that DP may result from poorly healing ulcers and is linked to comorbidities like diabetes, chronic obstructive lung disease, rheumatoid arthritis, cirrhosis, chronic kidney disease, and radiotherapy. Case Description/Methods: A 41-year-old man with past medical history of chronic liver disease with prior inconclusive liver biopsy, chronic kidney disease stage 3b, diabetes mellitus, presents with abdominal distention, bilateral lower limb swelling, and worsening anemia (Figure 1). On admission, labs showed normocytic anemia, negative hepatitis screen, normal alpha-1-antitrypsin levels, and non-reactive HIV test. Antibodies for liver-kidney microsomal, smooth muscle, mitochondrial M2 antibodies were normal. Family history was negative for hepato-pancreatic neoplasms, liver disease, and genetic conditions. Social history negative for intravenous drug use, high-risk sexual practices, and travel history. Model for end-stage liver disease score was 16-18. Esophagogastroduodenoscopy (EGD) showed a duplicated pylorus with multiple erosions on antral surface and ulcerations which were likely a potential cause of bleeding. The duodenal bulb did reveal multiple erosions and the post-bulbar duodenum was normal. Biopsy was positive for Helicobacter pylori in stomach and antrum. Liver biopsy showed bridging fibrosis with nodule formation consistent with Ishak 6/6, Metavir F4 Fibrosis. Discussion: The likely mechanism of DP in our patient is fistulization due to poorly healing ulcer complicated by liver cirrhosis. Treatment should prioritize addressing factors hindering proper healing. Although many cases respond well to proton pump inhibitor (PPI) therapy, surgery becomes necessary for free perforations, obstructions - that are refractory to endoscopic treatment-, and refractory bleeding. Notably, even with treatment, fistulae persist in 67%, fusion in 28%, and self-resolution in 5% of cases. This case highlights the need for heightened awareness and caution during EGD or endoscopic retrograde cholangiopancreatography in such patients to prevent procedural complications and adverse patient outcomes. Follow-up endoscopies can be performed to monitor for disease course.

Internal Medicine

Rehman S, **Abusuliman M**, **Chaudhary AJ**, **Alluri S**, **Nabaty R**, **Saleem A**, and **Kutait A**. Risk Factors for Esophageal Variceal Ligation Ulcer Bleeding. *Am J Gastroenterol* 2024; 119(10):S437. Full Text

S. Rehman, Henry Ford Health, Detroit, MI, United States

Introduction: Esophageal Variceal Ligation (EVL) ulcer bleeding is defined as endoscopically confirmed bleeding from a post banding ulcer with no alternative bleeding source. EVL ulcer bleeding is a rare

complication, difficult to manage and has a high rate of mortality. The data on the risk factors and treatment of EVL ulcer bleeding is limited. This study aims to identify risk factors for the development of EVL ulcer bleeding to better understand patients who may be at higher risk. Methods: Through a retrospective case control study, ICD 10 codes were used to identify patients who were 18 years or older with a history of cirrhosis who underwent EVL between 1/2016-12/2023 within our tertiary health system. We excluded patients who did not undergo EVL in our health system and those who had GI bleeding for any other reason besides EVL ulcer. We compared patients who had at least 1 episode of EVL ulcer bleeding as defined above to those with no episode of EVL ulcer bleeding by collecting demographic data, lab values at time of initial EVL and initial EVL endoscopy findings. We ran independent T test for continuous variables with equal variance and normal distribution, Mann-Whitney U Test for continuous variables with non-normal or non-parametric distribution and Chi square test for categorial variables. Results: In this time, 407 patients underwent at least 1 session of EVL in our health system and of these patients, 375 had no episodes of EVL ulcer bleeding and 32 had EVL ulcer bleeding. Those who developed EVL ulcer bleeding at baseline were on average younger (mean age 55 +/- 11.3 years, P=0.036), had higher MELD scores at initial scope (19.8 +/- 9, P=0.015), had more banding sessions (mean 3.5 +/- 2.6 bands, P=0.000) with more number of bands (4.7, P=0.000) placed per session, had a history of variceal bleeding (59%, P=0.005) and hepatic encephalopathy (81%, P=0.000). On labs, EVL ulcer bleeding patients had lower albumin (2.7, P=0.009). Endoscopy findings of stigmata of recent bleeding (P=0.006), management post initial scope (P=0.000) and mortality within 6 months (P=0.010) were statistically significant between the 2 groups. Conclusion: Our results demonstrate both the presence of patient specific demographic risk factors and endoscopic findings that increase risk of EVL ulcer bleeding. Whether this was due to predominately our patient population or sample size is unknown. Further studies assessing the treatment of EVL ulcer bleeding itself based on these risk factors is warranted (see Table 1).

Internal Medicine

Rehman S, **Abusuliman M**, **Chaudhary AJ**, **Alluri S**, **Saleem A**, **Nabaty R**, and **Kutait A**. Esophageal Variceal Ligation Ulcer Bleeding: Outcomes of Different Modalities Used for Treatment. *Am J Gastroenterol* 2024; 119(10):S438. Full Text

S. Rehman, Henry Ford Health, Detroit, MI, United States

Introduction: Esophageal Variceal Ligation (EVL) ulcer bleeding, defined as endoscopically confirmed bleeding from an ulcer due to slippage of a band with no alternative bleeding source, poses a challenge as there exists no standardized guidelines for treatment. Hemospray is a nonabsorbable hemostatic powder used for various gastrointestinal bleeding, however limited data exists for its use in EVL bleeding. This study aims to assess the treatment outcomes of different modalities used in EVL ulcer bleeding including the use of hemospray to shed insight into management strategies. Methods: We used ICD 10 codes to identify patients over the age of 18 with a history of cirrhosis who underwent EVL within our tertiary health system between 1/2016-12/2023. We excluded patients who did not have any EVL and those who had GI bleeding for any other reason besides EVL ulcer as defined above. Primary outcome was management of EVL ulcer and secondary outcomes were rebleeding, readmission within 3 months and mortality within 6 months. Results: 407 patients underwent at least 1 session of EVL in this time and of these, 32 (7.9%) developed EVL ulcer bleeding. Of the EVL ulcer bleeding patients, the mean age was 55 ±11.3 years and alcoholic cirrhosis was the most common cause of cirrhosis (59%, n=19). Mean MELD at initial EVL scope was (19.8± 9.25) compared to MELD at EVL ulcer bleeding scope (21.5± 9.98). On average, 10.76 ±5.01 days was time to repeat scope and hematemesis was most common indication for second scope (n= 21,54%). EVL ulcer bleeding was most frequently managed with rebanding (n=16, 50%), followed by endoscopic injection sclerosis (n=9, 28%) and hemospray (n=7, 22%). 17 patients (53%) had rebleeding post intervention, 12 were (38%) readmitted within 3 months and of these 6 (50%) had rebleeding as the most common reason for readmission.14 (44%) of EVL ulcer bleeding patients died within 6 months. When comparing management of EVL ulcer bleeding scope to rate of rebleed, no statistical significance across the different modalities (P=0.283) including hemospray and rebleeding risk (P=0.112). Conclusion: Our data suggests there is no standard treatment of EVL ulcer bleeding that prevents rebleeding including hemospray. Whether this is due to the small sample size or time frame remains unknown. Further studies should assess known risk factors for EVL ulcer bleeding

with treatment outcomes to establish other underlying factors that impact EVL treatment bleeding outcomes in addition to modality used (see Table 1).

Internal Medicine

Rehman S, Garg N, **Rahman T**, **Jamil M**, **Abusuliman M**, **Alluri S**, Almasri W, **Nabaty R**, and **Jafri SM**. Effect of Mammalian Target of Rapamycin (mTOR) Inhibitor Everolimus Upon Skin and Other Malignancy Following Liver Transplantation. *Am J Gastroenterol* 2024; 119(10):S1323. Full Text

S. Rehman, Henry Ford Health, Detroit, MI, United States

Introduction: Malignancy after solid organ transplant especially skin cancers is common phenomenon. Some case reports and small single center studies highlight various antioncogenic effects of mammalian target of rapamycin (mTOR) inhibitor class of immunosuppressants especially everolimus. This study aims to assess the incidence of post transplant skin malignancy and outcomes among liver transplant recipients on everolimus. Methods: A retrospective chart review of liver transplant recipients transplanted at a large tertiary center between 1/2015-12/2019 was conducted. Patients were split into 3 groups: not on everolimus post transplant (group 1), started on everolimus within 1 year of transplant and discontinued before 3 years (group 2) and on everolimus for at least 3 consecutive years (group 3). Demographic data including age and gender were collected with primary outcome assessing the incidence of skin cancer post transplant. Secondary outcomes assessed other post transplant malignancies including non-hepatic gastrointestinal malignancy, transplant rejection and death. Results: Among 381 liver transplant recipients, 67% were in group 1 (n=257), 15% in group 2 (n=59), 17% in group 3 (n=65). 25 patients in group 1 (9.7%), 4 in group 2 (6.8%) and 6 (9.2%) in group 3 developed some skin malignancy with squamous cell carcinoma the most common among all 3 groups (group 1 vs 3, P 50.835; group 2 vs 3, P 50.513). 26 patients in group 1 (10.1%), 6 in group 2 (6.8%) and 5 (7.7%) developed some other type of malignancy, and among other malignancies, hematologic was most common in group 1 (n=6, 23%) and non-hepatic gastrointestinal was most common in group 2 (n=4, 67%) and 3 (n=4, 80%). There was no significant difference in incidence of skin malignancy (group 1 vs 3, P = 0.835; group 2 vs 3, P 50.513), death (group 1 vs 3, P = 0.502; group 2 vs 3, P 50.611) or transplant rejection among the 3 groups (group 1 vs 3, P = 0.305; group 2 vs 3, P 50.066). Conclusion: Our data demonstrates everolimus did not have a protective effect against skin malignancy, other post transplant malignancies, transplant rejection or mortality in liver transplant patients. The data demonstrated that the duration of evrolimus therapy also had no effect on these variables. Whether these study findings were related to short duration of therapy or to a small sample size is unclear. Further investigations are warranted over a longer period of time and with other mTOR agents (see Table 1).

Internal Medicine

Rothstein Costris A, **Davydov E**, and **Levy S**. Rare Case of Hyperparathyroidism in Third Trimester Pregnancy Requiring Urgent Parathyroidectomy. *J Endocr Soc* 2024; 8:A257-A258. Full Text

A. Rothstein Costris, Henry Ford Hospital, Detroit, MI, United States

Introduction: Primary hyperparathyroidism (PHPT) during pregnancy has risks to both the mother and her fetus. Complications include maternal pre-eclampsia, miscarriage, hyperemesis gravidarum, nephrolithiasis and pancreatitis. Fetal complications encompass hypocalcemia, tetany, intrauterine growth retardation and fetal demise. Though medical treatment is available, parathyroidectomy is the only definitive treatment. Traditionally, surgery is done in the second trimester of pregnancy. We report a case of a third trimester parathyroidectomy in a 29 yo female with PHPT. Case representation: A 29-year-old G1P0 woman at 28 weeks gestation presented with persistent nausea and vomiting, constipation, joint pain, and increased forgetfulness. She has moved to USA from Saudi Arabia and had not received prenatal care in the USA. She was found to have a PTH of 224 (15-65 pg/mL), Calcium of 13.5 (8.2-10.2 mg/dL), Ionized Calcium of 1.63 (1.00-1.35 mmol/L), and a corrected Calcium of 14.2 (8.7-10.1 mg/dL). Electrolyte abnormalities were also noticed, with a Potassium of 2.8 (3.5-5 mmol/L), Phosphorus of 1.7 (2.5-4.5 mg/dL) and Magnesium of 1.2 (1.8-2.3 mg/ dL). Vit. D levels were found to be extremely low <7 (20-40 ng/mL). Due to severe dehydration, persistent nausea, vomiting, and hypercalcemia, the patient received fluid resuscitation and Vit. D supplementation. A neck CT scan identified an 11 x 6 x 14 mm

arterially hyperenhancing soft tissue structure at T1-T2, suggesting a probable parathyroid adenoma in the right paratracheal region. Management options included surgery or conservative therapy with fluids and Cinacalcet. A joint decision was made between Maternal Fetal Medicine, ENT and Endocrinology to proceed with parathyroidectomy. Surgical excision revealed an enlarged, hypercellular right inferior parathyroid gland (0.51g). Postoperative laboratory studies at 2 weeks showed normal PTH, Ca, Ionized Ca. Conclusion: It is preferable to conduct surgery for PHPT during the second trimester of pregnancy. However, when PHPT leads to severe symptoms, surgery might be considered in the third trimester. The severity of our patient's symptoms led to inability to tolerate oral intake, deeming surgery necessary. The multidisciplinary team agreed that surgery in the third trimester would be the best course of treatment as it will result in normocalcemia immediately. Second trimester parathyroidectomy is viewed as safer due to the completion of organogenesis and lower teratogenicity risks. Performance of surgery during the third trimester may lead to an increase in the risk of premature birth. However, untreated hypercalcemia may increase fetal loss and thus third trimester parathyroidectomy can be considered as a treatment option for PHPT in pregnancy. It is also imperative to discuss all options with the patient. In our case, the patient had opted for surgery which was successful.

Internal Medicine

Rothstein Costris A, **Yaseen A**, and **Levy S**. A Case of Severe Myxedema Coma with Levothyroxine Allergy. *J Endocr Soc* 2024; 8:A970. Full Text

A. Rothstein Costris, Henry Ford Hospital, Detroit, MI, United States

Introduction: Myxedema coma is a life threatening condition with a mortality rate of 25-60%. Untreated, it can lead to fatal physiological changes. The treatment is thyroid hormone replacement therapy, alongside supportive care for complications. Clinical Case: A 65-year-old woman, who has been dealing with untreated hypothyroidism since 2012 and reported allergies to various levothyroxine brands, presented with falls, weakness, and exacerbated leg numbness. During the examination, she exhibited periorbital edema, non-pitting edema in the lower extremities, bradycardia, and hypothermia. The blood work revealed an elevation in TSH levels at 301 uIU/L (0.45-5.33 uIU/mL). The patient was administered IV Synthroid (200 mcg), Atropine, and Hydrocortisone due to concerns about myxedema coma. After four hours, the patient experienced angioedema and hypotension, necessitating intubation. This situation was complicated by a pulseless electrical activity (PEA) arrest. Following cardiopulmonary resuscitation and the administration of epinephrine, the patient achieved return of spontaneous circulation. The allergy team assessed the patient for potential anaphylactic shock from IV Synthroid. Subsequently, the patient was initiated onIV Liothyronine and Hydrocortisone, leading to improvement in mental status over a period of a few weeks, and no adverse effects were reported. Thyroid labs improved to TSH of 53 (0.45-5.33 uIU/mL), FT3 of 3.3 (2.5-4.4 pg/mL) and total T3 of 133 (87-178 ng/dl). Upon discharge, the patient was prescribed Liothyronine, with plans to perform a Levothyroxine desensitization test in the outpatient setting. Conclusion: Myxedema coma is an endocrine emergency. Patients usually present with deteriorating mental status, hypothermia, and multiple organ system abnormalities. The diagnosis relies more on the clinical presentation and physical examination than on laboratory results. Thyroid replacement therapy serves as the cornerstone of treatment, with a preference for T4 due to its greater availability and lower likelihood of adverse events compared to Liothyronine, which may increase the risk of mortality at higher doses. Despite associated risks, incorporating low doses of Liothyronine is still considered in treatment plans, driven by concerns about reduced T4 to T3 conversion in myxedema patients. Hypersensitivity reactions to Levothyroxine are uncommon but may manifest as widespread hives, swelling, eczema-like skin rashes, elevated body temperature, and compromised liver function, with only one case reporting an anaphylactic reaction to Levothyroxine. In summary, the potential for experiencing an anaphylactic reaction to Levothyroxine exists, highlighting the need to contemplate alternative treatments, such as Liothyronine. Desensitization methods can be considered once the patient's condition is stable.

Internal Medicine

Saleem A, **Al-Juburi S**, **Alomari A**, **Chaudhary AJ**, **Abusuliman M**, **Faisal MS**, **Omeish H**, **Samad M**, Nayeem M, **Rehman S**, Abbasi AF, and **Jafri SM**. Exploring the Limits: Minimizing Immunosuppression and Its Adverse Effects. *Am J Gastroenterol* 2024; 119(10):S1254. Full Text

A. Saleem, Henry Ford Health, Detroit, MI, United States

Introduction: Post liver transplantation survival has substantially improved over the last few decades. Post-transplant management remains particularly challenging due to the intricate balance between immunosuppression and its adverse effects. Excess immunosuppression can be associated with metabolic disease, infection, and malignancy. Our study aims to delineate this balance to guide clinicians in their ability to safely minimize immunosuppression without predisposing to rejection. Methods: Our study included patients who have had a 10-year liver transplant course starting in 2013 and were on tacrolimus immunosuppression. Patients who expired between 2018 - 2023 and those without adequate clinical data were excluded. Mean 5-year tacrolimus troughs 5 years after transplant (2018 - 2023) were calculated. A mean trough level of 4 was used as a cutoff to subcategorize our patients into those with a 5 year mean trough of ≤4 or >4. We compared the incidence of rejection, infection, malignancies, hyperkalemia, and nephrotoxicity between these 2 groups during this time period. Results: In 2013, 79 patients underwent liver transplants at our center; 33 expired or had inadequate data and were excluded. Forty-four patients met inclusion criteria, 17 Females (38%), 27 Males (61%). The mean age for our patients was 54.6 with a standard deviation of 8.9. Etiologies of cirrhosis were hepatitis C (45.45%), alcohol (18.18%), nonalcoholic steatohepatitis (18.8%), cryptogenic (9.09%), primary biliary cirrhosis (4.55%), primary sclerosing cholangitis (2.27%), and cystic fibrosis (2.27%). Twenty-three (52%) patients had a mean 5-year tacrolimus trough greater than 4 and 21 (48%) less than 4. Three patients experienced rejection in the .4 group and 1 in the , 4 group; 2 patients in each group were hospitalized for infection; 2 patients developed a malignancy in the >4 group and 3 in the ,<4 group. Two patients developed nephrotoxicity in the , 4 group and 1 patient in the >4 group. No significant relationship between the mean 5-year trough and incidence of rejection, hyperkalemia, infection, cancer, and nephrotoxicity was found in our analysis (Figure 1). Conclusion: Our findings underscore clinicians' abilities to down titrate tacrolimus levels without an associated increased risk of rejection. Higher tacrolimus levels were also not associated with an increased incidence of cancer, infections, nephrotoxicity, or hyperkalemia. This discussion may benefit from larger sample sizes for increased generalizability.

Internal Medicine
Saleem A, **Al-Juburi S**, **Saad Faisal M**, **Chaudhary A**, **Alomari A**, **Abusuliman M**, **Toiv A**, **Samad M**, **Haque M**, and **Jafri SM**. MINIMIZATION OF IMMUNOSUPPRESSION BEYOND FIVE YEARS FOLLOWING LIVER TRANSPLANT: LONG TERM OUTCOMES ON REJECTION, MALIGNANCY, AND MORBIDITY. *Hepatology* 2024; 80:S1073-S1074. Full Text

A. Saleem, Henry Ford Medical Center, United States

Background: Post liver transplantation survival and graft preservation has substantially improved over the last few decades. Post-transplant management remains particularly challenging due to the intricate balance between immunosuppression and its adverse effects. Excess immunosuppression can be associated with metabolic disease, infection, and malignancy. Our study aims to delineate this balance to guide clinicians in their ability to safely minimize immunosuppression without predisposing to rejection. Methods: Our study included patients who have had a 10-year liver transplant course. Patients who underwent transplantation in 2013 and initiated tacrolimus were included. Patients who expired between 2018 - 2023 and those without adequate clinical data were excluded. Mean 5-year tacrolimus troughs 5 years after transplant (2018 - 2023) were calculated. A mean trough level of 4 was used as a cutoff to subcategorize our patients into those with a 5 year mean trough of ≤4 or >4. We compared the incidence of rejection, infection, malignancies, and hyperkalemia between the groups during this period. Results: 79 patients underwent liver transplants at our center in 2013. 33 expired or had inadequate data and were excluded. 44 patients met inclusion criteria, 17 Females (38%), 27 Males (61%). The mean age for our patients was 54.6 with a standard deviation of 8.9. Etiologies of cirrhosis were Hepatitis C (45.45%), Alcohol (18.18%), Nonalcoholic Steatohepatitis (18.8%), Cryptogenic (9.09%), Primary Biliary Cirrhosis (4.55%), Primary Sclerosing Cholangitis (2.27%), and Cystic Fibrosis (2.27%). 23 (52%) patients had a mean 5-year tacrolimus trough greater than 4 and 21 (48%) less than 4. 3 patients experienced rejection in the >4 group and 1 in the <4 group during this period. 2 patients in each group were hospitalized for

infection. 2 patients developed a malignancy in the > 4 group and 3 in the < 4 group. No statistically significant relationship between the mean 5-year trough and incidence of rejection, hyperkalemia, and infection was found in our analysis (Table 1). Conclusion: Our findings underscore clinicians' abilities to down titrate tacrolimus levels without an associated increased risk of rejection. Conversely, higher tacrolimus levels were also not associated with an increased incidence of cancer, infections, or hyperkalemia. Our study's results may reassure providers regarding the safety of minimizing immunosuppression. This topic can benefit from larger sample sizes for increased generalizability in the future.

Internal Medicine
Saleem A, **Chaudhary AJ**, **Jamali T**, **Samad M**, and **Tosch K**. Ileal Neuroendocrine Tumor: A Rare Incidental Finding. *Am J Gastroenterol* 2024; 119(10):S3012. Full Text

A. Saleem, Henry Ford Health, Detroit, MI, United States

Introduction: Ileal neuroendocrine tumors (NET) are rare, slow growing tumors that originate from enterochromaffin cells in the GI tract. The incidence of these tumors has been on the rise over the last few decades. Patients with small bowel NETs may initially be asymptomatic or may experience vague symptoms. Despite their indolent nature, these tumors may metastasize to the liver necessitating prompt diagnosis and treatment. We present the case of a rare, ileal neuroendocrine tumor discovered as an incidental finding. Case Description/Methods: We present the case of an asymptomatic 68-year-old African American man with a history of chronic kidney disease and tobacco use who underwent magnetic resonance imaging of the abdomen for evaluation of renal cysts. Imaging demonstrated complex renal cysts in addition to an incidental finding of a non-fatty enhancement of the ileocecal valve measuring 36 mm. Positron emission tomography scan demonstrated increased uptake in the cecum corresponding to the lesion along with non-specific uptake in adjacent ileocecal lymph nodes with no distant metastatic disease noted. Subsequent colonoscopy identified a partially obstructing tumor spanning more than half the intestinal lumen in the terminal ileum (Figure 1A). The mass was biopsied, and pathology revealed a grade 1, well differentiated neuroendocrine tumor with tumor cells positive for Cam 5.2, synaptophysin, and Ki67 < 3% (Figure 1B). A laparoscopic right hemicolectomy with small bowel resection was performed. Four out of thirteen excised adjacent lymph nodes were positive for metastatic neuroendocrine tumor. Our patient's postoperative course was complicated by ileus with eventual resolution. The case was discussed in a multidisciplinary tumor board and the decision for surveillance alone was made with a repeat computed tomography scan in 3 months. Discussion: Small bowel tumors represent less than 0.6% of all cancers with neuroendocrine tumors being the most common in this subset. More than half of these patients present with liver metastasis at the time of diagnosis. Liver metastasis may increase 5-year mortality by 10% - 20%, however, patients with liver metastasis are more likely to be symptomatic expediting diagnosis. Clinicians should be wary of certain risk factors predisposing patients to this pathology such as smoking and the presence of Crohn's disease or genetic syndromes such as MEN1. Given its indolent nature and the mortality associated with liver metastasis, prompt diagnosis and treatment is necessary in these patients.

Internal Medicine
Saleem A, **Malick AN**, **Alomari A**, **Faisal MS**, **Abusuliman M**, **Rehman S**, **Chaudhary AJ**, Ibrahim AM, **Jamali T**, and **Suresh S**. Investigating Fecal Calprotectin: Unmasking the Sneaky Subtypes of Non-IBD Colitis. *Am J Gastroenterol* 2024; 119(10):S178. Full Text

A. Saleem, Henry Ford Health, Detroit, MI, United States

Introduction: The current gold standard for diagnosing non-inflammatory bowel disease (IBD) colitis is colonoscopy with biopsy. Imaging and stool-based tests are also often utilized during initial evaluation to screen for intestinal inflammation. Fecal calprotectin (FC) is a sensitive marker in assessing IBD disease activity, but its utility in non-IBD colitis has not been extensively evaluated. In this study, we aim to assess the utility of fecal calprotectin as a screening test for various subtypes of non-IBD colitis. Methods: This was a retrospective study of clinic patients at a tertiary care medical system who presented with subacute or chronic diarrhea between 2013-2023. Patients who had an abnormal FC during their clinic visit and

underwent a colonoscopy within 3 months of this test result were included. Patients with a new or prior diagnosis of IBD or infectious colitis were excluded. Baseline patient characteristics, FC levels, histologic, and endoscopic findings on colonoscopy were collected from medical records. FC levels in patients with non-IBD colitis were compared to those without colitis. Results: 282 patients met our inclusion criteria, of which 36 had specific types of non-IBD colitis diagnosed based on histology. These clinical subtypes included microscopic colitis (66%), immune checkpoint inhibitor (ICI) colitis (14%), nonsteroidal anti-inflammatory drug induced colitis (6%), ischemic colitis (8%), radiation colitis (3%), and segmental colitis associated with diverticulosis (SCAD) (3%) (Figure 1). 233 patients had no gross or histologic features of colitis. The mean FC level of patients with a specific clinical subtype of non-IBD colitis was 246 (SD 265) compared to 90 (SD 284) in patients without colitis. Figure 1 shows the mean FC levels of patients diagnosed with each clinical sub-type of non-IBD colitis. A Mann-Whitney test was performed demonstrating a significant difference in these 2 groups ($P < 0.001$). Conclusion: Our study demonstrates a significant quantitative difference in FC level between patients with non-IBD colitis and those without colitis. However, this difference was primarily seen in patients with microscopic colitis and ICI colitis whereas patients with NSAID induced, ischemic, radiation colitis, and SCAD had FC levels similar to patients without colitis. These preliminary findings suggest that although FC shows promise as a screening marker for non-IBD colitis, clinicians should not rely too heavily on this test, especially when a patient has risk factors for a specific type of colitis. (Table Presented).

Internal Medicine

Saleem A, **Malick AN**, **Alomari A**, **Haque M**, **Faisal MS**, **Abusuliman M**, **Chaudhary AJ**, **Jamali T**, **Brennan B**, and **Suresh S**. Unraveling the Role of Fecal Calprotectin and CT Imaging in Non-IBD Colitis. *Am J Gastroenterol* 2024; 119(10):S178-S179. Full Text

A. Saleem, Henry Ford Health, Detroit, MI, United States

Introduction: Current literature details the utility of computed tomography (CT) imaging and its correlation with pathologic inflammation in inflammatory bowel disease (IBD). Higher fecal calprotectin levels in IBD patients have been associated with a greater likelihood of abnormalities noted on CT imaging. This relationship has not been explored in non-IBD colitis. We seek to elucidate the correlation between abnormalities on imaging and histologic colitis in the context fecal calprotectin (FC) with the hopes of commenting on the utility of CT imaging in assessing disease activity in non-IBD colitis. Methods: This was a retrospective study of clinic patients at a tertiary care medical system who presented with subacute or chronic diarrhea between 2013 - 2023. Patients who had an abnormal FC test during their clinic visit followed by a colonoscopy within 3 months of this test result were included. Patients with a new or prior diagnosis of IBD or infectious colitis were excluded. Baseline patient characteristics, CT imaging findings within a 4-month window, FC levels, histologic, and endoscopic findings on colonoscopy were collected from medical records. Imaging findings were compared between patients with high (>50 mg/g) and normal (< 50 mg/g) FC levels in patients with histologically proven non-IBD colitis. Results: 282 patients met the inclusion criteria, of which 43 patients were diagnosed with non-IBD colitis based on histology. These 43 patients were stratified into 2 cohorts based on FC levels and the presence or absence of colitis on imaging. 28 patients had an elevated FC while 14 patients had normal FC. Of these 43 patients, 28 underwent CT imaging between their clinic visit and colonoscopy. 11 of these patients had abnormal CT imaging demonstrating colitis while 17 patients had normal imaging. A logistic regression analysis was performed to explore the relationship between FC and abnormal CT imaging which revealed no statistically significant correlation ($P = 0.6$). Figure 1 shows the distribution of normal and abnormal imaging findings in each cohort. Conclusion: Our study demonstrates no significant relationship between FC levels and CT imaging findings in patients with non-IBD colitis. This finding contrasts with studies showing an association between FC and abnormal imaging in patients with IBD. Clinicians should maintain high suspicion for non-IBD colitis in patients with high FC levels regardless of normal CT imaging and pursue appropriate diagnostic workup when otherwise indicated. (Table Presented).

Internal Medicine

Salem AE, Abosheaishaa H, Elfert K, Baqir SM, Zaaya M, Siriya P, Meribout S, Kodilinye SM, Mohammadrezaei F, **Abusuliman M**, Parraga CB, Mohamed I, Sandhu SPS, Ibrahim M, DiLeo DA, Roland BC, and Jovani M. Incidence of Gallstone Formation in Type 2 Diabetes Patients Treated With GLP-1 Agonists: A 24-Month Prospective Study. *Am J Gastroenterol* 2024; 119(10):S1534. Full Text

A.E. Salem, Maimonides Medical Center, Brooklyn, NY, United States

Introduction: This prospective study aimed to investigate the incidence of gallstone formation in patients with type 2 diabetes undergoing treatment with glucagon-like peptide-1 (GLP-1) agonists for weight loss. Methods: A cohort of 229 patients with type 2 diabetes prescribed GLP-1 agonists for weight management was followed over 24 months. Baseline data, including demographics, clinical characteristics, and metabolic profiles, were recorded. Regular ultrasonography was performed to detect gallstone development at baseline, 6, 12, 18, and 24 months. Logistic regression analysis was used to evaluate the association between GLP-1 agonist use and gallstone formation, adjusting for age, gender, duration of diabetes, body mass index (BMI), and GLP-1 agonist type. Subgroup analyses explored the impact of various GLP-1 agonists on gallstone risk. Results: Throughout the study period, 78 out of 229 patients (34%) developed gallstones. The cumulative incidence rate of gallstone formation was 33.6% (95% confidence interval [CI]: 27.6%-39.6%). Significant differences were observed across various subgroups. Patients with a diabetes duration longer than 10 years had an incidence rate of 44.6% (95% CI: 34.8%-54.4%), whereas those with a BMI over 30 had an incidence rate of 39.8% (95% CI: 31.1%-48.5%). Among the GLP-1 agonists, patients treated with liraglutide had a 35.7% incidence rate (95% CI: 27.2%-44.2%), while those on semaglutide had a 31.6% rate (95% CI: 24.1%-39.1%). At univariate logistic regression analysis the association between GLP-1 agonist therapy and gallstone development with an adjusted odds ratio (OR) of 2.1 (95% CI: 1.5-2.9, $P < 0.01$).Multivariable analysis adjusted for age, gender, duration of diabetes, BMI, and specific GLP-1 agonist preserved the strength of this association (adjusted OR 2.1; 95% CI: 1.5-2.9, $P < 0.01$), underscoring the heightened risk of gallstones in this patient population. Conclusion: In this prospective we found that there is an increased risk of gallstone formation in patients with type 2 diabetes treated with GLP-1 agonists for weight loss. The findings underscore the necessity for clinicians to recognize this potential complication and implement vigilant monitoring strategies. Tailored patient management plans, including regular ultrasonographic screening and individualized risk assessments, are recommended to mitigate the risk of gallstones in patients undergoing GLP-1 agonist therapy. .

Internal Medicine

Salem AE, Baqir SM, Zaaya M, Kodilinye SM, Abosheaishaa H, Parraga CB, Elfert K, Mohamed I, **Abusuliman M**, Meribout S, Elnaggar M, Chaudhry MA, Siriya P, Roland BC, DiLeo DA, and Jovani M. Pyloric Gastric Adenoma With Low Grade Dysplasia in an Asymptomatic 50-Year-Old Asian Female With Negative H. Pylori. *Am J Gastroenterol* 2024; 119(10):S2642. Full Text

A.E. Salem, Maimonides Medical Center, Brooklyn, NY, United States

Introduction: Pyloric gastric adenoma (PGA), a rare precancerous lesion, is prevalent in populations with a high incidence of gastric cancer. A meta-analysis indicates that tumors larger than 2 cm with a depressed or nodular surface may lead to increased dysplasia after endoscopic resection. This case details the incidental discovery of a 3 cm granular flat lesion in the cardia during esophagogastroduodenoscopy (EGD) in an asymptomatic 50-year-old Asian woman. The aim is to shed light on the management of pyloric gastric adenoma in the Western context, where its low prevalence makes it less recognized. Case Description/Methods: A 50-year-old East-Asian woman with a history of iron deficiency anemia underwent EGD, unveiling a 3 cm granular lesion (Paris 0-IIa, NICE type 2, pit pattern III) at the cardia/ fundus junction. Biopsies confirmed pyloric adenoma with low-grade dysplasia. No other gastric lesions seen. Decision was made to proceed to endoscopic submucosal dissection (ESD). A resected 8 x 4 cm specimen showed no reverse target sign. Pathology revealed pyloric adenoma with low-grade dysplasia, and margins were negative. Discussion: The 2019 WHO classification categorizes gastric adenomas into intestinal or gastric origin, with pyloric gland adenoma in Japan and highly differentiated adenocarcinoma for foveolar-type intraepithelial neoplasia/adenoma. More common

in Asia, these lesions are less frequent in the West. PGA is more common in females (3:1), possibly associated with autoimmune gastritis. Approximately 2% of gastric polyps are PGAs, typically in geriatric females with autoimmune gastritis or chronic mucosal damage, with an average age at diagnosis of about 60 years old. High-grade PGAs often exhibit tubulovillous architecture. Overall, PGAs progress to adenocarcinoma in 12%-47% of cases within 10-48 months (60%-85% for HGD and 23% for LGD). Hence, it is imperative to remove them early.No clear therapeutic guidelines exist for gastric low-grade dysplasia (LGD) management, necessitating case-by-case decisions. Given the patient's age and lack of comorbidities, a joint decision favored endoscopic resection, with ESD chosen over endoscopic mucosal resection (EMR) for its en-bloc capability. The patient underwent close follow-up with an EGD in 3 months. The scar from previous ESD was biopsied, and it was negative for recurrence. This case highlights a rare gastric lesion in Western countries and adequate endoscopic treatment of the same with ESD. (Figure Presented).

Internal Medicine
Salem AE, Mujtaba Baqir S, Meribout S, Abosheaishaa H, Zaaya M, **Abusuliman M**, Mohamed I, Parraga CB, Kodilinye SM, Siriya P, Elfert K, DiLeo DA, and Roland BC. Optimizing Clinical Outcomes: The Efficacy of Biofeedback Therapy (BFT) in Managing Resistant Fecal Incontinence. *Am J Gastroenterol* 2024; 119(10):S555. Full Text

A.E. Salem, Maimonides Medical Center, Brooklyn, NY, United States

Introduction: Fecal incontinence (FI) is widespread and socially devastating. Few effective treatments exist. Conservative therapy offers limited benefit. Prior studies show mixed success with biofeedback therapy (BFT) in FI. While BFT is established for dyssynergic defecation (DD), its efficacy in FI patients after failed conservative therapy is uncertain. Our aims were: 1) Assess BFT response in these patients; 2) Evaluate non-BFT therapy response rates; 3) Identify predictive risk factors for BFT treatment failure. Methods: We reviewed consecutive FI patients referred for high-resolution anorectal manometry at a single tertiary care center from 1/2021-7/2022. BFT was recommended for DD, weak sphincter tone, low resting pressure, or impaired/heightened intrarectal sensation. Additional therapeutic strategies assessed included conservative management, injection of “bulking agent” (e.g. Solesta), sacral nerve stimulation (SNS), & surgery. Conservative therapy included stool bulk forming agents and/or anti-diarrheals. Clinical success after 5 sessions of BFT was defined as at least 50% reduction in FI episode frequency/week. Results: A total of 513 completed ARM within the study period; 111 (22%) patients were referred for FI. Of this subgroup, 25 were initially treated with conservative measures, but only 6 (24%) reported benefit, while 19 (76%) reported no benefit ($P < 0.0001$). Overall, 46 (41%) patients were referred to BFT and of those, 29 (63%) completed the BFT therapy sessions. Of these, the majority reported benefit (n=22, 76% vs no benefit in 24%, $P < 0.0001$). Of the 7 patients who failed BFT, 4 were referred for additional treatments (SNS, n=1; Solesta, n=1; surgery, n=2). When looking at predictors of BFT failure, only pelvic organ prolapse and neurologic disease were significantly associated with lack of response. Conclusion: The management of FI remains challenging with limited therapeutic options. Our results show the majority of FI patients who fail to improve with conservative measures can improve with BFT. The only predictors of BFT treatment failure were pelvic organ prolapse and neurologic disease. Our findings suggest that BFT is of significant benefit in FI patients who have failed conservative therapies and may be considered a reasonable treatment strategy. Large-scale, prospective studies are needed to further delineate the efficacy of BFT and predictors of clinical response.

Internal Medicine
Salem AE, Zaaya M, Mujtaba Baqir S, Siriya P, Meribout S, Parraga CB, Kodilinye SM, Abosheaishaa H, **Abusuliman M**, Chaudhry MA, Sandhu SPS, Elfert K, Mohamed I, Roland BC, DiLeo DA, and Jovani M. Incidental Finding of Colitis Cystica Profunda in Routine Colorectal Screening. *Am J Gastroenterol* 2024; 119(10):S2144. Full Text

A.E. Salem, Maimonides Medical Center, Brooklyn, NY, United States

Introduction: Colitis Cystica Profunda (CCP) is a rare, non-malignant condition characterized by cysts filled with mucus in the submucosa and muscularis mucosa layer, bordered by flattened epithelial cells of

the colon. Recognizing CCP is crucial due to its potential to imitate well-differentiated rectal adenocarcinoma, possibly leading to unwarranted surgical resection. We report a case of CCP found during routine colonoscopy in a 48-year-old woman. Case Description/Methods: A 48-year-old woman with emphysema, generalized anxiety disorder, and latent tuberculosis (treated 16 years ago) was referred for her first colonoscopy for colorectal cancer screening. She was overweight (body mass index 29.41), an active smoker, and a cannabis user. Her family history included stomach cancer (maternal aunts and cousins died at ages 49 and 52 years-old). She denied symptoms or family history of colon cancer or inflammatory bowel disease. Her only medication was an albuterol inhaler. She had a robotic-assisted laparoscopic cholecystectomy 8 years prior. Her vital signs and physical exam were normal.The colonoscopy revealed a 2mm sessile polyp in the mid-rectum, 2 non-bleeding angiodysplasia lesions in the proximal ascending colon and recto-sigmoid colon, and small non-bleeding internal hemorrhoids. The patient went home without complications. Pathology report of the 2mm polyp showed CCP (submucosal herniation of mucosa), with no neoplastic component. The patient was asymptomatic during the follow-up visit after 3 weeks and was scheduled for a repeat colonoscopy in 3 years. Discussion: The pathophysiology of CCP involves congenital or acquired muscularis mucosa weakening from inflammation, infection, trauma, and ischemia. CCP can be classified as diffuse or localized. Endoscopic examination reveals polypoid lesions surrounded by normal, edematous, or ulcerated mucosa. Anorectal ultrasound shows a hypoechoic signal in the submucosal layers, without deeper infiltration. As CCP resembles rectal adenocarcinoma, early endoscopic submucosal dissection and biopsy are necessary for diagnosis and treatment. Management includes diet changes, biofeedback therapy, and medications like sucralfate and hydrocortisone enema. Surgery might be required for large lesions that cause obstructive symptoms, chronic hemorrhage, or rectal prolapse.

Internal Medicine

Samad M, **Desai S**, **Marougail V**, **Sherbin E**, **Saleem A**, **Dababneh YJN**, and **Suresh S**. Smoking Can Reduce Treatment Response in Microscopic Colitis. *Am J Gastroenterol* 2024; 119(10):S219. Full Text

M. Samad, Henry Ford Hospital, Rochester Hills, MI, United States

Introduction: While existing research has focused on the association of specific risk factors with the development of microscopic colitis (MC), investigation of determinants affecting treatment response for MC patients is limited. The study aims to analyze whether certain risk factors affect treatment response in patients receiving initial therapy for MC. Methods: A retrospective cohort study was conducted at a single urban quaternary care center and consisted of 176 patients that received a new diagnosis of MC in the ambulatory setting. Demographic data, chronic medication use, comorbidities, and smoking status were collected for each patient. Patients received initial treatment and their daily number of bowel movements were recorded before and after therapy. Their response to treatment was the primary outcome. Treatment response was recorded as remission (complete resolution), partial response (>50% response), non-response (< 50% response), or intolerance due to medication side effect. Results: In total, 58 patients (33% of total cohort) achieved clinical remission while 90 (51%) had a partial response and 25 (14%) patients had no response to treatment. An additional 3 (2%) patients had intolerance to initial treatment. A univariate analysis assessing individual risk factors revealed that patients who were actively smoking had a significantly higher frequency of non-response to initial therapy (22%) compared to non-smokers (10%) ($P = 0.007$). No other risk factors studied had a significant effect on response to initial treatment in MC. Conclusion: This study demonstrates an association between active smoking and poor response to initial treatment in patients with MC. While active smoking is a known risk factor for the development of MC, this study reveals that smoking cessation is also a key component in achieving successful remission of this disease process. Further prospective multicenter studies are needed to explore the relationship between smoking and decreased treatment response and to minimize confounding variables. (Table Presented).

Internal Medicine

Samad M, **Desai S**, **Marougail V**, **Sherbin E**, **Saleem A**, **Dababneh YJN**, and **Suresh S**. Pill Poppers and Poop Problems: How Drug Exposure Affects Microscopic Colitis Recurrence Rates. *Am J Gastroenterol* 2024; 119(10):S220. Full Text

M. Samad, Henry Ford Hospital, Rochester Hills, MI, United States

Introduction: There is growing evidence that certain medications are associated with the development of microscopic colitis (MC), especially in the elderly population. However, there is limited data on how patients who are on these medications respond to treatment for MC and if they are at higher risk for disease recurrence. The study aims to analyze whether specific chronic medications are associated with higher disease recurrence rates following initial treatment in patients with MC. Methods: A retrospective cohort study was conducted at a single, urban quaternary care center in the midwestern United States and consisted of 176 patients who received a new diagnosis of MC. Data points that were collected included chronic medication usage of beta blockers, proton pump inhibitors, H2 receptor antagonists, aspirin or non-steroidal anti-inflammatory, angiotensin receptor inhibitors, mineralocorticoid receptor antagonist, serotonin reuptake inhibitors, or oral hypoglycemic medications. Chronic medication usage was defined as taking the medication 3 times weekly for at least 2 weeks prior to presentation. The primary outcome measured was recurrence of symptoms, defined as lack of treatment response following initial therapy and re-presentation to the gastroenterology clinic within 1 year following initial treatment. Results: A univariate analysis of chronic medications and recurrence revealed a significant association between use of oral hypoglycemic medications and increased MC recurrence rates (Table 1). 15 patients from the cohort used oral hypoglycemic medications. A subgroup analysis revealed the most common drug used in this class was metformin. However, metformin was not independently associated with recurrence in patients treated for MC. Conclusion: Although oral hypoglycemic drugs have been previously shown to be a risk factor in development of MC, our study demonstrates that this class of medications is also associated with higher rates of symptom recurrence following an initial treatment course. While this does not necessarily establish a cause-effect relationship, future studies should focus on the proposed potential pharmacologic risk factors of oral hypoglycemic drugs on MC recurrence. (Table Presented).

Internal Medicine
Samad M, **Suresh S**, **Sherbin E**, **Desai S**, **Marougail V**, and **Dababneh YJN**. Prescriber Practices and Their Impact on Recurrence Rates in Microscopic Colitis. *Am J Gastroenterol* 2024; 119(10):S219-S220.
Full Text

M. Samad, Henry Ford Hospital, Rochester Hills, MI, United States

Introduction: Microscopic colitis (MC) is a challenging disease to manage due to the high likelihood of disease recurrence following initial treatment. Some studies have shown that up to 80% of patients initially treated with budesonide experience symptoms within 3 months of stopping the medication. This study aimed to examine how various initial treatments prescribed for patients with newly diagnosed MC impact rates of short-term disease recurrence. Methods: A retrospective cohort study was conducted at a single, urban quaternary care center in the midwestern United States and consisted of 176 patients who presented in the ambulatory setting and received a new histologic diagnosis of MC. Data points that were collected including various patient demographics and initial treatment prescribed. Primary outcome measured was recurrence of symptoms, defined as lack of sustained treatment response following initial therapy and re-presentation to the gastroenterology clinic within 1 year following initial treatment. Results: 59 (34%) patients were treated initially with a budesonide 2-month taper and 53 (30%) patients were treated with a fixed daily dose of budesonide defined as a 2-month course. Additional treatments included 22 (12%) patients who received loperamide, 2 (5%) patients who received bismuth subsalicylate and 3 (8%) patients who received bile acid sequestrants. Other treatments included prednisone, sulfasalazine, and diphenoxylate/atropine which were prescribed in 7 (19%) of patients. A total of 40 (23%) patients who were treated with these medications experienced short-term recurrence of symptoms. A univariate analysis revealed no significant association between initial therapy attempted and frequency of recurrence (Table 1). Conclusion: This study found that the choice of initial treatment does not seem to impact symptom recurrence rates in patients with MC. This suggests that clinicians may tailor their initial choice of therapy to each patient while considering factors such as potential drug interactions and financial constraints without being concerned about decreased efficacy. These findings would benefit from validation on a larger scale since most patients in our cohort received initial treatment with budesonide while other treatments were prescribed far more infrequently. (Table Presented).

Internal Medicine

Samad M, **White C**, **Rehman S**, **Brahmbhatt N**, **Memon M**, **Youssef RM**, **Saleem A**, **Ali H**, and **Jafri SM**. Safety and Tolerability of Orthopedic Surgery Following Liver Transplants. *Am J Gastroenterol* 2024; 119(10):S1359. Full Text

M. Samad, Henry Ford Hospital, Rochester Hills, MI, United States

Introduction: Immunosuppression poses a potential risk for infectious complications following surgery. While most elective and some non-elective orthopedic procedures are generally safe, their post operative infectious complications in liver transplant patients are understudied. Our purpose of this study is to evaluate risk factors for development of short-term infectious complications following elective and nonelective orthopedic surgeries in liver transplant patients. Methods: The study design is a retrospective cross-sectional study. Data extraction using SlicerDicer was used to identify patients who underwent liver transplantation and elective and non-elective orthopedic surgeries following transplantation from 2013-2022. Data collected included demographics, number of months following transplant, type of orthopedic surgery, and immunosuppression at time of orthopedic surgery. Primary outcomes included infection within 30 days of orthopedic surgery and death within 3 months. Results: A total of 87 patients were identified. The average patient age was 67.5 years at the time of orthopedic surgery. The mean length of time from transplantation to orthopedic surgery was 87 months. Elective surgeries comprised more of the population with 26 undergoing total knee arthroplasty (30%) and 19 undergoing total hip arthroplasty (22%). Non-elective surgeries included open reduction internal fixation (ORIF) and closed reduction internal fixation (CRIF) following acute fracture, comprising of 16 patients (18%). Infections within 30 days were identified in 4 patients, 2 of which underwent total hip arthroplasty. However, there is no significant association between infections within 30 days and type of surgery or immunosuppression at the time of surgery. Additionally, there were no patient deaths that resulted from infection. Conclusion: We evaluated outcomes following orthopedic surgeries in patients following liver transplantation. Our results support the safety and efficacy of these surgeries following liver transplantation.

Internal Medicine

Shahzil M, Akram Qureshi A, Hasan F, Jamil Z, Kashif TB, **Chaudhry AJ**, **Faisal MS**, Khaqan MA, and Farooq U. Efficacy and Tolerability of Linaclotide Combined with Polyethylene Glycol for Bowel Preparation: A Meta-Analysis. *Am J Gastroenterol* 2024; 119(10):S350-S351. Full Text

M. Shahzil, Penn State Health Milton S. Hershey Medical Center, Hershey, PA, United States

Introduction: Colonoscopy is the gold standard for both screening and prevention of colorectal cancer (CRC). The success of the procedure relies heavily on adequate bowel preparation to enhance diagnostic accuracy and therapeutic outcomes. Polyethylene glycol (PEG) is the standard bowel prep solution, but its high volume can cause patient discomfort and non-compliance. Combining PEG with linaclotide may offer comparable cleansing efficacy with better tolerability. This meta-analysis aims to evaluate the effectiveness and safety of linaclotide combined with PEG for bowel preparation. Methods: This meta-analysis, following Cochrane and PRISMA guidelines, compared linaclotide plus PEG versus PEG alone for bowel preparation. Comprehensive searches across multiple databases until March 2023 included randomized controlled trials with adults undergoing colonoscopy. Data extraction used PICOS criteria and a predefined Excel template. Statistical analyses were conducted using RevMan with a random-effects model, considering results significant at $p < 0.05$. Results: Of 1533 screened studies, seven with 3213 patients were included. The linaclotide plus PEG group had 1708 patients, and the PEG only group had 1505. Adequate bowel preparation showed no significant difference between groups (OR: 1.23; 95% CI: 0.94, 1.61; I2 = 0%). Total Boston Bowel Preparation Scale (BBPS) scores were also similar (MD: 0.30; 95% CI: -0.02, 0.62; I2 = 93%). The left colon BBPS score showed significant improvement with linaclotide (MD: 0.09; 95% CI: 0.01, 0.17; I2 = 77%). Fewer adverse events were noted in the linaclotide group, including less abdominal discomfort (RR: 0.42; 95% CI: 0.21, 0.83; I2 = 87%), pain (RR: 0.47; 95% CI: 0.24, 0.91; I2 = 43%), bloating (RR: 0.46; 95% CI: 0.24, 0.90; I2 = 72%), nausea (RR: 0.66; 95% CI: 0.49, 0.89; I2 = 25%), and vomiting (RR: 0.55; 95% CI: 0.33, 0.92; I2 = 38%). Other outcomes, including cecal intubation rate, polyp detection rate, adenoma detection rate, sleep disturbance, and withdrawal time, showed no significant differences. Conclusion: This meta-analysis suggests that linaclotide plus

PEG provides similar bowel cleansing efficacy to standard PEG with improved patient tolerability. Additionally, no substantial differences were observed in other procedural metrics, such as cecal intubation and detection rates. Further research is needed to standardize bowel preparation protocols, confirm these findings across diverse populations, and optimize colonoscopy outcomes. (Figure Presented).

Internal Medicine
Shahzil M, Azeem S, Jamil Z, **Chaudhry AJ**, Shabbir A, Rehmani M, **Faisal MS**, Khaqan MA, and Warraich MS. Comprehensive Evaluation of the Efficacy and Safety of the Clostridioides difficile Toxoid Vaccine: A Meta-Analysis. *Am J Gastroenterol* 2024; 119(10):S233-S234. Full Text

M. Shahzil, Penn State Health Milton S. Hershey Medical Center, Hershey, PA, United States

Introduction: Clostridioides difficile (C. difficile), a gram-positive bacterium, causes significant morbidity and mortality, particularly in hospitalized individuals over 65 and those recently on antibiotics. Current treatments include antibiotics and fecal transplants for recurrent cases. Given the role of humoral immunity, toxoid vaccines targeting toxins A (TcdA) and B (TcdB) show promise. This meta-analysis evaluates the safety, immunogenicity, and efficacy of the C. difficile toxoid vaccine. Methods: This meta-analysis followed Cochrane and PRISMA guidelines, comparing the efficacy of C. difficile toxoid vaccine (50, 100, and 200 ug doses) against a normal saline placebo. Comprehensive searches were conducted across PubMed, Embase, Scopus, and Cochrane CENTRAL databases up to January 2023, focusing on randomized controlled trials (RCTs). Data extraction adhered to PICOS criteria and utilized Excel. Statistical analyses were performed with RevMan using a random-effects model ($P < 0.05$). Results: From 3,057 screened studies, 8 were eligible, including 11,717 patients (7903 vaccine and 3814 placebo). Six studies in the day regimen showed significant increases in Geometric Mean Concentrations (GMC) for Toxin A (MD: 2048.05) and Toxin B (MD: 2453.98), and significant seroconversion rates for Toxin A (RR: 23.28) and Toxin B (RR: 19.23). Local adverse effects included increased pain (RR: 3.02), swelling (RR: 8.53), and erythema (RR: 6.78). The 100ug month regimen showed significant GMC increases for Toxin A (MD: 935.01) and Toxin B (MD: 3995.16), with increased pain (RR: 5.39), swelling (RR: 4.91), and erythema (RR: 4.17). The 200ug month regimen showed significant GMC increases for Toxin A (MD: 1246.80) and Toxin B (MD: 6700.23), with elevated seroconversion rates for Toxin A (MD: 77.97) and Toxin B (MD: 66.59). Local adverse effects included increased pain (RR: 5.46), swelling (RR: 4.02), and erythema (RR: 2.69). Systemic adverse effects varied, with some increases in headache and myalgia but overall manageable side effects. Conclusion: This meta-analysis shows that the C. difficile toxoid vaccine elicits robust immune responses and maintains a favorable safety profile across dosages. Despite some variability and evidence quality limitations, the vaccine shows promise in preventing CDI by targeting toxins A and B. Further research is needed to translate immunogenicity into clinical benefits, paving the way for an effective CDI vaccine. (Table Presented).

Internal Medicine
Shahzil M, **Chaudhry AJ**, Kashif TB, Khaqan MA, Jamil Z, Munir L, **Faisal MS**, and Ali H. Assessing the Effectiveness of Texture and Color Enhancement Imaging (TXI) versus White-Light Endoscopy (WLE) in Detecting Gastrointestinal Lesions: A Comprehensive Meta-Analysis. *Am J Gastroenterol* 2024; 119(10):S638-S639. Full Text

M. Shahzil, Penn State Health Milton S. Hershey Medical Center, Hershey, PA, United States

Introduction: Texture and Color Enhancement Imaging (TXI) is an innovative technology introduced by Olympus in the EVIS X1 endoscopy system. It enhances mucosal visualization and increases polyp detection rates without compromising the brightness or color spectrum of white-light endoscopy (WLE). This meta-analysis assesses TXI's effectiveness in detecting gastrointestinal (GI) lesions compared to WLE, aiming to evaluate TXI's clinical utility. Methods: This meta-analysis adhered to Cochrane guidelines and PRISMA standards, comparing TXI versus WLE for GI lesions. A comprehensive search across PubMed, MEDLINE, Embase, Scopus, and CENTRAL up to May 2024 included RCTs and observational studies of patients undergoing endoscopy. Data extraction followed PICOS criteria using Excel, and statistical analyses were conducted with RevMan using a random-effects model, with

significance at P < 0.05. Results: From 2,000 screened studies, 17 studies encompassing 15,929 patients undergoing endoscopic procedures were selected. The TXI group included 3,944 patients, while the WLE group had 11,985 patients. The primary outcomes demonstrated significant enhancements with TXI, specifically in the color difference between lesions and surrounding mucosa (Mean difference [MD]: 3.55; 95% CI: 2.63, 4.46) and the visibility score of lesions (MD: 0.42; 95% CI: 0.21, 0.63). Secondary outcomes revealed a marked increase in the adenoma detection rate (ADR) (Odds ratio [OR]: 1.84; 95% CI: 1.52, 2.22). Additionally, TXI showed superior efficacy in polypoid ADR (OR: 1.66; 95% CI: 1.31, 2.12) and visibility scores stratified by lesion characteristics, including vessel pattern (MD: 0.75; 95% CI: 0.47, 1.03), surface pattern (MD: 0.82; 95% CI: 0.60, 1.04), and margin pattern (MD: 0.55; 95% CI: 0.23, 0.87). Furthermore, visibility scores for sessile serrated lesions (SSL) and hyperplastic polyps (HP) (MD: 0.58; 95% CI: 0.15, 1.01), along with the mean adenoma detection rate per procedure (MD: 0.64; 95% CI: 0.32, 0.95), demonstrated significant improvement with TXI. Conclusion: This meta-analysis provides compelling evidence supporting the superiority of Texture and Color Enhancement Imaging (TXI) over White-Light Endoscopy (WLE) in detecting gastrointestinal lesions. The significant improvements in color differentiation, visibility scores, and adenoma detection rates underscore TXI's value as a powerful tool for endoscopic procedures, offering a promising advancement in gastrointestinal imaging (see Table 1).

Internal Medicine

Shahzil M, Fatima M, **Faisal MS**, Rehmani M, **Chaudhry AJ**, Khaqan MA, and **Faisal MS**. Efficacy of Submucosal Injection in Endoscopic Papillectomy for Ampullary Tumors: A Meta-Analysis. *Am J Gastroenterol* 2024; 119(10):S1157-S1158. Full Text

M. Shahzil, Penn State Health Milton S. Hershey Medical Center, Hershey, PA, United States

Introduction: Ampullary adenomas, originating from the ampulla of Vater (AoV), require complete resection due to their precancerous nature. Endoscopic papillectomy offers a less invasive alternative to surgery, but the use of submucosal injection (SI) in this procedure is not standardized, and its efficacy remains unclear due to the unique anatomy of the AoV. This meta-analysis evaluates the clinical efficacy of SI versus no injection before endoscopic papillectomy, focusing on complete resection rates and prevention of complications. Methods: This meta-analysis followed Cochrane and PRISMA guidelines, comparing submucosal injection versus no injection in endoscopic papillectomy for ampullary tumors. We searched PubMed, Embase, Scopus, and Cochrane CENTRAL databases up to May 2024, including RCTs and observational studies. Data extraction followed PICOS criteria using Excel, and statistical analyses were performed with RevMan using a random-effects model (P < 0.05). Results: From 203 screened studies, 4 studies with 322 patients undergoing endoscopic papillectomy were selected. The SI group included 134 patients, while the non-SI group had 116 patients. Primary outcomes assessed included en bloc resection (OR: 1.17; 95% CI: 0.49, 2.77), complete resection (OR: 0.55; 95% CI: 0.27, 1.15), and no evidence of residual tumor after long-term follow-up (OR: 0.55; 95% CI: 0.21, 1.42), with no significant differences between groups. Secondary outcomes showed no significant differences in positive deep resection margin (OR: 1.88; 95% CI: 0.62, 5.73), positive lateral resection margin (OR: 2.19; 95% CI: 0.71, 6.72), and overall positive resection margin (OR: 0.65; 95% CI: 0.19, 2.16). Pathologic findings of adenocarcinoma and adenoma were similar. Adverse events, including post-papillectomy bleeding, pancreatitis, perforation, cholangitis, and papillary stricture, showed no significant differences between the SI and non-SI groups. Conclusion: This meta-analysis provides comprehensive evidence indicating no significant benefit of submucosal injection (SI) over no injection in endoscopic papillectomy for ampullary tumors. The lack of significant differences in en bloc resection, complete resection, absence of residual tumors after long-term follow-up, and adverse events suggests that routine SI in endoscopic papillectomy may not offer additional clinical advantages. Further research and broader clinical evaluations are needed to optimize endoscopic techniques for treating ampullary tumors. (Table Presented).

Internal Medicine

Shahzil M, Habiba U, **Qureshi MA**, **Faisal MS**, Mukhtar R, Khaqan MA, and **Chaudhry AJ**. Evaluating Outcomes and Perioperative Complications of Combined Heart and Liver Transplantation in Patients With Failing Fontan Physiology: A Systematic Review. *Am J Gastroenterol* 2024; 119(10):S1377. Full Text

M. Shahzil, Penn State Health Milton S. Hershey Medical Center, Hershey, PA, United States

Introduction: Significant advancements in treating single-ventricle congenital heart disease have improved survival rates, leading to an increase in adults with Fontan physiology who require heart transplants due to end-stage heart failure. Concurrently, the incidence of Fontan-associated liver disease (FALD) has risen, necessitating more combined heart and liver transplants (CHLT). However, data on posttransplant outcomes for these patients remain limited and inconclusive. This systematic review evaluates perioperative complications, post-transplant survival, and factors influencing outcomes in patients undergoing CHLT for FALD, aiming to improve patient selection and timing for these complex procedures. Methods: This systematic review followed Cochrane guidelines and PRISMA standards to evaluate CHLT outcomes for failing Fontan physiology. Comprehensive searches across PubMed, Embase, Web of Science, and Cochrane CENTRAL up to May 2024 included randomized controlled trials and observational studies. Data extraction used PICOS criteria via Excel. Due to varied findings, a meta-analysis was not feasible; thus, a narrative synthesis was conducted. Results: From 437 screened studies, 8 studies encompassing 305 patients undergoing CHLT for FALD and heart failure were included. The mean patient age was 37.7±14 years, and 45% were male. The mean cardiopulmonary bypass time was 282±125 minutes. Red blood cell transfusions ranged from 3 to 46 units. Intensive care unit stay ranged from 7.5 to 11 days, and hospital length of stay varied from 16 to 42 days. Mechanical circulatory support was required in 15% of patients, while renal replacement therapy was needed in 26%. Tracheostomy was performed in 19% of patients. The overall survival rate was 82% at one year and 74% at 5 years. Infection rates varied, with 7 out of 9 patients affected, and reoperation rates due to complications were noted. Conclusion: This systematic review highlights the complexity of CHLT for patients with failing Fontan physiology, including FALD. Despite diverse perioperative outcomes, the high one-year and 5-year survival rates affirm the viability and advantages of CHLT. Future research should focus on refining patient selection, optimizing perioperative outcomes, and comparing CHLT to orthotopic heart transplantation (OHT) to establish comprehensive guidelines for managing failing Fontan physiology.

Internal Medicine

Shahzil M, Hasan F, Kazmi K, Banatwala UESS, **Chaudhary A**, **Faisal MS**, Khaqan MA, Gangwani M, Williams K, Mohan B, and Tofani C. EFFICACY AND SAFETY OF PEGBELFERMIN IN MASH CIRRHOSIS-A META-ANALYSIS AND SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS. *Hepatology* 2024; 80:S1256-S1257. Full Text

M. Shahzil, Department of Internal Medicine, Penn State Health Milton S. Hershey Medical Center, PA, United States

Background: Metabolic dysfunction-associated steatohepatitis (MASH), an advanced form of fatty liver disease, is characterized by liver inflammation and fibrosis, affecting 1.5-6.5% of adults globally. Lifestyle changes and medications are primary management options, with an emerging interest in fibroblast growth factors (FGF) like FGF21 and its analogs, particularly pegbelfermin (PGBF). This systematic review and meta-analysis evaluates the efficacy and safety of pegbelfermin in treating MASH-related cirrhosis. Methods: This meta-analysis followed Cochrane guidelines and PRISMA standards. A comprehensive search of CENTRAL, PubMed, MEDLINE, Embase, and Scopus databases up to January 2023 focused on RCTs comparing pegbelfermin to placebo for MASH. Two reviewers independently extracted data, and bias was assessed using the RoB 2.0 tool. Meta-analyses, performed with RevMan 5.4 using a random-effects model, set statistical significance at $p < 0.05$ and evaluated heterogeneity with Chi-square and Higgins I2 tests. Results: Data from 452 participants across three RCTs were analyzed, with 227 in the PGBF group (113 received 10 mg, 114 received 20 mg). Significant improvements in adiponectin concentration were observed in both the 10 mg (MD = 18.23, 95% CI: 6.35-30.11, P = 0.003) and 20 mg (MD = 18.09, 95% CI: 5.88-30.31, P = 0.004) PGBF groups compared to placebo. Significant reductions in PRO-C3 concentration were noted in both the 10 mg (MD = -25.50, 95% CI: -43.95 to -7.05, P = 0.007) and 20 mg (MD = -19.54, 95% CI: -33.33 to -5.76, P = 0.005) groups indicating hepatic benefits and reduced fibrosis. Significant improvement in MASH was seen in the 10 mg group (RR = 2.84, P = 0.02), but not in the 20 mg group (RR = 3.24, P = 0.15). No significant improvements in liver stiffness (10 mg: RR = 1.31, P = 0.23; 20 mg: RR = 1.41, P = 0.07), Modified Ishak scores (10 mg: RR = 1.25, P = 0.37; 20

mg: RR = 1.01, P = 0.98), or collagen proportionate area (10 mg: RR = 0.87, P = 0.63; 20 mg: RR = 0.88, P = 0.38) were observed in either the 10 mg or 20 mg groups compared with placebo. ALT and AST levels showed no significant reductions in either group. There was no significant risk of treatment-emergent adverse events (TEAEs) in either group, except for diarrhea in the 20 mg group (RR = 2.28, P = 0.005). Conclusion: Pegbelfermin, a promising therapy for MASH cirrhosis, has demonstrated effectiveness at 10 mg, significantly improving MASH and biomarkers such as adiponectin and PRO-C3. Despite mild gastrointestinal side effects, it maintains a generally safe profile. Further research with larger randomized controlled trials and extended follow-up is warranted to explore Pegbelfermin's role in enhancing MASH and liver fibrosis outcomes, particularly in combination with Resmetirom.

Internal Medicine

Shahzil M, Munir L, Alvi Z, Akram Qureshi A, Fatima M, **Faisal MS**, Mukhtar R, and **Chaudhry AJ**. Trends and Disparities in Chronic Liver Failure (CLF)-Related Deaths in the United States: A 1999-2020 Analysis. *Am J Gastroenterol* 2024; 119(10):S1377. Full Text

M. Shahzil, Penn State Health Milton S. Hershey Medical Center, Hershey, PA, United States

Introduction: Chronic liver disease (CLD) and cirrhosis cause 2 million deaths annually. US mortality rates increased during the COVID-19 pandemic, reaching 16.4 per 100,000 in 2022. The pandemic heightened risks for CLD patients, disrupted healthcare, and increased mortality, especially among younger individuals and those with alcoholic liver disease. This study examines US CLD and cirrhosis mortality trends from 1999 to 2020, identifying demographic and regional patterns using age-adjusted mortality rates (AAMR) to inform targeted interventions. Methods: Data from the Centers for Disease Control Wonder database were analyzed for chronic liver failure-related deaths (International Classification of Diseases-10 code K72.1) from 1999 to 2020. Ageadjusted mortality rates per 1,000,000 of the US Standard 2000 population were calculated. Trends were examined using Joinpoint Regression, stratified by gender, race, urbanization, and US census regions. Age groups included pediatric, young adults, middle adults, and older adults. The Monte Carlo Permutation Procedure analyzed trends, with significance set at $P<0.05$. Results: The investigation cataloged 13,547 chronic liver failure (CLF)-related deaths over the study period. Mortality rates rose from 1999 to 2002 (APC: 9.12), declined from 2002 to 2010 (APC: -3.46), and increased significantly from 2010 to 2020 (APC: 11.05). Higher mortality was observed among 65-74-year-olds (AAMR: 5.37), males (AAMR: 2.32), and White Americans (AAMR: 1.86). Males saw trends including an initial rise from 1999 to 2003 (APC: 11.18), a decline from 2003 to 2006 (APC: -11.42), a slight rise from 2006 to 2012 (APC: 1.36), and a significant increase from 2012 to 2020 (APC: 11.63). Females showed stability from 1999 to 2010 (APC: -1.24), followed by a rise from 2010 to 2020 (APC: 11.47). The Northeast saw a rise from 2013 to 2020 (APC: 14.07), while the South increased from 2011 to 2020 (APC: 12.77). Urbanization trends showed lower mortality in metropolitan areas. Large central metros declined from 1999 to 2012 (APC: -1.42) and rose from 2012 to 2020 (APC: 11.61). Conclusion: The study highlights the significant burden of chronic liver disease (CLD) and cirrhosis on US mortality (Figure 1). Rising mortality rates among older adults, males, and White Americans emphasize the need for targeted public health interventions. Regional and racial disparities, particularly among Black Americans, call for tailored healthcare strategies. Addressing these trends is crucial for reducing CLF-related mortality and ensuring equitable healthcare access.

Internal Medicine

Shamaa O, **Chavarria-Viales M**, **Alhaj Ali S**, **Al Khouly M**, **Varban O**, and **Zuchelli T**. Management of Gastro-Jejunal Anastomotic Strictures: Comparing Endoscopic Outcomes in Primary vs Conversion Roux-en-Y Gastric Bypass Patients. *Am J Gastroenterol* 2024; 119(10):S1118-S1119. Full Text

O. Shamaa, Henry Ford Health, Detroit, MI, United States

Introduction: Conversion surgery from sleeve gastrectomy (SG) to Roux-en-Y gastric bypass (RYGB) is a common intervention for GERD and weight recurrence. There is limited data on post-surgical gastrojejunal anastomotic strictures (GJAS) endoscopic therapy outcomes in patients with sleeve gastrectomy to Roux-en-Y gastric bypass (SG-RYGB) conversion surgeries. Our study aims to compare the outcomes of primary RYGB (P-RYGB) and SG-RYGB GJAS when treated with through-the-scope

balloon dilation (TTS BD) and lumen-apposing metal stent (LAMS). Methods: This is a single center retrospective study, that included patients diagnosed with GJAS post P-RYGB and SG-RYGB surgeries who underwent TTS BD or intraluminal LAMS placement. Data was collected between 2/1/2013 - 1/1/2023. Primary outcomes were technical success, clinical success, surgical revision & mortality. Secondary outcomes included immediate clinical success and the number of endoscopic sessions needed to achieve clinical success. Results: A total of 22 patients were identified to have GJAS, 13 post P-RYGB (age 55 67) & 9 post SG-RYGB (age 45.5 66). Among the P-RYGB group, 4 patients were treated with TTS BD (median stricture diameter 5 mm) and 9 with LAMS (median stricture diameter 5.5 mm). Whereas within the 9 SG-RYGB patients, 7 received TTS BD (median stricture diameter 8.5 mm), and 2 underwent LAMS placement (median stricture diameter 7 mm). All 22 patients had a 100% technical success rate with no mortality or need for surgical revision. Half (n=2/4) of the P-RYGB patients had clinical success with TTS BD compared to 89% (n=8/9) of those who received LAMS. In SG-RYGB patients, almost half of those who received TTS BD (n=3/7) & LAMS stents (n=1/2) had immediate clinical success following first intervention. During the duration of the study, 4/7 (57%) TTS BD and 2/2 (100%) LAMS SG-RYGB patients maintained clinical success without symptom recurrence. One P-RYGB case experienced intraprocedural LAMS mis-deployment. Post-procedure adverse event rates were reported in 1 P-RYGB TTS BD patient & 3 P-RYGB LAMS patients (Table 1). Conclusion: This study demonstrates that both TTS BD and LAMS are effective in the management of GJAS following primary as well as conversion bariatric surgery. LAMS generally exhibited higher immediate and maintenance clinical success rates compared to TTS BD, especially in P-RYGB patients. Further multicenter research involving larger patient cohorts is warranted to optimize patient outcomes in this population. (Table Presented).

Internal Medicine

Shams S, **Ahmed M**, and **Fnu R**. The Small but Mighty Tumor: Small Cell Neuroendocrine Carcinoma of Pancreas. *Am J Gastroenterol* 2024; 119(10):S1826. Full Text

M. Ahmed, Henry Ford Macomb Hospital, Clinton Township, MI, United States

Introduction: Pancreatic neuroendocrine tumors are classified into 2 major types: Neuroendocrine tumors (NETs) and Neuroendocrine carcinomas (NECs). Pancreatic neuroendocrine carcinomas are further classified into either large cells or small cells. Primary pancreatic small cell carcinoma is extremely rare and accounts for less than 1% of all pancreatic malignancies. Case Description/Methods: A 61-year-old man with a history of hypertension and hyperlipidemia presented to the emergency department with sharp, intermittent right-sided abdominal pain and decreased appetite for one week. During a recent routine annual visit, the patient was also found to have elevated transaminases. An abdominal ultrasound showed multiple liver masses. Subsequently, a computed tomography (CT) scan of the abdomen revealed a pancreatic head mass measuring 6x3 cm and multiple liver masses concerning for metastasis. Biopsy of the pancreatic mass revealed small cell carcinoma. A liver biopsy was consistent with metastatic small cell neuroendocrine carcinoma. The patient started chemoimmunotherapy with carboplatin, etoposide, and atezolizumab. A restaging scan after 2 cycles showed significant improvement in tumor burden. High dose steroids were initiated because atezolizumab maintenance therapy resulted in hepatitis and the patient was off immunotherapy for 9 months due to intolerance. A repeat CT revealed progression of the tumor along with newly enlarged portocaval lymph nodes. Carboplatin and etoposide were restarted. During a recent visit with oncology, there was ongoing discussion regarding the patient's enrollment in CAPTEM versus FOLFIRI clinical trial as second-line therapy. Discussion: Neuroendocrine carcinomas of pancreas are nonfunctional and are metastatic at the time of presentation, as seen in our case. The most common sites of metastasis are the peripancreatic lymph nodes, liver, lungs, bone marrow, bone, colon, adrenal gland, and brain (2). Small cell cancer of the pancreas is usually diagnosed with Endoscopic Ultrasound-Guided Fine Needle Aspiration (EUS-FNA) (3) and Immunohistochemistry (IHC). Ki-67 labeling index is usually >20. IHC commonly shows positivity for synaptophysin, neuron-specific enolase. In our case, IHC was diffusely positive for AE1/AE3 and focally positive for synaptophysin. Ki-67 index was > 50%, Loss of RB, and overexpression of P53 in tumor cells. Pancreatic NECs are extremely rare and treatment should be established by a multidisciplinary team, while closely monitoring for side effects.

Internal Medicine

Singh B, **Ethakota J**, **Bai S**, **Ranjan N**, **Quereshi A**, **Ramanan S**, Sridhar N, Hau Koo T, Kaur G, **Maraj D**, **Zreik H**, **Santos R**, and **Bern M**. Uncanny Association Between Clostridioides difficile and Microscopic Colitis. *Am J Gastroenterol* 2024; 119(10):S1929. Full Text

B. Singh, Henry Ford Jackson Hospital, Jackson, MI, United States

Introduction: Chronic diarrhea is often misdiagnosed as irritable bowel syndrome with diarrhea, especially in women with anxiety, depression, or fibromyalgia. This case highlights the need for thorough evaluation of chronic diarrhea. Causes like bile salt diarrhea post-cholecystectomy, small intestinal bacterial overgrowth in diabetics or post-anastomotic surgery, chronic pancreatitis in type 1 diabetics, and giardiasis near water bodies should be considered. Celiac disease and inflammatory bowel disease should be explored especially with family history. After years of empiric treatment, a colonoscopy during an acute exacerbation of chronic diarrhea led to a diagnosis of microscopic colitis (MC), prompting the discontinuation of selective serotonin reuptake inhibitors (SSRIs), which are a known risk factor. Concurrently, Clostridioides difficile diarrhea, initially missed due to a negative antigen test, was correctly identified via polymerase chain reaction. MC and C. difficile have a reciprocal relationship, where one can predispose to the other. Case Description/Methods: A 47-year-old woman with anxiety, migraines, and chronic diarrhea post-cholecystectomy presented with worsening symptoms. She developed diarrhea after 2 courses of Augmentin for sinusitis, with a subsequent computed tomography revealing pancolitis. Initial stool cultures were negative. Despite a course of ciprofloxacin and Flagyl, her symptoms worsened post-treatment. Family history included Crohn's disease. Daily medications included Escitalopram and cholestyramine. She had leukocytosis, and stool studies including C. difficile toxin were negative. Due to high suspicion, a polymerase chain reaction for C. difficile was ordered and returned positive. Treatment with oral vancomycin improved her symptoms significantly. A follow-up colonoscopy with biopsies diagnosed lymphocytic colitis. SSRI discontinuation was advised, and a tapering course of Budesonide was initiated. Discussion: MC, including collagenous colitis and lymphocytic colitis, presents with chronic watery diarrhea. MC is associated with medications like proton pump inhibitors, SSRIs, and nonsteroidal antiinflammatory drugs. Diagnosis requires colonoscopy and biopsies, as the colon appears normal macroscopically. Treatment typically involves a budesonide taper. Persistent diarrhea or recurrent C. difficile infections warrant colonoscopy with random biopsies to check for MC. This case suggests a possible link between C. difficile infection and lymphocytic colitis, supported by recent studies. MC risk factors include older age, female sex, and smoking. Prior gastrointestinal infections, including C. difficile, are more common in MC patients.

Internal Medicine

Singh B, **Kaur P**, **Bai S**, **Ethakota J**, **Ranjan N**, and **Quereshi A**. Dupilumab and Non-EOE GI Disorders. *Am J Gastroenterol* 2024; 119(10):S1609. Full Text

P. Kaur, Henry Ford Jackson Hospital, Jackson, MI, United States

Introduction: Eosinophilic gastrointestinal disorders are characterized by eosinophil-rich inflammation in the gastrointestinal tract, with no known cause for eosinophilia. These disorders are divided into specific types based on their location such as - Eosinophilic esophagitis, Eosinophilic gastroenteritis or duodenitis, and eosinophilic colitis, proctitis, or proctocolitis. The etiology of these disorders is still no fully understood. Treatment includes steroids but recent approval of dupilimab for esophagitis has prompted interest in other eosinophilic conditions. Methods: Pubmed and Google Scholar were looked into with MeSH terms dupilumab, eosinophilic gastritis/enteritis/colitis/proctitis. Prisma guidelines were adhered to, a total of 12 results were brought on including 2 case series, 3 case reports, 3 incomplete randomized control trials and a meta-analysis comparing biologics in eosinophilic conditions. Rest were duplicates. The case series and reports were included. Results: The first case series included 12 pediatric patients with eosinophilic gastritis, duodenitis or both. All of them had failed initial steroid treatment and treatment with dupilumab led to remission in 5/12 patients and histologic improvement in 8/8 patients studied as measured by eosinophils/high power field. Similarlythe second series had steroid resistant gastritis, enteritis(jejunal and ileal) and colitis. All 3 patients had histologic improvement. Symptomatic improvement of at least 1 symptom was achieved in all patients. Rest 3 were case series, including

eosinophilic colitis, egg-induced eosinophilic gastritis and ulcerative colitis with eosinophilic infiltrate. Symptomatic improvement was seen in all cases with histologic remission only studied in colitis case which showed reduced eosinophils per high powered field. Conclusion: Non-eosinophilic esophagitiseosinophilic diseases are rare but pose challenges of steroid dependence or resistance. With introduction of dupilumab in the field of eosinophilic esophagitis, interest has increased in all conditions with similar pathology. Our review shows promising results, there are phase 2 trials with dupilumab in these conditions especially ulcerative colitis with eosinophils.

Internal Medicine
Singh B, Koo TH, Sridhar N, and **Ramanan S**. The Role of Steroids in Eosinophilic Esophagitis: A Meta-Analysis. *Am J Gastroenterol* 2024; 119(10):S409. Full Text

B. Singh, Henry Ford Jackson Hospital, Jackson, MI, United States

Introduction: Eosinophilic esophagitis (EoE) is a chronic immune-mediated inflammatory disease of the esophagus characterized by eosinophilic infiltration. Swallowed topical steroids have been the preferred medications for EoE as they relieve symptoms and restore the pathology to normal levels. This meta-analysis aims to evaluate the effectiveness of topical steroids in improving histologic, clinical, and endoscopic outcomes compared to placebo in patients with EoE. Methods: A comprehensive literature search was performed from major databases (PubMed, EMBASE, Medline, ISI Web of Science, and Cochrane Database of Systematic Reviews) from inception to May 2023 to identify relevant randomized controlled trials (RCTs) that compared topical steroid therapy with placebo to treat EoE. The primary outcomes assessed were histological response, clinical response rate, and endoscopic response rates in EoE patients treated with topical steroids compared to placebo. Pooled estimates were calculated using a random-effects model with 95% confidence intervals (CI) using odds ratios (OR) for dichotomous diseases. The statistical analysis was performed using Review Manager (RevMan) software. Results: Nine randomized controlled trials (RCTs) were included, with 193 participants in total, 102 receiving topical steroids, and 91 being included in the placebo group. Topical corticosteroids were significantly more effective than placebo in inducing histologic response (OR 37.81, 95% CI: 14.98 to 85.64, $P < 0.00001$). They were also more effective in inducing clinical response (OR 2.53, 95% CI: 1.14 to 5.60, $P = 0.02$). The endoscopic response rate was higher in the steroid group (OR 3.51, 95% CI: 1.51 to 8.14, $P = 0.004$). The heterogeneity among studies for histologic, clinical, and endoscopic outcomes was low to moderate ($I2 = 0\%$ to 60%). Conclusion: Topical steroids demonstrate significant efficacy in improving histologic, clinical, and endoscopic outcomes in patients with EoE. The observed low to moderate heterogeneity among studies suggests a consistent benefit of steroid therapy despite the fact that infections, the most frequently reported side effects, were mild and almost always tolerated without severe consequences. Further research is necessary to confirm long-term safety and efficacy and to refine treatment regimens.

Internal Medicine
Singh B, Koo TH, Sridhar N, and **Ramanan S**. The Role of SGLT2 Inhibitor in the Treatment of Non-Alcoholic Fatty Liver Disease: A Meta-Analysis. *Am J Gastroenterol* 2024; 119(10):S1248. Full Text

B. Singh, Henry Ford Jackson Hospital, Jackson, MI, United States

Introduction: Non-alcoholic fatty liver disease (NAFLD) is intricately linked with metabolic disorders and insulin resistance, which is a primary driver of type 2 diabetes mellitus (T2DM), leading to hepatic steatosis and further liver damage. Sodium-glucose co-transporter 2 (SGLT2) inhibitors have emerged as potential pharmacological treatments offering benefits beyond glucose control. This meta-analysis aims to evaluate the effectiveness of SGLT2 inhibitors in reducing liver fat content and quantify their impact on elevated liver enzymes, alanine transaminase (ALT), and aspartate transaminase (AST) levels in NAFLD patients. Methods: A comprehensive literature search was performed from major databases from January 2018 to January 2024. The primary outcomes assessed were the reduction in liver fat content and liver enzyme levels (Alanine transaminase (ALT) and Aspartate aminotransferase (AST)) in NAFLD patients treated with SGLT2 inhibitors compared to placebo or conventional treatments. The secondary outcomes included the effect on the Fibrosis-4 (FIB-4) index and Hemoglobin A1C (HbA1c) levels. Pooled estimates

were calculated using a random-effects model with 95% confidence intervals (CI). The statistical analysis was performed using Review Manager (RevMan) software. Results: Ten randomized controlled trials (RCTs) were included, with 571 participants in total, 281 receiving SGLT2 inhibitors, and 290 being included in the control group (either conventional medicine or a placebo). The duration of treatment in the included studies ranged from 12 weeks to 52 weeks. SGLT2 inhibitors significantly reduced ALT levels (WMD -5.36, 95% CI: -8.86 to -1.85, P = 0.003) and AST levels (WMD -2.57, 95% CI: -3.84 to -1.30, P<0.0001). The FIB-4 index also showed a significant reduction (WMD -0.06, 95% CI: -0.10 to -0.02, P = 0.0010). However, the reduction in HbA1c levels was not statistically significant (WMD -0.16, 95% CI: -0.38 to 0.06, P = 0.16). Conclusion: SGLT2 inhibitors show promise in reducing liver fat and improving liver function in NAFLD patients, particularly those with concurrent diabetes and obesity. The heterogeneity among studies underscores the need for personalized treatment approaches. Further research is necessary to confirm long-term safety and efficacy.

Internal Medicine
Singh B, **Lazarczyk P**, **Ramanan S**, Kaur G, **Ethakota J**, **Bern M**, and Gamarra R. There is Some Dump in the Sump. *Am J Gastroenterol* 2024; 119(10):S1711-S1712. Full Text

B. Singh, Henry Ford Jackson Hospital, Jackson, MI, United States

Introduction: Sump syndrome is a long-term complication of choledochoduodenostomy for biliary drainage in the setting of stones or strictures in days before endoscopic retrograde cholangiopancreatography (ERCP) was common. Symptoms of cholangitis, 5-10 years after the initial procedure, lead to the suspicion of sump syndrome. ERCP acts both diagnostic and therapeutic with debris removal, and/or stenting and/or sphincterotomy. Case Description/Methods: 62-year-old man with pancreatic cancer post gastrojejunostomy and cholecystojejunostomy followed by chemo-induced remission 12 years ago presented with nausea, vomiting, and right-sided flank pain. He had been presenting with similar presentations over the past year leading to multiple ERCPs. Upon the last 2 ERCPs, the patient was found to have multiple gall stones in the stump of the common bile duct draining into the duodenum treated with biliary stents. Upon admission, the patient was afebrile with normal vitals and liver function tests. Imaging showed a patent stent in the common bile duct. Given his recent history of cholangitis and choledocholithiasis in the common bile duct stump, requiring ERCP-guided stenting, a diagnosis of Sump syndrome was made with the patient developing biliary stasis in the stump causing recurrent obstruction and subclinical infections. General surgery was brought on board to explore the possibility of a Whipple's procedure versus hepaticojejunostomy to completely resect the frequently affected region altogether. Discussion: Pre-ERCP, treatment for choledocholithiasis included anastomosis between the common hepatic duct or proximal common bile duct and duodenum with a distal stump draining into the ampulla of Vater. Following the surgery air in the biliary tree acted as the sole indication of functional anastomosis. However, 5-10 years after the procedure, these patients sometimes presented with ascending cholangitis. This phenomenon of the development of stones and subclinical or clinical infection is known as Sump syndrome. The distal duct draining into the ampulla of Vater acts as a recess where static bile and debris keep accumulating, acting as a home for bacterial proliferation. This generally leads to pancreatitis or recurrent cholangitis. For imaging, an ultrasonogram may reveal stones and ductal dilation which might hint at the diagnosis. Finally, ERCP is both diagnostic and therapeutic with sphincterotomy and endoscopic removal. Adequate antibiotic coverage is necessary. Surgical Roux-en-Y hepaticojejunostomy proves to be a definitive treatment if the patient requires multiple ERCPs (Figure 1).

Internal Medicine
Singh B, **Patel-Rodrigues P**, **Khan MZ**, Kaur G, **Bai S**, **Bern M**, and **Jafri SM**. A Rare Case of Immune Checkpoint Cholangitis. *Am J Gastroenterol* 2024; 119(10):S1711. Full Text

B. Singh, Henry Ford Jackson Hospital, Jackson, MI, United States

Introduction: Immune checkpoint inhibitor cholangitis (IMC) due to its rarity poses difficulties in diagnosis and treatment. IMC includes a range of biliary tract injuries with different clinical and pathological characteristics, from small-duct to large-duct involvement. Case Description/Methods: A 32-year-old man presented hospital with presyncope, nausea , and vomiting. Upon computed tomography, he was found

to have multiple cryptogenic liver lesions. He had a history of lung adenocarcinoma on maintenance Keytruda. He had multiple admissions related to Keytruda complications which included pancreatitis requiring high-dose steroids, esophagitis, and gastritis (last esophagogastroduodenoscopy showing Severe hemorrhagic gastritis, gastric stenosis). A magnetic resonance cholangiopancreatography was obtained for cholestatic elevation of transaminases and showed intrahepatic and extrahepatic biliary dilatation with periductal enhancement. A liver biopsy was inconclusive. However, the findings could be associated with obstructive changes. The likely differentials were primary versus secondary sclerosing cholangitis. In the setting of prolonged use of pembrolizumab for 1.5 years and taking into consideration the timeline of symptoms, secondary sclerosing cholangitis was diagnosed. She was treated with steroids and keytruda and paclitaxel were discontinued with improvement in symptoms. Discussion: Immune checkpoint inhibitors(ICI) can affect any organ system, including the liver, causing cholangitis, although this is less common than immune-mediated hepatitis. Cholangitis induced by ICIs is categorized into 3 types: small-duct, large-duct, and mixed. Small-duct cholangitis is likely underreported due to the need for liver biopsy for diagnosis. Its pathology includes bile duct loss, minor bile duct injuries, and mixed inflammatory cells, predominantly CD81 T cells, diffuse fibrosis in the extrahepatic bile duct with imaging showing nonobstructive dilatation or stenosis. For treatment, the Barcelona criterion is used, where alkaline phosphatase normalization indicates complete resolution, a 40% decrease suggests a partial response, and less than 40% is unsatisfactory. Steroids alone or with immunosuppression show similar results. It's crucial to differentiate ICI-induced cholangitis from cholangiocarcinoma, which doesn't respond to steroids, and IgG4-related disease, which does. Taxanes can produce a similar picture and may need discontinuation if ICI-related cholangitis is suspected.

Internal Medicine

Singh B, **Ramanan S**, Kaur G, Singh W, and **Bern M**. MASH 2B TRIALS-A SYSTEMATIC REVIEW. *Hepatology* 2024; 80:S1265. Full Text

B. Singh, Henry Ford Health Jackson, United States

Background: Non-alcoholic fatty liver disease (NAFLD), now termed metabolic dysfunction-associated fatty liver disease (MAFLD), is the leading cause of chronic liver disease in the U.S., encompassing conditions from simple steatosis to cirrhosis and hepatocellular carcinoma. Early symptoms like fatigue and abdominal pain are non-specific, often delaying diagnosis until advanced stages. Systemic insulin resistance leads to lipid accumulation in the liver, triggering inflammatory responses. The gut microbiome and gut-liver axis also play significant roles. Diagnosis uses the NAFLD Activity Score (NAS) and the NASH Clinical Research Network (CRN) fibrosis score to assess disease activity and progression. Treatments emphasize weight loss and lifestyle changes, with promising pharmacological options targeting insulin sensitivity, lipid metabolism, and inflammation. These include PPAR agonists, SGLT-2 inhibitors, GLP-1 inhibitors, and the recently approved Resmetirom. Current research focuses on phase 2b trials to evaluate the efficacy and safety of these treatments. Methods: This study follows PRISMA-2020 guidelines. Three researchers conducted a literature search across multiple databases for phase 2b trials from the past 5 years. Studies were selected using PICO criteria and data were extracted per the Cochrane Handbook. Quality assessment was done using the Cochrane Risk of Bias Tool (2.0). Results: This study includes 11 randomized control trials (RCTs), all double-blinded, with 10 being placebo-controlled, involving adults with histologically confirmed NASH. The trials ranged from 100 to 392 participants. PPAR agonists were tested in the EMMINENCE and NATIVE trials, with NATIVE showing significant fibrosis and NASH resolution at higher doses. FGF21 and FGF19 pathways were targeted in six trials. The Harmony trial with efruxifermin showed significant fibrosis improvement, while the Enliven trial with pegozafermin also demonstrated significant fibrosis reduction at higher doses. The Falcon trials with pegbelfermin did not achieve significant primary outcomes. Alpine 2/3 and Alpine 4 trials with aldafermin showed mixed results, with significant fibrosis improvement only in specific doses. The TANDEM trial, comparing Tropifexor and Cenicriviroc, focused on safety and efficacy, showing ALT, AST, and GGT reductions. ICONA trial with Icosabutate showed potential in NASH patients with T2DM. Belapectin, a galectin-3 inhibitor, did not significantly reduce portal pressure. Outcomes frequently measured NAS or SAF score improvements, highlighting potential in combined drug mechanisms and specific comorbidities. Conclusion: RCTs in NASH treatment showed mixed outcomes. Lanifibranor and

icosabutate showed promise, especially in T2D patients. FGF21 analogues like efruxifermin improved fibrosis, while FGF19 trials had variable results. Further research is needed.

Internal Medicine
Singh H, **Bachour C**, **Metcalf D**, **Luthra K**, and **Kak V**. Hyponatremia as a Predictive Marker of Mortality in Hospitalized COVID- 19 Patients: A Healthcare System Analysis. *Am J Respir Crit Care Med* 2024; 209. Full Text

H. Singh, Internal Medicine, Henry Ford Jackson Hospital, Jackson, MI, United States

Rationale: There is documented evidence of the association between hyponatremia and mortality in hospitalized patients, including patients admitted with coronavirus disease-2019 (COVID-19) pneumonia. One of the proposed mechanisms of hyponatremia in COVID-19 is the syndrome of inappropriate antidiuretic hormone (SIADH) due to circulating cytokines such as IL-6. These cytokines are proposed to be associated with lung inflammation and correlate with respiratory failure and in-hospital mortality. Immunomodulators, tocilizumab and baricitinib, acting against the cytokine response, are known to reduce mortality in hospitalized COVID-19 patients. This study was undertaken to associate the severity of hyponatremia with in-hospital mortality in patients admitted with COVID-19 in multiple hospitals over a single health system network. Methods: After obtaining appropriate institutional review board (IRB) approval, a retrospective chart review was conducted from 03/01/2020 to 06/01/2021, which included all admitted patients with positive COVID-19 polymerase chain reaction tests at the time of admission. Individuals less than 18 years of age, incarcerated, and pregnant patients were excluded. Performance analytics and improvement (PAI) tool was used to extract patient records. The patients were categorized based on their admission sodium values into the following groups: normal sodium (>=136 mEq/L), mild hyponatremia (131 to 135 mEq/L), moderate hyponatremia (121 to 130 mEq/L), and severe hyponatremia (<=120 mEq/L). Primary and secondary outcomes calculated were hospital mortality and length of stay. IBM SPSS software was used to perform the data analysis. Chi-square tests and ANOVA tests were run to evaluate these outcomes. Results: Data for 2561 patients was extracted using the above method. 14 cases with severe hyponatremia were not included because of the small case count and its minute impact on the analysis and the interpretation of the results. Hence, 2547 patients were analyzed in this study. The percentage of in-hospital mortality in patients with normal sodium, mild hyponatremia, and moderate hyponatremia was found to be 8.7% (109/1260), 8.9% (84/945), and 15.8% (54/342) respectively; with Chi-Square p-value of <0.001 comparing mortality between the moderate hyponatremia group with the rest of the individual groups. Hospital length of stay of groups with normal sodium, mild hyponatremia, and moderate hyponatremia was 8.03, 7.99, and 9.44 days, respectively, with ANOVA F-Test P-value of 0.012. Conclusion: Admission hyponatremia of <130 mEq/L in COVID-19 patients is associated with a higher in-hospital mortality. Hence, admission sodium level may be used as a prognosticating factor and possible variable in the future COVID-19 treatment trials.

Internal Medicine
Sohail A, Bhinder M, Aslam A, **Chaudhary A**, and Brown K. REDUCTION IN HEPATOCELLULAR CARCINOMA RISK WITH SGLT2 INHIBITORS IN PATIENTS WITH CO-EXISTING HEPATITIS C AND TYPE 2 DIABETES: A GLOBAL MULTICENTER PROPENSITYMATCHED STUDY. *Hepatology* 2024; 80:S1420-S1421. Full Text

A. Sohail, University of Iowa Hospitals and Clinics, United States

Background: Chronic Hepatitis C infection (CHC) and Diabetes Mellitus Type 2 (T2DM) are independent risk factors for the development of Hepatocellular Carcinoma (HCC). Preclinical studies suggest that Sodiumglucose cotransporter-2 receptor inhibitors (SGLT2i) regulate pathways implicated in HCC progression and may inhibit oncogenesis. However, clinical studies are lacking. Using a large research network, this study aimed to evaluate the effect of SGLT2i on the incidence of HCC in patients with concomitant T2DM and CHC. Methods: In this retrospective cohort study and time-toevent analysis, we utilized the TriNetX electronic health records network, encompassing over 120 million patients from January 1, 2005, to December 31, 2022. We included patients aged 18 years or older diagnosed with co-existing T2DM and chronic hepatitis C who had received either previous or current antiviral treatment.

Patients with and without SGLT2 inhibitor treatment were matched using propensity scores for age, gender, race, comorbidities, liver-related characteristics, BMI, and background medications. Patients with a prior history of HCC, liver transplant, type 1 diabetes mellitus, or end-stage renal disease were excluded. Using a Cox proportional hazards regression model, we evaluated the association between SGLT2i use and the incidence of HCC in both groups. Results: We identified 1,478 patients in the SGLT2i group and 14,044 patients in the non-SGLT2i group. A total of 1,448 patients were included after propensity matching from both groups. Table 1 contains the baseline demographics, comorbid conditions, and baseline medications before and after propensity matching. The incidence of HCC was 6.63% in the SGLT2i group vs. 10.42% in the non-SGLT2i group (RR = 0.64, 95% CI(0.49-0.81), P < 0.01). This association remained significant regardless of age, gender, ethnicity, diabetes, hypertension, cirrhosis, and background diabetic medications (metformin, sulfonylurea, glitazone, DPP4i,alpha-glucosidase inhibitors, glucagon-like peptide 1 receptor agonists, and insulin). Conclusion: Based on a large global retrospective study of patients with co-existing CHC and T2DM, SGLT2i use was associated with a significantly lower risk of HCC. However, confirmation through future large-scale prospective studies is required. (Figure Presented).

Internal Medicine

Subramaniam S, Haider M, Mir J, Javed N, Singh S, Sandesara D, Sengodan P, Sattar Y, **Chaudhary AJ**, and Hamza M. Cardiovascular and Bleeding Outcomes of Proton-Pump Inhibitor and Clopidogrel Co-Therapy After Percutaneous Intervention: A Meta-analysis. *Am J Gastroenterol* 2024; 119(10):S690-S692. Full Text

S. Subramaniam, Ohio State University, Columbus, OH, United States

Introduction: Data regarding the concurrent use of proton pump inhibitor (PPI) with clopidogrel in patients with acute coronary syndrome (ACS) is conflicting. On one hand, there is data to support PPI and concomitant use of clopidogrel to decrease bleeding whereas, on the other hand, the concomitant use of PPIs and clopidogrel may diminish clopidogrel activity in preventing platelet aggregation by inhibiting major enzymes that activate the conversion of clopidogrel into its active metabolite. We conducted a meta-analysis evaluating the outcomes for concurrent use of these medications and comparing various PPIs in their interaction with clopidogrel. Methods: We searched PubMed and Embase, screened 1071 articles, and included seven articles meeting our inclusion criteria: randomized control trials comparing different PPIs to control (no PPI) in patients on clopidogrel with CAD for six months. The outcomes of interest were major adverse cardiovascular events (MACE), myocardial infarction (MI), heart failure (HF), arrhythmia, bleeding, all-cause death, and cardiovascular (CV) death. Pooled risk ratios (RR) and 95% confidence intervals (CI) were calculated using a random-effects model. We assessed heterogeneity between studies and the P-value was assigned to , 0.05 for statistical significance. A subgroup analysis was also done comparing individual PPIs including pantoprazole and omeprazole. Results: Seven studies with 5146 patients (PPI group: 2585, No-PPI: 2561). Our analysis shows that using PPI with clopidogrel is associated with fewer bleeding outcomes. Subgroup analysis showed that this was consistent for both pantoprazole and omeprazole compared to no PPI. Table 1. Our analysis showed no difference in all-cause mortality and cardiovascular outcomes (myocardial infarction, major cardiovascular events, onset of heart failure, arrhythmias, and cardiovascular mortality). Our subgroup analysis showed no difference in the subgroup analysis for both pantoprazole and omeprazole in all-cause mortality, and cardiovascular mortality Figure 1. Conclusion: In patients taking clopidogrel, both pantoprazole and omeprazole are associated with decreased bleeding outcomes. Our study showed no difference in terms of mortality and cardiovascular outcomes. Further randomized controlled trials are needed to validate these results.

Internal Medicine

Taleb M, **Stephan J**, **Vo T**, and **Estrada K**. A Delayed Diagnosis of Diabetic Myonecrosis: Case Report. *J Endocr Soc* 2024; 8:A341. Full Text

M. Taleb, Henry Ford Health System, Detroit, MI, United States

Background: Diabetic myonecrosis, also termed diabetic muscle infarction, isa raremicrovascular complicationofdiabetes mellitus (DM). Although it can manifest in patients with all types of DM, it is more

common in type 1 DM. It presents with pain and swelling localized in a muscle group and is associated with significant morbidity. The most commonly affected area is the anterior thigh, followed by the posterior thigh or calf. Clinical Case: A 34-year-old woman presented with two months of left thigh pain and swelling. She had a history of long-standing type 1 DM complicated by end-stage kidney disease for which she had been initiated on peritoneal dialysis (PD) six months prior to presentation. Her localized symptoms started after a fall and persisted since then. Our patient's initial workup showed an elevated CPK level of 1340 IU/L (normal <178 IU/L), and limb radiographs were negative for fracture or dislocation. Her symptoms were attributed to musculoskeletal pain. She subsequently presented to the emergency departments multiple times with the same symptoms. On one presentation, she was diagnosed with nontraumatic rhabdomyolysis in the setting of hematuria and persistent left thigh pain. On another presentation, CT of the left femur was done and showed skin thickening, subcutaneous fat stranding, and edema without osseous abnormalities; she was diagnosed with complex regionalpainsyndrome (CRPS)anddischarged home on gabapentin, which did not improve her symptoms. Ultimately, she was admitted to the hospital with the inability to ambulate due to her persistent and severe symptoms. MRI of the left hip and femur showed signs of diffusemyositis and areas of myonecrosis consistent with diabeticmyonecrosis. Prior to initiation of PD, our patient's HbA1c had been well controlled at the target of <7%.Due to the high dextrose content in dialysate, she had an increase in her HbA1c to 9.0% within a span of three months despite no changes in her medications or diet. Once the diagnosis was established, aspirin was initiated and insulin regimen was adjusted for tighter glucose control. Two weeks after treatment our patient had resolution of her symptoms.Conclusion:We highlight a case of diabetic myonecrosis, a complication of DM, that can bemissed due to its rarity and nonspecific presentation. Index of suspicion should be high in patients with persistent unexplained musculoskeletal symptoms. Despite MRI being the diagnostic modality of choice, obtaining it was delayed due to multiple factors including initial radiologic findings negative for acute fractures and previous misdiagnosis of rhabdomyolysis and CRPS. Management of diabetic myonecrosis is centered around tight glycemic control. This highlights the importance of close monitoring of glycemic control when initiating a patient with diabetes mellitus on PD, given the constituents of the dialysate used, to prevent complications of diabetes.

Internal Medicine

Toiv A, **Baldwin H**, and **Jafri SM**. Is Age Really Just a Number? A Comparison of Outcomes in Intestinal Transplant Recipients ,50 and 50 Years Old. *Am J Gastroenterol* 2024; 119(10):S1597. Full Text

A. Toiv, Henry Ford Hospital, Detroit, MI, United States

Introduction: With the continued development of therapeutic advances in surgical approaches and post-transplant immunosuppression that consistently improve transplant outcomes, the transplant community has been revising previously held notions regarding age criteria in the transplant evaluation. Historically, younger patients have been prioritized for transplantation due to concerns about posttransplant outcomes in older patients; however, emerging evidence suggests that the impact of age on transplant eligibility criteria may need to be reevaluated. Few studies have explored the impact of age on serious outcomes after intestinal transplantation (IT). This study aims to compare visceral transplant outcomes between IT recipients , 50 and ≥ 50 years old. Methods: We conducted a retrospective chart review of all patients who underwent IT at an academic transplant center from 2010 to 2023. The primary outcome was patient survival, analyzed with Kaplan- Meier survival analysis. Results: Among the 50 IT recipients, there were 21 IT recipients , 50years old and 29 IT recipients ≥50 years old (Table 1). The median age at transplant in the , 50 group was 37 years (range, 17-48) and in the ≥50 group was 55 years (range, 50-68). In both groups, the majority of transplants were exclusively IT, however they included multivisceral transplantation as well. Kaplan-Meier survival analysis (Figure 1) revealed that the , 50 group has a higher survival probability over time compared to the ≥50 group (P 5, 0.01). Although there was a greater incidence of reoperation within 1 and 3 months and the development of chronic kidney disease in the ≥50 group it did not reach statistical significance (P 5.0.05). No significant differences were observed between the groups for graft failure at 1 or 3 years or moderate-to-severe rejection at 1 or 3 years. Conclusion: Although recently published transplant literature has been highlighting that with carefully selected patients age does not impact transplant-related outcomes, this study found that IT recipients ≥50-year-old demonstrated significantly lower survival rates following IT compared to younger patients. Despite not

reaching statistical significance, the higher incidence of reoperation within 3 months and the development of chronic kidney disease in the older group suggest that this may be due to potential age-related differences in post-operative complications. .

Internal Medicine
Toiv A, **Baldwin H**, and **Jafri SM**. Does Sex Matter? A Comparison of Outcomes in Men and Women Intestinal Transplant Recipients. *Am J Gastroenterol* 2024; 119(10):S1595-S1596. Full Text

A. Toiv, Henry Ford Hospital, Detroit, MI, United States

Introduction: Researchers are increasingly investigating the possible differences in transplant-related outcomes between men and women. However, few studies have explored whether patient sex is associated with serious outcomes after intestinal transplantation (IT). This study aims to compare visceral transplant outcomes between men and women transplant recipients. Methods: We conducted a retrospective chart review of all patients who underwent IT or multivisceral transplant (MVT) at an academic transplant center from 2010 to 2023. The primary outcome was patient survival, analyzed with Kaplan-Meier survival analysis. Results: Among the 50 IT recipients, there were 20 men and 30 women (Table 1). The median age at transplant was 50 years (range, 22-64). Of the transplants, 58% were exclusively IT, while 42% were MVT. Kaplan-Meier survival analysis (Figure 1) revealed no significant mortality difference between the groups when analyzed by sex (P =0.28) or when comparing IT alone to MVT (P 5.0.05 in all subgroups). Male IT recipients showed a higher need for reoperation within 1 month (P =0.01) but not within 3 months (P =0.44). No significant differences were observed between the sexes in graft failure at 1 or 3 years, moderate-to-severe rejection at 1 or 3 years, or the development of post-transplant chronic kidney disease. Conclusion: Although the literature has highlighted differences in transplant-related outcomes based on patient sex, this study found no significant survival or transplant-related differences between men and women IT and MVT recipients. These findings can help address sex-based disparities in transplant outcomes and inform clinicians as to whether sex is an important consideration for IT evaluations. .

Internal Medicine
Toiv A, **Harris K**, **Zarrar Khan M**, **Theisen BK**, **Varma AK**, **Fain C**, and **Kaur N**. Rare EBV-Positive Recurrent Post-Transplant Lymphoproliferative Disorder With Barely Detectable EBV Viremia: A Diagnostic Challenge. *Am J Gastroenterol* 2024; 119(10):S1985. Full Text

A. Toiv, Henry Ford Hospital, Detroit, MI, United States

Introduction: Post-transplant lymphoproliferative disorders (PTLD) are complications arising from post-transplantation immunosuppressive therapy. Epstein-Barr virus (EBV) viremia is often seen in PTLD, but it is not a diagnostic feature. We report a rare case of recurrent PTLD in a transplant recipient who had high EBV viremia in her first PTLD episode, however, her recurrent episode had barely detectable EBV viremia, delaying diagnosis. Case Description/Methods: A 26-year-old woman with a heart transplant (EBV donor1/recipient-) and Crohn disease presented to the emergency department with severe abdominal pain and bloody diarrhea. Her heart transplantation was 7 years previously and she was maintained on high-dose immunosuppression. Notably, she had been diagnosed with EBV-positive PTLD 4 years previously and successfully treated with rituximab. That PTLD presentation was diagnosed with substantial EBV viremia (> 700,000 copies/mL). At this presentation, she had been treated for recurrent inflammatory bowel disease (IBD) flares over the preceding months before her symptoms escalated. Initial laboratory tests revealed high C-reactive protein, low EBV viral load below 50 IU/mL, and no lymphocyte abnormalities on peripheral smear. Computed tomography abdomen revealed severe pancolonic wall thickening and fat stranding, with multiple prominent pericolonic lymph nodes. She was started on methylprednisolone for presumed IBD flare. Due to a lack of clinical response, colonoscopy was pursued on day 3 of admission and showed inflammation with deep continuous and circumferential ulcerations from the rectum to the sigmoid, with pronounced serpiginous ulcers in the sigmoid colon. Pathology analysis (Figure 1) of colonic biopsies revealed mucosal architectural distortion, Paneth cell metaplasia, and increased lamina propria plasmacytic inflammation. Further histologic staining revealed EBV-positive plasma cell hyperplasia with no evidence of cytomegalovirus or granulomata supporting a

diagnosis of recurrent early PTLD. Discussion: This case illustrates the challenge of diagnosing rare gastrointestinal recurrent PTLD. Our patient's diagnosis was delayed because her symptoms resembled an IBD flare and she had barely detectable EBV, unlike her first PTLD episode. When evaluating a transplant recipient manifesting severe gastrointestinal symptoms, we recommend maintaining a heightened suspicion for PTLD and adopting a low threshold for early endoscopy with biopsy analysis for EBV.

Internal Medicine
Toiv A, **Kumar V**, **Patel A**, and **Jafri SM**. Protocol for the Management of Hepatitis C Transferred Through Kidney Transplantation. *Am J Gastroenterol* 2024; 119(10):S1320. Full Text

A. Toiv, Henry Ford Hospital, Detroit, MI, United States

Introduction: The effectiveness of direct-acting antiviral (DAA) drugs for treating hepatitis C virus (HCV) infection may substantially increase the number of available organs for transplants by allowing organ transplantation from HCV-positive (HCV1) donors into HCV-negative (HCV-) recipients. This study describes the outcomes of HCV- recipients who received kidneys from HCV1 donors, highlighting the benefits of post-transplant DAA therapy. Methods: This was a single center retrospective case series of all HCV- recipients who underwent kidney transplantation with organs from HCV1 donors at our transplant center from October 2020 to May 2023. Results: There were 11 HCV- recipients who underwent deceased donor kidney transplantation (DDKT) with organs from HCV+ donors: 9 men (82%) and 2 women (18%). There was 1 patient who received both liver and kidney. The median age was 60 years (range 41-76). The mean organ wait time spent on dialysis was 1.9 years. All patients were confirmed HCV- by quantitative nucleic acid amplification test at the time of transplant, and 9 (82%) patients tested HCV+ after transplantation. Of these 9 HCV infections, 6 were genotype 1a, 1 was 1b, and 2 were 2b. Notably, 8 of these 9 patients received DAA therapy for 12 weeks (6 sofosbuvir/velpatasvir and 2 glecaprevir/pibrentasvir), and all 8 patients had undetectable virus at 8 weeks of treatment with no side effects requiring early treatment termination. Also, none developed graft rejection or glomerulonephritis from HCV infection, although 2 patients had delayed graft function that improved. Within 1 year of transplant, 2 of the 8 patients died due to comorbidities unrelated to HCV or transplant. The 1-year survival for all kidney transplant recipients at our center between 2021 and 2022 was 96%. Conclusion: All HCV- patients who received an HCV+ DDKT and were treated with DAA therapy for post-transplant HCV infection had complete resolution of HCV. Patients receiving an HCV+ DDKT underwent transplant much earlier than expected, at around 1.9 years of dialysis waiting (DDKT wait time for type O patients is 5 years in Michigan). Effective DAA therapy now allows kidneys from HCV1 donors to be a safe source of organs for transplantation.

Internal Medicine
Toiv A, **Nabaty R**, **Saleh Z**, **Saleem A**, **Heppell O**, **Rahman A**, **Watson A**, and **Piraka C**. Entangled Pathways: Duodenal Obstruction Caused by Celiac Artery Dissection. *Am J Gastroenterol* 2024; 119(10):S3040. Full Text

A. Toiv, Henry Ford Hospital, Detroit, MI, United States

Introduction: Spontaneous celiac artery dissection is a rare subtype of visceral arterial dissection. While it may be incidentally discovered in asymptomatic individuals, it typically manifests as acute, severe abdominal pain and symptoms indicative of intestinal ischemia. This case introduces a novel diagnosis of acute celiac artery dissection causing duodenal obstruction. Case Description/Methods: A healthy 61-year-old man with no significant past medical history presented with subacute worsening nausea and vomiting, leading to an inability to eat or drink. Upon presentation, his vital signs were within normal range, and his abdominal physical examination was benign. Initial laboratory studies yielded normal results. Computed tomography of the abdomen revealed a 6.8 x 3.6 cm lobulated collection beneath the duodenum, compressing the duodenum. MR-cholangiopancreatography revealed dilation and aneurysm of the celiac trunk accompanied by a heterogeneous hemorrhagic mass enveloping and externally constricting the duodenum, causing duodenal obstruction. Esophagogastroduodenoscopy identified a narrowed, edematous 5 cm segment of the duodenum beyond D2, with all biopsies demonstrating normal

mucosa. Subsequent computed tomography-angiography revealed a celiac artery dissection with preserved flow and a 4 cm pancreaticoduodenal artery pseudoaneurysm. Interventional radiologists successfully embolized the pancreaticoduodenal pseudoaneurysm using microcoils. Anticipating that the obstructive process would improve after aneurysm microcoiling, clinicians did not place a duodenal stent. Instead, the patient was treated conservatively with nasogastric decompression. After several days of monitoring, the obstruction improved, allowing the patient to be discharged with the ability to consume a liquid diet. The patient was eventually able to return to eating a normal diet. Discussion: To our knowledge, this is the first reported case of a patient with a celiac artery dissection and pancreaticoduodenal pseudoaneurysm leading to external duodenal compression and obstruction. This case underscores a need for broadening the differential diagnosis for duodenal obstruction to encompass pathologies associated with the surrounding vasculature. Furthermore, it supports a conservative approach to managing this compressive duodenal obstruction with aneurysm coiling, rather than placing a permanent duodenal stent.

Internal Medicine
Toiv A, **Saleem A**, **Obri M**, **O'Brien H**, and **Jafri SM**. ADVANCING LIVER TRANSPLANTATION INTO THE NEXT DECADE: LIVER TRANSPLANT OUTCOMES IN PATIENTS 70 YEARS OR OLDER. *Hepatology* 2024; 80:S974. Full Text

A. Toiv, Henry Ford Hospital, United States

Background: Since the introduction of direct-acting antivirals for hepatitis C virus, liver transplantation (LT) has undergone a change in patient demographics, with patients receiving increasingly more LT for other chronic liver diseases and at older ages. Historically, younger patients have been prioritized for LT due to concerns about post-transplant outcomes in older patients; however, emerging evidence suggests that the impact of age on transplant eligibility criteria may need to be reevaluated. This study describes the clinical characteristics and postoperative LT outcomes of patients ≥ 70 years compared to patients < 70 years old. Methods: Single center retrospective chart review of all patients who underwent LT at a high-volume academic transplant center between January 1, 2014, and September 26, 2023. Results: Of 999 liver transplant recipients (36% women; 64% men), 43 were ≥ 70 years old (median 71 y; range 70-75) and 956 were < 70 years old (median 58 y; range 16-69). The older group had more baseline comorbidities but a lower median MELD at LT (21 vs 25; p =.014). Indications for LT differed between groups; while the younger group had a higher rate of alcoholic cirrhosis (39% vs 14%; p = < .001), the older group had greater proportions of patients with metabolic dysfunction-associated steatohepatitis (51% vs 23%; p = <.001), primary biliary cholangitis (9.3% vs 2.8%; p= .040), and cryptogenic cirrhosis (14% vs 5%; p= .022). Older and younger patients had similar postoperative liver function laboratory values, biliary complication rates, need for further procedures, and hospital readmission. The older cohort had a significantly longer mean length of stay (25.5 vs 14.0 days; p= .002), an association that was confirmed on regression analysis (p < .001). Notably, no differences in mortality or graft failure at 1, 3, and 5 years were observed between older and younger LT recipients. Conclusion: LT recipients ≥ 70 years-old had positive post-transplant outcomes and similar patient and graft survival as patients < 70 years old, although older age was associated with a longer hospital stay. Overall, LT evaluation and eligibility age criteria may need to be reevaluated to be more age inclusive.

Internal Medicine
Vemulapalli K, **Khan MZ**, and **Al Shammari M**. Uncomplicated Diverticulitis Masquerading as Symptomatic Ovarian Cyst in a Young Female. *Am J Gastroenterol* 2024; 119(10):S1973. Full Text

K. Vemulapalli, Henry Ford Health, Detroit, MI, United States

Introduction: Diverticulitis is an overwhelmingly common diagnosis in the field of gastroenterology. However, it is currently a diagnosis of high suspicion only in elderly to middle aged patients. Signs and symptoms of diverticulitis overlap with many alternative diagnoses. The differential is particularly broad in young female patients. Here we present a case of diverticulitis in a young female patient that was previously masquerading as symptomatic ovarian cyst. Case Description/Methods: A 19-year-old woman with prior history of symptomatic ovarian cyst requiring resection months prior presented with 4-day

history of right lower quadrant pain associated with nausea and diarrhea. She denied fevers or chills. She reported symptoms consistent with recurrence of prior episodes of symptomatic ovarian cyst. Exam was pertinent for right lower quadrant tenderness. Vitals signs remarkable for initial tachycardia with lab work showed leukocytosis to 13.0, unremarkable liver profile, lipase, urinalysis and pregnancy testing. Computed tomography Abdomen Pelvis with contrast was performed and showed findings of wall thickening and pericolonic fast stranding with multiple colonic diverticula at the level of mid ascending colon to the hepatic flexure concerning for diverticulitis. She was started on amoxicillin-clavulanate and noted to have significant improvement. She was discharged with a 5-day course of antibiotics to follow-up outpatient for colonoscopy. Discussion: Acute diverticulitis is 1 of the leading gastrointestinal-related causes of hospitalization with diagnostic delay resulting in increased risk of associated complications including abscess formation, fistulation, and sepsis. Recent trends have demonstrated a rising incidence of diverticulitis in younger patients resulting in a disconnect between clinical suspicion and disease prevalence. Moreover, studies have indicated diverticulitis in younger patients can present with increased severity and likelihood of recurrence. Differential diagnoses of recurrent abdominal pain should remain broad even with prior diagnoses of gynecologic etiology. Guidelines for treatment are not standardized therefore early intervention and appropriate follow-up should be arranged to ensure adequate long-term care of affected patients (see Figure 1).

Internal Medicine

Vemulapalli K, **Khan MZ**, **Patel-Rodrigues P**, **Hammad T**, and **Watson A**. Intrapapillary Mucinous Neoplasm Complicated by Spontaneous Pancreaticogastric Fistula. *Am J Gastroenterol* 2024; 119(10):S1836-S1837. Full Text

M.Z. Khan, Henry Ford Health, Detroit, MI, United States

Introduction: Intraductal Papillary Mucinous Neoplasms (IPMNs) consist of a range of presentations varying in malignant potential. Mainly characterized by papillary growth and significant mucin secretion, IPMNs can present with various complications including obstructive jaundice or cholangitis. Rarely, IPMN can fistulize into the adjacent organs. Here we present the case of a patient found to have benign IPMN complicated by 20mm pancreatico-gastric fistula. Case Description/Methods: An 85-year-old woman with history of heart failure presented with several week history of progressive epigastric pain accompanied by poor appetite and nausea. She remained hemodynamically stable with lab work showing unremarkable liver enzymes, blood counts, and lipase. Computed tomography abdomen pelvis showed dilated pancreatic duct with communication to the stomach. Magnetic resonance cholangiopancreatography (MRCP) showed moderate intrahepatic and severe extrahepatic biliary ductal dilation with the main pancreatic duct dilated up to 20mm. A 20mm fistula between the pancreatic body duct to posterior wall of the stomach was noted. The patient underwent Esophagogastroduodenoscopy/endoscopic retrograde cholangiopancreatography (ERCP) which demonstrated a 20mm fistula with copious amounts of mucin pouring out of the lesser curvature opening. The main pancreatic duct was visualized with features of main duct IPMN. Biopsy demonstrated features consistent with low-grade IPMN. Sphincterotomy and balloon extraction of choledocholithiasis was performed. A fully covered metal stent was placed into the common bile duct to maintain biliary drainage. Multidisciplinary discussion was held with the patient's family, gastroenterology team, and oncology team and decision to pursue resection was deferred in favor of symptomatic care. The patient recovered well and was discharged to follow-up for outpatient ERCP for further stent management. Discussion: IPMN resulting in fistulation into the stomach is an exceedingly rare presentation that can mimic many other pathologies of abdominal pain. Our patient's presentation with non-specific symptoms of epigastric pain, nausea, and early satiety requires a high degree of suspicion for biliary pathology. The identification of such a diagnosis requires complex decision-making involving multidisciplinary insight as well as shared decision-making regarding the potential for malignancy and surgical versus conservative management (see Figure 1).

Internal Medicine

Venkat D, **Chaudhary AJ**, **Elshebiny H**, and **Jafri SM**. Incidence, Management, and Prognosis of Wilson's Disease. *Am J Gastroenterol* 2024; 119(10):S1263. Full Text

D. Venkat, Wayne State University, School of Medicine, West Bloomfield, MI, United States

Introduction: Wilson's disease is an autosomal recessive condition caused by mutation in the Wilson's disease protein (ATP7B) gene, which results in an excessive copper buildup in the body. In this study, we present a retrospective analysis of the incidence, prognosis, and management of Wilson's disease at an academic medical center. Methods: We evaluated medical records of all patients with Wilson's disease seen at an academic medical center over the past 10 years. Each patient's presentation, management, and overall disease course was reviewed. This includes demographics, laboratory testing, 24-hour copper urine testing, symptoms, hepatology evaluation, therapy, side effects, liver complications, transplantation, and mortality. Results: A total of 88 patients with Wilson's disease were included; 43% are older than 50 years at diagnosis, with mean age 46.6 (range 13 to 83); 55% were female. Of the 17 with an initial 24-hour urine copper test recorded at our center, 29% had urine copper greater than 100 mcg at first clinic visit. Of those with initial and most recent 24-hour urine copper testing documented, 78% showed decreased urine copper and 22% showed no change or increase in urine copper. In total, 51% were asymptomatic, 15% had only gastrointestinal (GI) symptoms, 22% had only neuropsychiatric symptoms, and 2% had both GI and neuropsychiatric symptoms, 52% had documented visits with hepatology forWilson's disease. Of those who saw hepatology, 23% had 1 follow-up visit each year, and 77% had 2 or more visits per year. Only 28% of patients had documented therapy. Of patients on treatment, 28% were placed on trientine only, 36% were on zinc only, 24% received a combination of trientine, zinc and/or penicillamine. For those taking medications, 24% demonstrated intolerance to medications. 16% required a liver transplant. In total, 26% of the patients had cirrhosis, and 11% received a transplant. The mortality rate was 11%, but none of the deaths were related to Wilson's disease. Conclusion: Wilson's disease is a complex condition in which follow-up and assessment of fibrosis and successful therapy are important. We found that a large number of patients did not have referral to hepatology in spite of the diagnosis. Further, only 28% of patients with diagnosis of Wilson's disease had documented therapy at any time. Closer attention is warranted to ensure treatment and follow-up of patients with this progressive condition.

Internal Medicine

Venkatesh HK, **El-Kateb M**, and **Hussain A**. A Possible Correlation between Nephronophthisis and Glaucoma. *J Am Soc Nephrol* 2024; 35:1288. Full Text

H.K. Venkatesh, Henry Ford Macomb Hospital, Clinton Township, MI, United States

Introduction: Cilia perceive extracellular signals like growth factors, chemicals and light for normal kidney development and maintenance. 'Ciliopathies' are autosomal recessive genetic diseases caused by their dysfunction. Most commonly affected are the kidneys causing Nephronophthisis (NPH), but the brain, eye, face, liver, heart and skeleton are also involved. Several associations between NPH and other conditions have been discovered. This case report describes an unusual combination of glaucoma and NPH leading to profound visual and renal function loss. Case Description: A 20-year-old African American male presented with progressive vision loss after undergoing retinal cryotherapy and laser at the age of 4 for an unknown retinopathy. He had end-stage renal disease (ESRD) secondary to infantile NPH confirmed by genetic testing, having already failed transplantation twice. Eye examination noted decreased visual acuity bilaterally with only preserved light perception; he also had horizontal nystagmus, elevated intraocular pressure, retinal dystrophy and optic atrophy. Despite the discontinuation of steroids after the failure of his second allograft, tonometry continued to suggest open-angle glaucoma, concerning for a different disease process. Discussion: Over 90 gene mutations are involved in ciliopathies, of which more than 20 give rise to NPH. NPH has 3 forms - infantile, juvenile and adult; while the latter two produce tubulointerstitial fibrosis, infantile NPH causes a more severe medullary cystic kidney disease that quickly progresses to ESRD. Retinopathy in conjunction with NPH, is a rare autosomal recessive disease affecting 1 in a million, called Senior-Loken syndrome that presents with childhood-onset hyperopia, photophobia and nystagmus. Glaucoma has been recognized in other ciliopathies. In this case, despite the estimated 3% risk of permanent glaucoma following steroid cessation, dysfunctional cilia impairing aqueous humor outflow in the anterior segment of the eye may be responsible. Life expectancy with NPH may vary depending on the onset of ESRD. Although renal transplantation is the only solution currently, specific signaling pathways like cAMP/PKA, mTOR and Hedgehog are potential

sites for therapy. Identification of patients with NPH and new associations adds to the literature and maximizes pathological discoveries, thus paving the way for better treatment.

Internal Medicine

Youssef RM, **Yanamandra A**, and **Jafri SM**. Outcomes of Liver Transplantation in Arab American Patients: A Single Center Experience. *Am J Gastroenterol* 2024; 119(10):S1339. Full Text

A. Yanamandra, Wayne State University, School of Medicine, Detroit, MI, United States

Introduction: Arab American patients are a unique population poorly studied following liver transplantation. We aimed to evaluate the outcomes following liver transplant in self-identified Arab American Patients at a single academic center. Methods: This is a single-center qualitative study using a retrospective database of all patients who self-identify as Arab that received a liver transplantation. Patients were evaluated for demographics, clinical outcomes and disease recurrence. Results: Of the 28 patients included in our population, the average age at transplant is 56.3 (30.3 to 67.8) years of age and 71.4% of patients are male. The etiologies leading to cirrhosis are alcoholic cirrhosis (42.9%), hepatitis C (25.0%), hepatitis B cirrhosis (7.1%), autoimmune hepatitis (7.1%), primary sclerosing cholangitis (7.1%), nonalcoholic steatohepatitis (3.6%), cryptogenic cirrhosis (3.6%), and autoimmune cholangitis (3.6%). Survival at 1 year is 85.7%, at 3 years is 78.6%. Graft survival at 1 year is 85.7%, at 3 years is 78.6%. 7.1% of patients had histologic evidence of graft rejection and rejection occurred at a mean of 2.75 months post-liver transplant. 50% of patients with rejection survived to 1- and 3-years post-transplant. 10.7% of patients had histologic evidence of recurrent cirrhosis. 6 patients have died. Their etiology of cirrhosis varied with separate patients each having autoimmune hepatitis, hepatitis B, hepatitis C, cryptogenic, nonalcoholic steatohepatitis, alcoholic cirrhosis respectively. The causes of death for each separately are cardiac arrest, cholangiocarcinoma, cholangiosarcoma, graft failure, angiosarcoma, graft versus host disease respectively. Of the deceased patients, 33.3% survived 1 year post-liver transplant, while 0.0% survived 3 years. 16.7% had recurrent cirrhosis. Conclusion: Arab Americans are a growing group of patients with potential differences in metabolic disease, underlying liver disease recurrence and complications. Survival is worse than expected, especially in the face of rejection. Further study of this population is needed for an understanding of risk factors to better care for these patients following liver transplantation.

Nephrology

Morse P, **Chouman A**, **Tamr A**, **Saleem A**, **Cunningham C**, and **Umanath K**. CMV Colitis in Immunocompetent Host. *Am J Gastroenterol* 2024; 119(10):S2432-S2433. Full Text

P. Morse, Wayne State School of Medicine, Detroit, MI, United States

Introduction: Cytomegalovirus (CMV) is a double-stranded DNA virus which causes disease in humans based on their immune status. Despite being a common infection in immunocompromised hosts, CMV colitis rarely occurs in the immunocompetent. Symptoms of CMV colitis are nonspecific, including diarrhea, abdominal pain, fever, and rectal bleeding. We present an immunocompetent patient who was identified as having biopsy proven CMV colitis. Case Description/Methods: A 55-year-old woman with a history of well-controlled type 2 diabetes and end-stage renal disease (ESRD) on dialysis presented to the hospital with painless hematochezia and diarrhea for two months with acute worsening in the last week. Imaging several weeks before presentation to the ED was suggestive of ischemic colitis, but no further studies were completed at that time. Her hemoglobin on presentation was 8.4 g/dL. The next day, her hemoglobin dropped to 6.5 g/dL requiring blood transfusion. The patient's white blood cell count was mildly decreased at 3.6 K/mL with a normal differential. She underwent esophagogastroduodenoscopy, which was normal, and colonoscopy, which showed diffuse inflammation and a colonic ulcer which was biopsied. Pathology showed features of ischemic colitis and stained positive for CMV. Serum CMV quantitation at this time was 1474 IU/mL. She started intravenous ganiciclovir, which was transitioned to oral valganciclovir at discharge. Upon outpatient follow up two weeks later, the patient reported compliance with the valganciclovir and resolution of her symptoms. Serum CMV quantitation was undetectable at this visit. Discussion: Here we present a patient with well-controlled diabetes and ESRD on dialysis who presented with CMV colitis. Despite multiple comorbidities, she was immunocompetent.

Given the patient's positive biopsy staining for CMV, elevated serum CMV quantitation, and complete resolution of symptoms on valganciclovir, CMV colitis is the most likely diagnosis. Diabetes and ESRD on dialysis are known to be comorbid conditions with CMV colitis in immunocompetent hosts. Additionally, prior research indicates that being age 55 or over is also a risk factor. It is hypothesized that these comorbidities contribute to a weakening of the immune system, facilitating CMV colitis to develop in patients traditionally considered immunocompetent. Clinicians should consider CMV colitis in otherwise unexplained abdominal symptoms, particularly in patients with multiple comorbidities like diabetes, ESRD, and age 55 or greater.

Nephrology

Obeidat A, Yassine AA, Aldiabat M, **Mahfouz R**, and Gavin M. MALNUTRITION IMPACT ON PATIENTS WITH CIRRHOSIS; A NATIONWIDE ANALYSIS. *Hepatology* 2024; 80:S477-S478. Full Text

A. Obeidat, Presbyterian Health System

Background: Malnutrition, sarcopenia and cachexia are common conditions in patients with cirrhosis. Malnutrition has been reported in 20% of patients with compensated cirrhosis and in more than 50% of patients with decompensated cirrhosis. The pathophysiology of malnutrition in cirrhotic patients is complex and multifactorial. In this study we examine the potential impact of malnutrition on the in-hospital mortality as well as other secondary outcomes in cirrhotic patients admitted to the hospital in the period between 2019-2021. Methods: The United States Nationwide Inpatient Sample (NIS) database was used to extract hospitalization data of patients admitted between 2019 to 2021. Using ICD10 revision codes, we identified adults with the diagnosis of cirrhosis with concomitant malnutrition, including sarcopenia and cachexia. The control group included cirrhotic patients without malnutrition. The primary outcome was the inhospital mortality. Secondary outcomes included encephalopathy, ascites, variceal bleed, sepsis, respiratory failure (RF), acute kidney injury (AKI), hepatorenal syndrome (HRS) and length of stay (LOS). Multivariate logistic regression was used to adjust for relevant variables. Results: An estimated 212,067 patients were admitted with cirrhosis during the study period. Of these, 25,331 patients had the diagnosis of malnutrition. In malnourished cirrhotic patients, the mean age was 56.44 years vs 55.7 patients without malnutrition. 35.8% were females and 68.8% were Caucasians. 12.08% of malnourished cirrhotic patients died during hospitalization compared to 6.35% of cirrhotics without malnutrition. Further, total hospital charges were more in the malnourished group compared to the non-malnourished group (133,054 $ vs 75,661$). When adjusted to other relevant variables, malnutrition was associated with increased inhospital mortality in cirrhotic patients (OR 1.93; P-value 0.00). Age and Caucasian race were also associated with increased in-hospital mortality. On multi-variate analysis, malnutrition was associated with an increased chance of developing sepsis, AKI, RF, HE, ascites, HRS and prolonged LOS. Interestingly, malnourished cirrhotic patients had a lower chance for variceal bleeding (see Table 1). Conclusion: Malnutrition is a common complication in patients with cirrhosis. In this study, cirrhotic patients with malnutrition had an increased chance of in-hospital mortality. Moreover, they had higher chances for decompensation including HE and ascites, and other in-hospital complications such as AKI, HRS and RF, which can lead to increased LOS and increased financial burden. Therefore, we recommend clinicians to pay close attention to cirrhotic patients with malnutrition and to have a multi-disciplinary approach which involve other team members in treating them.

Nephrology

Obeidat A, Yassine AA, Aldiabat M, **Mahfouz R**, and Holman G. Impact of Cirrhosis on Patients Admitted With Acute COPD Exacerbation: A Nationwide Study. *Am J Gastroenterol* 2024; 119(10):S1374. Full Text

A. Obeidat, Presbyterian Hospital, Albuquerque, NM, United States

Introduction: Chronic obstructive pulmonary disease (COPD) has increasingly been identified as a major cause of death worldwide. The management of acute COPD exacerbation depends on severity. In cases of severe exacerbation, hospitalization is required. We study the potential impact of cirrhosis on the in-hospital mortality as well as other secondary outcomes in patients admitted with acute COPD exacerbation. Methods: The United States Nationwide Inpatient Sample (NIS) database was used to extract hospitalization data of patients admitted between 2019 to 2021. Using International Classification

of Diseases 10 revision codes, we identified adults with the primary diagnosis of COPD exacerbation. We divided patients into 2 groups; cirrhosis vs no cirrhosis. The primary outcome was the in-hospital mortality. Secondary outcomes included sepsis, respiratory failure (RF), arrhythmias, pneumothorax, pulmonary embolism (PE), acute kidney injury (AKI) and length of stay (LOS). Multivariate logistic regression was used to adjust for relevant variables. Results: An estimated 914,498 patients were admitted with COPD exacerbation. 38,310 patients had the diagnosis of cirrhosis. In cirrhotic patients, the mean age was 62.2 years. 31.5% were females and 79.5% were Caucasians. 10.5% of cirrhotic patients died during hospitalization compared to 5.8% of non-cirrhotics. Alcohol use, smoking and malnutrition were more prevalent among cirrhotics. Cirrhotic patients had a longer LOS (8.4 vs 6.3), and more financial burden with total hospital charges of 101,061≥ vs 74,363≥. When adjusted to other relevant variables, cirrhosis was associated with increased in-hospital mortality (OR 1.26; P-value <0.001). Further, cirrhosis was associated with an increased chance of developing sepsis, AKI, encephalopathy and prolonged LOS. Moreover, cirrhosis increased the chance of developing an arrhythmia and cardiac arrest, however, this association was not significant. Interestingly cirrhotic patients had a lower chance for PE, pneumothorax and RF (Table 1). Conclusion: COPD exacerbation is a common cause of hospitalization in the US. In this study, we concluded that cirrhosis is associated with increased in-hospital mortality among patients with acute COPD exacerbation. Moreover, it can increase the chance of developing other in-hospital complications that will lead to an increased LOS and total hospital charges. We advise clinicians to be attentive when treating cirrhotic patients with acute COPD exacerbation, and to closely monitor for in-hospital complications.

Nephrology

Obeidat A, Yassine AA, **Mahfouz R**, Holman G, and Aldiabat M. Prevalence of Different Malignancies Among Liver Transplant Recipients: A Nationwide Study. *Am J Gastroenterol* 2024; 119(10):S1373-S1374. Full Text

A. Obeidat, Presbyterian Hospital, Albuquerque, NM, United States

Introduction: Liver transplantation (LT) is lifesaving for patients with acute, end-stage liver disease and liver cancer. Prolonged immunosuppression is associated with carcinogenesis, most commonly skin cancer followed by lymphoproliferative diseases. We will highlight the prevalence of most common malignancies among LT recipients, excluding liver cancer, and will include demographics of LT recipients with these malignancies. Methods: The United States Nationwide Inpatient Sample (NIS) database was used to extract hospitalization data of patients admitted between 2019 to 2021. Using International Classification of Diseases10 revision codes, we identified adults who underwent LT. We identified patients with a diagnosis of malignancy except liver cancer. The control group included LT recipients without malignancy. We compared both groups in terms of demographic and clinical characteristics. Moreover, we studied the prevalence of different malignancies among LT recipients. Results: An estimated 26,371 patients with a history of LT were admitted during the study period. 5,585 patients had the diagnosis of one of the cancers studied below. Among LT recipients, 2,540 patients had hepatitis B, 9,150 patients had hepatitis C and 5,155 had alcohol related cirrhosis. Cancer was more prevalent among older patients with a mean age of 64.4 years. Moreover, cancer was more prevalent in Whitesand males. LT recipients with cancer had more prevalence of malnutrition, smoking and chronic lung diseases. On the other hand, patients with no cancer had more prevalence of alcohol use, obesity, diabetes mellitus and congestive heart failure. LT recipients with cancer had increased length of stay (LOS) (6.7 days vs 5.9 days) and mean total hospital charges (95,878 ≥ vs 81,252 ≥). Excluding liver cancer, lymphoma was the most prevalent malignancy among LT recipients (27.8%). This was followed by lung cancer (23.7%), melanoma (13.4%), leukemias (11.9%) and squamous cell cancer of the skin (6.5%). cholangiocarcinoma, colon cancer, basal cell skin cancer, gastric cancer and pancreatic cancer constitute the rest (Figure 1). Conclusion: Malignancy is a known complication in patients with LT. Most LT recipients with cancer are elderly and malnourished. Therefore, it is important to pay more attention to signs and symptoms that may represent malignancy among LT patients to diagnose them earlier for better management and prognosis. Our study showed that pancreatic cancer occurred less frequently than expected among LT recipients and this merits further investigation.

Nephrology

Venkatesh HK, **El-Kateb M**, and **Hussain A**. A Possible Correlation between Nephronophthisis and Glaucoma. *J Am Soc Nephrol* 2024; 35:1288. Full Text

H.K. Venkatesh, Henry Ford Macomb Hospital, Clinton Township, MI, United States

Introduction: Cilia perceive extracellular signals like growth factors, chemicals and light for normal kidney development and maintenance. 'Ciliopathies' are autosomal recessive genetic diseases caused by their dysfunction. Most commonly affected are the kidneys causing Nephronophthisis (NPH), but the brain, eye, face, liver, heart and skeleton are also involved. Several associations between NPH and other conditions have been discovered. This case report describes an unusual combination of glaucoma and NPH leading to profound visual and renal function loss. Case Description: A 20-year-old African American male presented with progressive vision loss after undergoing retinal cryotherapy and laser at the age of 4 for an unknown retinopathy. He had end-stage renal disease (ESRD) secondary to infantile NPH confirmed by genetic testing, having already failed transplantation twice. Eye examination noted decreased visual acuity bilaterally with only preserved light perception; he also had horizontal nystagmus, elevated intraocular pressure, retinal dystrophy and optic atrophy. Despite the discontinuation of steroids after the failure of his second allograft, tonometry continued to suggest open-angle glaucoma, concerning for a different disease process. Discussion: Over 90 gene mutations are involved in ciliopathies, of which more than 20 give rise to NPH. NPH has 3 forms - infantile, juvenile and adult; while the latter two produce tubulointerstitial fibrosis, infantile NPH causes a more severe medullary cystic kidney disease that quickly progresses to ESRD. Retinopathy in conjunction with NPH, is a rare autosomal recessive disease affecting 1 in a million, called Senior-Loken syndrome that presents with childhood-onset hyperopia, photophobia and nystagmus. Glaucoma has been recognized in other ciliopathies. In this case, despite the estimated 3% risk of permanent glaucoma following steroid cessation, dysfunctional cilia impairing aqueous humor outflow in the anterior segment of the eye may be responsible. Life expectancy with NPH may vary depending on the onset of ESRD. Although renal transplantation is the only solution currently, specific signaling pathways like cAMP/PKA, mTOR and Hedgehog are potential sites for therapy. Identification of patients with NPH and new associations adds to the literature and maximizes pathological discoveries, thus paving the way for better treatment.

Neurology

Contreras J, Nadeem M, Akhter N, **Hoda N**, **Ahmad AS**, Ducruet AF, Bhatia K, and Ahmad S. Remote ischemic post-conditioning (RIC) mediates neuroprotection in murine traumatic optic neuropathy (TON). *Invest Ophthalmol Vis Sci* 2024; 65(7):3953. Full Text

J. Contreras, Translational Neuroscience, Barrow Neurological Institute, Phoenix, AZ, United States

Purpose : Traumatic optic neuropathy (TON) has been regarded a vision threatening condition caused by either ocular or blunt/penetrating head trauma which is characterized by direct or indirect TON. Injury happens during sports, vehicle accidents and mainly in military war and combat exposure. TON results optic nerve damage that leads to profound loss of central vision. There is stiil a lack of TON managment. Here, we used remote ischemic post-conditioning (RIC) therapy to reduce TON related retinal dysfunction. Earlier, we have demonstrated that RIC therapy is protective in TON via AMPKα1 activation in mice. AMPKα1 is the catalytic subunit of the heterotrimeric enzyme AMPK, the master regulator of cellular energetics and metabolism. The α1 isoform predominates in immune cells including macrophages (Mφs). Methods : We generated myeloid specific AMPKα1 KO mice by using LysMcre to carry out the study. We induced TON in mice by using controlled impact system as reported previously. RIC therapy was given every day (5-7 days following TON). Western blotting, Immunohistochemistry, Flow cytometry and TEM technique, and Unisense sensor system for retinal oxygenation were used to generate research data. Results : Immunofluorescence and western blot data showed increased microglial activation and decreased retinal ganglion cell (RGCs) marker Brn3 and axonal regeneration marker GAP43 expression in TON [AMPKα1F/F] vs Sham group but TON+RIC [AMPKα1F/F] attenuated expression level of these markers. Interestingly, higher microglia activation was observed in myeloid AMPKα1F/F KO group with TON and RIC didn't show any significant difference. Flow cytometry, ELISA and retinal tissue oxygen data revealed that RIC therapy significantly reduced the pro-inflammatory signaling markers and

increased anti-inflammatory markers, and improved oxygen level however, myeloid AMPKα1 KO mice didn't show any changes after TON with RIC. Transmission electron microscopy (TEM) data of optic nerve showed increased demyelination and axonal degeneration in TON [AMPKα1F/F] group and TON+RIC [AMPKα1F/F] showed improved myelination. RIC has no significant effect in myeloid AMPKα1 KO group following TON. Conclusions : Overall, these data suggested that RIC therapy provides protection against inflammation and neurodegeneration via myeloid AMPKα1. Further investigation of RIC and AMPKα1 signaling is warranted in TON.

Neurology
Snyder J, Alford SH, Kumar T, Pindolia K, **Poisson L**, Mahatma S, and **Mikkelsen T**. ONCOPATH: OPTIMIZED TREATMENT GUIDELINE CONCORDANT PATHWAY PRESENTED ON A VISUALINTERACTIVE DASHBOARD FOR CLINICAL DECISION SUPPORT COMPUTED BY OVERLAYING PATIENT LONGITUDINAL DATA ON A KNOWLEDGE GRAPH. *Neuro Oncol* 2024; 26:viii172. Full Text

J. Snyder, Henry Ford Health, Detroit, United States

BACKGROUND: OncoPath provides a visual analysis of a brain tumor patient's longitudinal clinical data overlayed on disease specific pathways with the goal of reducing knowledge discordant care and insurance authorization burden. By ingesting, curating and visually presenting the patient experience on guidelines, OncoPath aims to streamline clinical decision making and related processes. Understanding the patient's journey compared to treatment guidelines is of value in addressing health equity and guideline adoption in real world settings. METHODS: Data from 44 glioma patients diagnosed and treated between 2016-2021 were uploaded to OncoPath using natural language processing and other tools to capture abstractable data elements. The data was overlayed on guidelines using recursive graph modeling. Using the knowledge graph of a patient's history, the model also recommends treatment options in an interactive visual dashboard representing NCCN guidelines. The dashboard includes the guidelines in graphical format with associated references and notation. RESULTS: 28 males and 16 females age 21-38 years at diagnosis were abstracted. Cases represented 4 oligodendrogliomas, 13 astrocytomas, and 27 glioblastomas. Data was available through second line therapy, discharge to hospice or death. Cases were matched to the NCCN 2021 guidelines which was used for treatment decisions until November 2022. The patient data matched OncoPath except in 3 cases where KPS was not available resulting in premature pathway truncation. For these cases we inferred KPS based on subsequent treatment received to optimize the historic data. CONCLUSION: To our knowledge, this is a first-of-a-kind technology in neuro-oncology that may improve time to treatment, reduce health utilization resources and can serve as a benchmarking tool for care delivery. The feasibility of clinically implementing such tools for decision support was demonstrated. This type of tool could be particularly useful in low-resource areas where disease specific expertise may not be available or to illuminate care discrepancies.

Neurology
Zhang Y, **Zhang L**, **Chopp M**, **Zhang ZG**, **Mahmood A**, and **Xiong Y**. N-Acetyl-Seryl-Aspartyl-Lysyl-Proline (AcSDKP) as a Potential Novel Treatment for Experimental Traumatic Brain Injury. *J Neurotrauma* 2024; 41(15-16):A117. Full Text

Y. Zhang, Department of Neurosurgery, Henry Ford Health, Detroit, United States

Objective: N-acetyl-seryl-aspartyl-lysyl-proline (AcSDKP) exhibits multiple functions, such as immunomodulation, anti-inflammation, anti-fibrosis, and pro-angiogenesis. This study was aimed to determine efficacy and mechanism of AcSDKP treatment for traumatic brain injury (TBI). Methods: Young (2-3 months) male Wistar rats were subjected to moderate TBI. Subcutaneous infusion of AcSDKP at a dose of 0.8 mg/kg/day or Vehicle (0.01N acetic acid) was initiated 1h after injury and continued for 3 days. Modified neurological severity score (mNSS), foot-fault, Morris water maze tests were performed. Animals were sacrificed 1 day or 35 days after injury and brain sections processed for histological analyses of neuronal loss, neuroinflammation, BBB damage, angiogenesis, neurogenesis and histone deacetylase 4 (HDAC4). One-way ANOVA followed by post hoc Tukey's tests was used to compare the

differences in functional and histological outcomes. P value <0.05 was considered significant. Results: Compared to the Vehicle treatment, AcSDKP treatment led to significant (p<0.05): 1) improvements in spatial learning in the Morris water maze test and sensorimotor function in foot-fault and mNSS tests, 2) reductions of lesion volume and hippocampal neuronal cell loss (NeuN), BBB damage (Fibrin deposit), and neuroinflammation (CD68+ microglia/macrophages and GFAP+ astrocytes), 3) enhancement of angiogenesis (BrdU/EBA staining) and neurogenesis (BrdU/NeuN staining), and 4) blockage of neuronal HDAC4 nuclear translocation, which increased histone H3 acetylation in rats after TBI. Conclusions: Our data reveal a novel mechanism that AcSDKPinduced beneficial effects on TBI recovery are associated with its selective inhibition of neuronal HDAC4 nuclear translocation.

Neurosurgery
Dunbar E, Lee S, Peach MS, Wanbo J, Smith C, Hansfit S, Mertitz K, Berkowitz A, Sloan L, Ferreira C, Neil E, Kotecha R, Nowlan A, McCracken D, Patel T, Wardak Z, Richardson A, Shah M, Chowdhary S, DiNapoli V, Floyd J, Nagib M, Wasilewski A, Patel A, Rao G, Pham H, Ryan R, Shen C, **Robin A**, **Lee I**, Leng L, Hoang K, Olson J, Choutka O, Mercado C, Chamoun R, Camarata P, Smith W, Babu H, Piccioni D, Sevak P, Zhu J, Haydon D, Aizenberg M, Hoeprich M, Williams B, Dickinson L, Baskin D, Farach A, and Rodriguez A. TRIALS IN PROGRESS: REGISTRY OF SAFETY and EFFICACY IN ADULTS WITH PRIMARY and METASTATIC INTRACRANIAL TUMORS TREATED WITH START (GAMMATILES (CS-131 SOURCE BRACHY-THERAPY)): NCT04427384. *Neuro Oncol* 2024; 26:viii114-viii115. Full Text

E. Dunbar, Piedmont Brain Tumor Center, Atlanta, United States

INTRO: This is the first observational registry study of R+STaRT, delivered by Cs-131 sources in permanently implanted resorbable collagen tile carriers, for patients with intracranial tumors. METHODS: Since October 2020, 37 sites to-date have enrolled 359 patients with primary and metastatic intracranial tumors into the R+STaRT registry to assess the safety and efficacy of the addition of Gamma Tile to medically needed resection. Local control, overall survival, QOL, neurocognition, functional decline, and surgical and radiation associated AE's are collected at 1, 3, 6, 9,12, 18 and 24 months, then every 6 months through 5 years. RESULTS: Demographics include 359 patients, avg. age 57 y.o. 162 malignant gliomas, 125 metastatic tumors, 38 meningiomas, and 34 rare other tumors. 197 Males (163 White, 23 Black, 5 Asian, and other races) and 157 Females (White 121, 28 Black, 0 Asian, and 8 other races). No unexpected outcomes reported in the hands of experienced providers have occurred, although close clinical-radiographic follow-up, to ensure early detection of possible treatment-effects, is paramount. Steroid-use, and above endpoints, continue to be collected. CONCLUSIONS: In this observational registry of Gamma Tiles (Cs-131 source brachy-therapy) added to medically needed resections for patients with primary and metastatic intracranial tumors continues. Data will be used to benchmark clinical outcomes of R+STaRT therapy and allow for comparisons to existing standard-of-care treatments. The outcome measures captured will allow for evaluation of the potential risks and benefits of this treatment approach for patients in a real-world setting.

Neurosurgery
Elder JB, Hanft S, **Lee IY**, Farrell C, Boockvar JA, Zacharia BE, Kim L, Schulder M, Correia CES, Ramakrishna R, Wong ET, Wu J, Agarwal V, Amankulor N, Bhatia A, Evans LT, Brennan C, Gill BJ, Sengupta S, Quinones-Hinojosa A, Giglio P, Wu K, Wu SH, Falo C, **Walbert T**, **Robin A**, Alnahhas I, Vojnic M, Wernicke AG, Aregawi D, Maurer R, Ghatan S, Singer S, Jeyapalan S, Magge R, Malik AN, Patel N, Chan A, Iwamoto F, Hormigo A, Higgins D, Dey M, Moss NS, Sherman W, Neese L, Pennock GK, Scott C, Perez-Olle R, and Andrews DW. EARLY SAFETY DATA FROM A RANDOMIZED, MULTICENTER, DOUBLE-BLIND, PHASE 2B STUDY OF IGV-001, AN AUTOLOGOUS CELL IMMUNOTHERAPY, VERSUS PLACEBO, IN NEWLY DIAGNOSED GLIOBLASTOMA (NDGBM). *Neuro Oncol* 2024; 26:viii87-viii88. Full Text

J.B. Elder, Ohio State University, Columbus, United States

Standard of care (SOC) for ndGBM begins with maximal safe resection followed by adjuvant radiotherapy and temozolomide, and maintenance temozolomide. IGV-001 is an autologous biologic-device combination immunotherapy for the treatment of ndGBM that consists of autologous GBM tumor cells and

an antisense oligonucleotide against IGF-1R mRNA, irradiated and administered via biodiffusion chambers implanted in the abdomen. In a phase 1b study, IGV-001 was well tolerated without unexpected adverse events in subjects with ndGBM. Multiple efficacy signals were observed, including significant improvements in progression-free survival (PFS), overall survival (OS), radiographic evidence of tumor response, and changes in immune response biomarkers. Here, we present early safety data from the phase 2b randomized, multicenter, double-blind, placebo-controlled study (NCT04485949) designed to assess efficacy and safety of IGV-001 in subjects with ndGBM across 20 sites in the United States. After surgical resection, subjects were randomized 2:1 and treated with IGV-001 or placebo followed by SOC. The primary outcome is PFS, defined as the time from randomization to first progression, as determined by blinded central radiology review, or death. Secondary outcomes include OS, defined as the time from randomization to death due to any cause, and safety. As of May 22, 2024, 99 subjects were randomized and 95 implanted with IGV-001 or placebo plus SOC. A total of 39/45 (86.7%) subjects had sufficient follow-up time after initiated treatment with concurrent radiation and temozolomide. Nine of 72 randomized (12.5%) discontinued treatment, including 7 who stopped during the SOC treatment period. None ceased treatment for adverse events, protocol deviations, or death. A total of 11/72 (15.3%) randomized subjects discontinued the study after randomization. A review of blinded safety data did not show any emerging risk and supports no change to the benefit-risk profile of IGV-001 versus placebo. Updated data will be presented.

Neurosurgery

Faddah R, **Walbert T**, **Snyder J**, **Gadgeel S**, **Philip P**, and **Lange L**. STREAMLINING THE STUDY INTAKE PROCESS AT THE CANCER CLINICAL AND TRANSLATIONAL RESEARCH OFFICE (CCTRO). *Neuro Oncol* 2024; 26:viii261. Full Text

R. Faddah, Henry Ford Health, Detroit, United States

Challenges in the Protocol Intake/Activation process at the Henry Ford Cancer Center, particularly during the budget negotiation and coverage analysis (CA) phases, hamper operational efficiency and financial prospects. This study aimed to improve budget time and process efficiency. Process flow mapping, Value Stream Mapping (VSM), and cause-effect analysis using a fishbone diagram were used to identify and analyze key bottlenecks, focusing on the budget negotiation and CA phases. Budget negotiation took an average of 121.5 days in 2023 due to multiple procedures and a lack of standardized practices. Delays ranged from 127.75 days in August to a low of 69.84 days in November of 2023. The budget build process averaged 13.31 days, with an additional 7.57 days for approval, totaling 20.89 days. The CA phase had an average cycle time of 10.82 days (range 2-10 days). To improve approval times, it was recommended to implement an Electronic Document Management System to automate routing, signing, and tracking of budget and CA-related documents, standardized budget templates to streamline negotiations, a detailed electronic checklist to streamline task lists for document collection and budget negotiation, automated reminders for internal and external stakeholders to ensure timely submission of necessary documents, and timely submission policies enforced by a dedicated finance member on committees. Newly developed Key Performance Indicators (KPIs) such as 'time to collect documents,' 'time between committees,' and 'time for budget negotiation process,' along with a dual tracking system in Excel, were proposed to monitor and improve these metrics. The recommendations are expected to significantly enhance the efficiency of the Protocol Intake/Activation process. By reducing the budget negotiation phase to less than 60 days and optimizing the CA process, faster study initiation, better resource utilization, and improved responsiveness to research opportunities will be achieved. This study underscores the critical need to address operational challenges in clinical trial management to enhance CCTRO's capability to conduct timely and effective research.

Neurosurgery

Gordeyeva Y, Dalm B, Almeida L, De Jesus S, Fasano A, Foote K, Jimenez-Shahed J, Pathadan DS, Pouratian N, Rolston J, Rosenow J, Safarpour D, **Schwalb J**, Siddiqui M, Spindler M, Tsai A, Wong J, and Verhagen-Metman L. CLINICAL TRENDS AND CLINICIAN PERCEPTIONS REGARDING ASLEEP AND AWAKE DBS. *Stereotact Funct Neurosurg* 2024; 102:222-223. Full Text

Y. Gordeyeva, Poznan University of Medical Sciences, Poznan, Poland

Introduction: DBS clinical practice continues to evolve leading to a wide variability in intraoperative methods, and consensus regarding optimal workflow is lacking. Our objective is to determine trends and perceptions regarding Asleep and Awake Deep Brain Stimulation (DBS) in the USA and abroad. Methods: A panel of DBS clinicians created a REDCap survey regarding DBS practice in the US and abroad. The survey was sent out to the Functional Neurosurgery Working Group of the Parkinson Study Group, DBS Think Tank, World Society for Stereotactic and Functional Neurosurgery, and Movement Disorder Society members with stated DBS interest. Results: There were 321 individual respondents from 38 countries and six continents. Sixty percent were neurosurgeons, 37% neurologists and 3% Advanced Practice Providers. Fifty-eight percent perform both awake and asleep DBS procedures, 26.8% awake only, and 15.5% asleep only. Of 117 centers performing both awake and asleep DBS, 70% choose awake for STN, 45% choose awake for GPi, and 92% choose awake for VIM. When asked to agree or disagree to: asleep DBS is equal to or more effective than awake DBS for each target, respondents agreed/disagreed as follows: VIM:12.7%/60.6%, GPi: 57.4%/23.8%, STN: 29.4%/41.3% (remainder 'similar' or 'no experience'). Of 162 respondents who perform asleep DBS, 21.6% use intra-operative MRI (iMRI). Out of the 78.4% who do not use iMRI for asleep DBS, 54.3% use microelectrode recording (MER). Of 187 respondents who perform awake DBS, the most commonly used tools reported were: pre-op MRI (95.2%), MER (91.4%) and test stimulation (stim, 95.1%). When presented with 7 techniques for awake/asleep DBS, the choice for the Most optimal technique for each target, was 'awake+MER+stimulation+/-intraoperative imaging' for STN and VIM. For GPi, 'Asleep i-MRI' and 'awake+MER+stimulation+/-intraoperative imaging' received a similar number of responses. For the Least optimal technique for each target, respondents chose 'asleep iCT/Oarm' for STN, GPi and VIM. Conclusions: Results confirmed high variability in the use of intraoperative methods. There was a preference for the use of Awake DBS for VIM and STN, while the results for GPi were equivocal. These results provide only a snapshot of current DBS trends, and perceptions may change with further technological advances.

Neurosurgery

Kagithala D, **Rademacher A**, **Pawloski J**, **Latack K**, **Fadel H**, **Dallo F**, **Snyder J**, **Lee I**, and **Robin A**. ADJUVANT RADIATION THERAPY IN ATYPICAL MENINGIOMA TREATMENT DOES NOT IMPROVE PROGRESSION FREE SURVIVAL OR OVERALL SURVIVAL: A RETROSPECTIVE COHORT STUDY. *Neuro Oncol* 2024; 26:viii229. Full Text

D. Kagithala, Department of Neurosurgery, Henry Ford Health, Detroit, United States

Treatment of atypical meningiomas (AMs) presents a challenge due to their aggressive nature and tendency to recur. While there is clear evidence for the role of surgical resection of AMs, the use of adjuvant radiation therapy (ART) is a topic of ongoing debate. The aim of this study is to explore the impact of ART following surgical resection of AMs. The primary outcomes of interest are progression free survival (PFS) and overall survival (OS). Records were reviewed for all patients treated for Ams at our institution between January 1, 2014 and January 1, 2024. Patients were grouped into two cohorts, those who were initially treated with surgical resection only and those who also received adjuvant RT. PFS and OS were compared between the two groups using Kaplan Meier curves and Log Rank test. Additionally, multivariable cox proportional hazard models were used to adjust for age, MIB, and resection Simpson grading. There were 76 patients who were initially treated with surgery only and 23 patients who had surgery and ART. No significant difference in PFS or OS was observed between the groups (p=0.3522 and p=0.3636, respectively); including after adjusting for age, MIB, and Simpson grading (HR= 1.55 [0.64-3.76], p= 0.330; and HR = 0.95 [0.31-2.93] p= 0.934, respectively). On multivariate analysis, MIB >10 was associated with a significant difference in PFS (HR=2.76 [1.15-6.59], p=0.023). With ART, PFS was 91% at 12 and 60% at 36 months (versus 89% and 57%, respectively, with surgery only). OS was 95% at 12 and 88% at 36 months (versus 91% and 85%, respectively, with surgery only). In this series, ART was not observed to significantly improve PFS or OS compared to surgery alone. Larger series are needed to determine if there is a subset of patients who benefit from ART.

Neurosurgery

Kotecha R, Lee S, Peach MS, Patel T, Wardak Z, Floyd J, McGinity M, Hanft S, **Robin A**, **Lee I**, Sloan L, Shen C, Rodriguez A, Bojanowski-Hoang K, Wanebo J, Smith K, Shah M, Richardson A, Chamoun R, Camarata P, Milligan B, Leng L, Seid P, Wasilewski A, Monyak D, Nowlan A, McCracken D, Dunbar E, Ranjan T, DiNapoli V, Pham H, Ryan R, Mercado C, Avgeropoulos N, Choutka O, Patel A, Jalali A, Haydon D, Deb N, Zhu J, Piccioni D, Hoeprich M, Ansari MA, Baskin D, Sevak P, Brachman D, Garcia M, and Patel S. RECURRENT BRAIN METASTASES (RBM) TREATED WITH SURGICALLY TARGETED RADIATION THERAPY (START): PRELIMINARY SAFETY EVALUATION FROM A MULTIINSTITUTIONAL PROSPECTIVE REGISTRY. *Neuro Oncol* 2024; 26:viii286. Full Text

R. Kotecha, Baptist Health Miami Cancer Institute, Miami, United States

BACKGROUND: Resection and intraoperative brachytherapy for operable recurrent brain metastasis allows for pathologic confirmation of recurrent disease, mass effect relief, and immediate initiation of radiotherapy (RT). In this analysis, we report patterns-of-use and treatment-related adverse events (AEs) for rBM patients treated with Cs-131 collagen tiles, an FDA-cleared intracranial brachytherapy device. METHODS: Patients with rBM who underwent resection and surgically-targeted radiation therapy (GammaTile, GT Medical Technologies Inc., Tempe, AZ USA) on a prospectively enrolling phase 4 registry study (NCT04427384) were analyzed. AEs were graded per CTCAE v5.0. RESULTS: Between 11/2020 and 2/2024, 56 rBM in 51 consecutive patients underwent STaRT at 19 centers, with 5 patients having 2 metastases implanted concurrently. 44 patients (86%) had prior same-site RT (median interval 14.5 mo, range 3-56). Primary tumor histologies were lung (27), melanoma (8), breast (7), renal (4), colon (2), and other (3). Median pre-operative maximum diameter was 3.0 cm (range 1.4-5.7); age 63 (range 28-81); 53% females; KPS median 90 (range 40-100); and median implantation time 3 minutes. 26 patients were implanted at a 1st, 15 at a 2nd, and 10 at ≥ 3rd same-site recurrence (range 1-9). At a median follow-up of 6.2 months (range <1-35.1), 6/51 patients (11.8%) experienced ≥Gr 3 AEs at a median of 12 (range 1-69) days postoperatively (POD). No radiation necrosis (RN) events were observed, and no AEs occurred in multi-implant cases or where STaRT was the initial form of RT. CONCLUSIONS: In this prospective multi-institutional study, STaRT demonstrated an excellent safety profile in a cohort of larger rBM, even in the setting of multi-recurrent disease. Accrual and follow-up are on-going and will provide data on tumor control and long-term RN rates.

Neurosurgery

Lita A, Sjöberg J, Pcioianu D, Celiku O, Dowdy T, Pun A, Gilbert MR, **Noushmehr H**, Petre I, and Larion M. RAMAN-BASED MACHINE LEARNING PLATFORM REVEALS UNIQUE METABOLIC DIFFERENCES BETWEEN IDHMUT AND IDHWT GLIOMA. *Neuro Oncol* 2024; 26:viii191. Full Text

A. Lita, Neuro-Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, United States

BACKGROUND: Formalin-fixed, paraffin-embedded (FFPE) tissue slides are routinely used in cancer diagnosis, clinical decision-making, and stored in biobanks, but their utilization in Raman spectroscopy-based studies has been limited due to the background coming from embedding media. METHODS: Spontaneous Raman spectroscopy was used for molecular fingerprinting of FFPE tissue from 46 patient samples with known methylation subtypes. Spectra were used to construct tumor/non-tumor, IDH1WT/IDH1mut, and methylation-subtype classifiers. Support vector machine and random forest were used to identify the most discriminatory Raman frequencies. Stimulated Raman spectroscopy was used to validate the frequencies identified. Mass spectrometry of glioma cell lines and TCGA were used to validate the biological findings. RESULTS: Here we develop APOLLO (rAman-based PathOLogy of maLignant glioma) - a computational workflow that predicts different subtypes of glioma from spontaneous Raman spectra of FFPE tissue slides. Our novel APOLLO platform distinguishes tumors from nontumor tissue and identifies novel Raman peaks corresponding to DNA and proteins that are more intense in the tumor. APOLLO differentiates isocitrate dehydrogenase 1 mutant (IDH1mut) from wildtype (IDH1WT) tumors and identifies cholesterol ester levels to be highly abundant in IDHmut glioma. Moreover, APOLLO achieves high discriminative power between finer, clinically relevant glioma methylation subtypes, distinguishing between the CpG island hypermethylated phenotype (G-CIMP)-high

and G-CIMPlow molecular phenotypes within the IDH1mut types. CONCLUSIONS: Our results demonstrate the potential of label-free Raman spectroscopy to classify glioma subtypes from FFPE slides and to extract meaningful biological information thus opening the door for future applications on these archived tissues in other cancers.

Neurosurgery
Nagaraja T, and **Lee I**. RECURRENT GLIOBLASTOMA AFTER LASER ABLATION OF THE PRIMARY TUMOR IN A PRECLINICAL ORTHOTOPIC MODEL EXHIBIT INCREASED GENETIC SIGNATURES OF CELL CYCLE AND CELL MOTILITY. *Neuro Oncol* 2024; 26:viii325. Full Text

T. Nagaraja, Henry Ford Hospital, Detroit, United States

Image-guided laser interstitial thermal therapy (LITT) is a minimally invasive tumor cytoreductive treatment for recurrent gliomas and tumors in eloquent loci. We have adapted this technique to develop an image-guided glioblastoma (GBM) ablation model, its recurrence and have tested the efficacy of imaging biomarkers in evaluating tumor ablation and recurrence. The cytopathology and molecular signatures of the primary and recurrent tumors were compared. Immune-compromised female rats were implanted with U251N tumor cells in one brain hemisphere (n=20). Tumor growth was monitored using magnetic resonance imaging (MRI). When tumors reached about 4 mm in diameter, they were ablated using a clinical LITT system (Visualase®), under MRI guidance. Five other rats implanted with U251N tumors were used as unablated controls. MRI data were acquired at 24 h post-LITT, and at 2 and 4 weeks. Rats were sacrificed for histopathology at 2 and 4 weeks, and brain sections stained for hematoxylin and eosin, human major histocompatibility complex, Ki67, a cell proliferation marker and sex determining region Y)-box 2 (SOX2), a stem cell transcription factor. An additional cohort of rats with primary (n=4) and post-LITT recurrent (n=4) U251N tumors were used for analysis of their molecular composition using RNA-Seq approach. In the treated groups, MRI showed little tumor tissue at 24 h, evidence of recurrence at 2 weeks and significant tumor tissue at 4 weeks. Tumor DCE-MRI parameters showed elevated intra-tumoral vascular permeability (i.e., Ktrans) values at pre-LITT imaging, that shifted to peri-ablation periphery at 24 h. A trend of progressive decrease in Ktrans was seen until 1-week post-ablation. Increasing Ktrans values at 2 weeks and after 4 weeks coincided with tumor recurrence. RNA-Seq data showed that cell cycle, cellular movement and inflammatory disease genes were the most differentially expressed genes in the recurrent tumors suggesting increased infiltration may primarily underlie treatment resistance.

Neurosurgery
Pathadan DS, Dalm B, De Almeida LB, De Jesus S, Fasano A, Foote K, Gordeyeva Y, Jimenez-Shahed J, Pouratian N, Rolston J, Rosenow J, Safarpour D, **Schwalb J**, Siddiqui M, Spindler M, Tsai A, Wong J, and Verhagen-Metman L. CLINICAL TRENDS IN ASLEEP AND AWAKE DBS: COMPARING NORTH AMERICA AND EUROPE. *Stereotact Funct Neurosurg* 2024; 102:242. Full Text

D.S. Pathadan, Ramaiah Medical College, Bengaluru, India

Introduction: DBS practices may vary geographically. We aim to compare trends and perceptions regarding Asleep and Awake DBS in North-America (NA) and Europe (EU). Methods: A panel of DBS clinicians sent a survey to DBS clinicians of the Parkinson Study Group, DBS Think-Tank, World Society for Stereotactic and Functional Neurosurgery, and Movement Disorder Society. Results: There were 214 respondents from NA (53% neurosurgeons, 43% Neurologists and 4% APP) and 61 from EU (69%, 30%, and 1%, respectively In NA, 54% perform both asleep and awake, 28% awake only, and 18% asleep only. In EU, these numbers were 66%, 18%, and 16%. In NA, centers performing both awake and asleep DBS (N=60), 75% choose awake for STN, 45% for GPI, 90% for VIM. In EU centers performing both (n=33), 30% choose awake for STN, 0% for GPI and 80% for VIM. For asleep-DBS, NA centers offer i-MRI in 37%, vs EU centers 0%. In NA, microelectrode-recording (MER) is used during asleep-DBS in 27% vs in EU 69% of cases. Whether awake or asleep, single-channel MER is most common in NA vs 2-3 or 4-5 channels in EU. When asked to agree or disagree with: asleep-DBS is equal to or more effective than awake-DBS for each target, NA respondents agreed/disagreed as follows: STN: 28%/43%; GPI: 53%/29%; VIM: 13%/64% vs EU respondents: STN: 53%/35%; GPI: 73%/15%; VIM: 15%/56%

(remainder: 'similar' or 'no experience'). When presented with 8 techniques for awake/asleep DBS, the choice for the 'Most optimal technique for each target', was 'awake+MER+test stimulation for STN and VIM (not GPI) in NA and EU. Similarly, when choosing the 'least optimal technique for each target', NA and EU agreed on 'asleep iCT/Oarm' for STN, GPI and VIM. Conclusions: Both continents preferred Awak- DBS for VIM and STN, and Asleep-DBS for GPI. 'The most optimal technique' in NA and EU was 'awake+MER+stim' for STN and VIM, and 'asleep iMRI' for GPI. 'The least optimal technique' for all 3 targets was 'asleep iCT/Oarm' (without physiology) in both continents. In EU, but not NA, asleep-DBS was performed with MER in the majority of cases.

Neurosurgery

Rademacher A, **Imran Z**, **Fadel H**, **Pawloski J**, **Anzalone A**, **Latack K**, and **Lee I**. ACCURACY OF THE ROSA ONE BRAIN ROBOTIC PLATFORM FOR THE PLACEMENT OF NEUROBLATE AND VISUALASE LASER INTERSTITIAL THERMAL THERAPY PROBES. *Neuro Oncol* 2024; 26:viii282. Full Text

A. Rademacher, Department of Neurosurgery, Henry Ford Health, Detroit, United States

Laser interstitial thermal therapy (LITT) is a minimally invasive treatment option for patients with intracranial lesions. The success of LITT is dependent on accurate placement of the laser probe in target tissue. Placement can be facilitated by various stereotactic methods, including the Robotic Surgical Assistant (ROSA) ONE Brain robotic platform. The aim of this study is to examine the accuracy of stereotactic probe placement utilizing the ROSA robot. Primary outcomes were entry distance, target distance, and entry angle error. Accuracy differences between two major LITT platforms, the Neuroblate (Monteris Medical) and Visualase Systems, were compared. A prospective institutional database was used to identify all patients who underwent LITT for intracranial tumors utilizing the ROSA robot between 2013-2023. The sign test was used to compare error values to test their difference from a null value of 0. Spearman correlation was used to assess the relationship between angle of error and trajectory length. Kuskal-Wallis test was used to compare errors and trajectory length between the two companies. Of the 105 patients who underwent LITT during the study period, 337 probes were placed. For Visualase probes, median entry distance (1.1mm, IQR=0.4-2.0), target distance (1.6mm, IQR =0.9-2.4), and entry angle error (1.5°, IQR=0.9-2.5), were significantly different than zero (p=<.0001). For Neuroblate probes, median entry distance (1.5mm, IQR=1.0-2.1), target distance (1.8mm, IQR=1.1-2.4), and entry angle error (1.8°, IQR=1.1-2.5) were significantly different than zero (p=<.0001). When comparing laser systems, there was a significant difference in median entry distance error with Neuroblate having a higher error (1.5mm, IQR=1.0- 2.1) than Visualase (1.1mm IQR=0.4-2.0, p=0.0041). Stereotactic placement of LITT probes utilizing the ROSA robotic system was not able to achieve perfect alignment with the planned trajectory. When comparing the systems, Visualase probes were placed more accurately at the entry point than Neuroblate probes.

Neurosurgery

Rademacher A, **Kagithala D**, **Pawloski J**, **Latack K**, **Fadel H**, **Dallo F**, **Snyder J**, **Lee I**, and **Robin A**. RADIATION-RELATED MORBIDITY OUTCOMES IN ATYPICAL MENINGIOMA PATIENTS: A RETROSPECTIVE COHORT STUDY. *Neuro Oncol* 2024; 26:viii228-viii229. Full Text

A. Rademacher, Department of Neurosurgery, Henry Ford Health, Detroit, United States

Atypical meningiomas present with unique challenges in management and prognosis. Given their tendency to recur, adjuvant radiation therapy (ART) is frequently utilized, however there are few reports on radiation-related morbidity in this patient population. The study aims to investigate the radiationrelated complications in atypical meningioma patients treated with or without ART. The primary outcomes were the incidence and severity of RT-related morbidity. All patients treated for atypical meningiomas at our institution between January 1, 2014 and January 1, 2024 were retrospectively analyzed. Patients were grouped into two cohorts, those who were initially treated with surgical resection only and those who also received adjuvant RT. Radiation morbidity grading was assigned for all patients that received radiation treatments during their clinical course based on established grading systems. Fisher's Exact and Kruskal-Wallis tests were used to determine associations between the two groups. There were 76 patients who

were initially treated with surgery only and 23 patients who had surgery and ART. Mean length of follow-up among all patients was 55.6 months. Significantly lower rates of RT-related morbidity in the surgery only group were observed compared to the surgery and RT cohort (15.8% vs. 60.9%, $p < 0.0001$). Among patients in the surgery only cohort, 23 patients received RT at recurrence or progression. When comparing this subgroup to those who underwent ART, there was no significant difference in the severity of RT-related morbidity ($p=0.2724$). In this series, patients receiving ART experienced a higher incidence of radiation-related morbidity. When comparing only those who received RT, there was no difference in the incidence or severity of radiation-related morbidity between the two cohorts.

Neurosurgery
Ser MH, Baykal D, White JD, Breen WG, Parney IF, **Walbert T**, Forsyth P, Etame A, Macaulay R, Pina Y, and Sener U. LONG TERM FOLLOW-UP OF A LYNCH SYNDROMEASSOCIATED GLIOBLASTOMA RESISTANT TO STANDARD-OFCARE CHEMORADIATION. *Neuro Oncol* 2024; 26:viii120. Full Text

M.H. Ser, Mayo Clinic, Rochester, United States

BACKGROUND: Lynch syndrome is caused by pathogenic germline variants in the DNA mismatch repair (MMR) genes, predisposing individuals to malignancies, including glioblastoma (GBM). MMR-deficient tumors are resistant to monofunctional alkylators such as temozolomide but not to bifunctional alkylators such as the nitrosourea lomustine. Anti-programmed cell death protein 1 (PD1) immune checkpoint inhibitor (ICI) pembrolizumab represents another treatment option, which is approved by the United States Food and Drug Administration (FDA) for the treatment of mismatch repair deficient cancers. METHODS: We present a patient with multifocal GBM and Lynch syndrome who experienced rapid progression following standardof- care chemoradiation, followed by durable responses to lomustine and then to pembrolizumab. RESULTS: A 58-year-old man with Lynch syndrome (MSH2 mutation) and prior history of colon cancer presented with seizures. Magnetic resonance imaging (MRI) brain identified right frontal and left parietal masses. Right frontal tumor was resected; pathology was consistent with GBM, IDH wildtype, MGMT-unmethylated. Both lesions were treated with radiation therapy (60 Gy, 30 fractions) with concurrent and adjuvant temozolomide. After two cycles of adjuvant temozolomide, his left parietal tumor progressed and was subtotally resected, followed by four cycles of lomustine (stopped due to myelotoxicity). He remained progression-free for 15 months. Surveillance MRI identified new enhancement involving the left frontal lobe, left periventricular white matter, and right internal auditory canal, concerning for leptomeningeal dissemination. MRI spine identified no additional lesions. Cerebrospinal fluid cytology was negative for tumor cells on two occasions. Patient was treated with pembrolizumab. He remains on treatment with stable disease four months after ICI initiation and 31 months after GBM diagnosis. CONCLUSIONS: Patients with MMR-deficient GBM resist standard chemoradiation. Alternatives such as nitrosourea or ICI therapy may achieve durable responses. While data is insufficient to administer these agents as upfront therapy in this specific setting, both should be considered as options for recurrent disease.

Neurosurgery
Snyder J, Alford SH, Kumar T, Pindolia K, **Poisson L**, Mahatma S, and **Mikkelsen T**. ONCOPATH: OPTIMIZED TREATMENT GUIDELINE CONCORDANT PATHWAY PRESENTED ON A VISUALINTERACTIVE DASHBOARD FOR CLINICAL DECISION SUPPORT COMPUTED BY OVERLAYING PATIENT LONGITUDINAL DATA ON A KNOWLEDGE GRAPH. *Neuro Oncol* 2024; 26:viii172. Full Text

J. Snyder, Henry Ford Health, Detroit, United States

BACKGROUND: OncoPath provides a visual analysis of a brain tumor patient's longitudinal clinical data overlayed on disease specific pathways with the goal of reducing knowledge discordant care and insurance authorization burden. By ingesting, curating and visually presenting the patient experience on guidelines, OncoPath aims to streamline clinical decision making and related processes. Understanding the patient's journey compared to treatment guidelines is of value in addressing health equity and guideline adoption in real world settings. METHODS: Data from 44 glioma patients diagnosed and treated between 2016-2021 were uploaded to OncoPath using natural language processing and other tools to

capture abstractable data elements. The data was overlayed on guidelines using recursive graph modeling. Using the knowledge graph of a patient's history, the model also recommends treatment options in an interactive visual dashboard representing NCCN guidelines. The dashboard includes the guidelines in graphical format with associated references and notation. RESULTS: 28 males and 16 females age 21-38 years at diagnosis were abstracted. Cases represented 4 oligodendrogliomas, 13 astrocytomas, and 27 glioblastomas. Data was available through second line therapy, discharge to hospice or death. Cases were matched to the NCCN 2021 guidelines which was used for treatment decisions until November 2022. The patient data matched OncoPath except in 3 cases where KPS was not available resulting in premature pathway truncation. For these cases we inferred KPS based on subsequent treatment received to optimize the historic data. CONCLUSION: To our knowledge, this is a first-of-a-kind technology in neuro-oncology that may improve time to treatment, reduce health utilization resources and can serve as a benchmarking tool for care delivery. The feasibility of clinically implementing such tools for decision support was demonstrated. This type of tool could be particularly useful in low-resource areas where disease specific expertise may not be available or to illuminate care discrepancies.

Neurosurgery
Tsai A, Dalm B, De Almeida LB, De Jesus S, Fasano A, Foote K, Gordeyeva Y, Jimenez-Shahed J, Pathadan DS, Pouratian N, Rolston J, Rosenow J, Safarpour D, **Schwalb J**, Siddiqui M, Spindler M, Wong J, and Verhagen-Metman L. PERCEPTIONS REGARDING ASLEEP AND AWAKE DBS AMONG NEUROLOGISTS AND NEUROSURGEONS. *Stereotact Funct Neurosurg* 2024; 102:257. Full Text

A. Tsai, Ohio State University, College of Medicine, Columbus, United States

Introduction: DBS is a multidisciplinary treatment with NSXs performing the procedure and NLGs optimizing clinical outcome. Whether their respective viewpoints regarding asleep and awake DBS procedures converge is of potential interest but has not been studied. Our objective is to compare trends and perceptions regarding Asleep and Awake deep brain stimulation (DBS) between neurologists (NLGs) and neurosurgeons (NSXs) in the USA and abroad. Methods: A panel of DBS clinicians created a REDCap survey regarding DBS practice in the US and abroad. The survey was sent out to the Functional Neurosurgery Working Group of the Parkinson Study Group, DBS Think Tank, World Society for Stereotactic and Functional Neurosurgery, and Movement Disorder Society members with stated DBS interest. Results: Of 321 individual respondents from 38 countries and 6 continents 60% were NSXs, 37% NLGs, and 3% Advanced Practice Providers. Fifty-eight percent perform both awake and asleep DBS procedures, 26.8% awake only, and 15.5% asleep only. Focusing only on 117 respondents who offer both options, 70% choose awake for STN, 45% choose awake for GPI, 92% choose awake for VIM. When asked to agree or disagree with asleep DBS is equal to or more effective than awake DBS for each target, NLGs agreed/disagreed as follows: VIM: 11.8%/62.8%, STN: 26%/47%, GPI: 49%/31%, vs NSXs: VIM: 13.6%/58%, STN: 32.6%/37.1%, GPI: 64.1%/18% (remainder: 'similar' or 'no experience'). When asked to choose the 'most optimal technique' out of 7 awake/asleep DBS techniques, both NLGs and NSXs selected 'awake+microelectrode recording (MER)+test stimulation (stim)' for STN and VIM. For GPI, NLGs preferred 'awake+MER+stim', while NSXs preferred 'asleep interventional-MRI' (iMRI). For 'least optimal technique for each target', NLGs and NSXs both chose 'asleep iCT/Oarm' for STN, GPI and VIM. Conclusions: In this survey, NLGs and NSXs showed similar preferences for awake DBS when targeting VIM and STN, while for GPI the results were more variable. Compared to NLGs, NSXs had a more favorable opinion on asleep procedures, especially iMRI, while NLGs preferred physiological confirmation for all targets. These results provide only a snapshot of current DBS trends, and perceptions may change with future technological advances.

Neurosurgery
Um H, Ismail M, Hill V, Puri S, Yu J, Lu L, Nayate A, **Rogers L**, Prasanna P, Bardhan M, Li C, Basree M, Baschnagel A, McMillan A, Bhatia A, Ahluwalia M, Veronesi M, and Tiwari P. AI-DRIVEN RISK-OF-PROGRESSION (AIRIP) CLASSIFIER FOR DISTINGUISHING RECURRENT BRAIN METASTASES FROM RADIATION TREATMENT EFFECT: A MULTI-INSTITUTIONAL COMPARATIVE STUDY WITH ADVANCED MULTIMODAL IMAGING. *Neuro Oncol* 2024; 26:viii32. Full Text

H. Um, University of Wisconsin-Madison, Madison, United States

Following radiation therapy, a significant challenge in brain metastases (BM) management is differentiating radiation-induced-treatment effect (TrE) from tumor recurrence (TuR). TrE can be indistinguishable from TuR using conventional MRI. Advanced imaging techniques (e.g., perfusion MRI, PET/MRI) are not consistently used, and the standardized Response Assessment in Neuro-Oncology for brain metastases (RANO-BM) is sensitive to inter-reader variability. The performance of an artificial intelligence (AI)-driven risk-of-progression (AiRiP) classifier, which has been shown to capture pathophysiologic differences between TrE and TuR on routine MRI, was compared to that of clinical assessments and advanced imaging methods, in a multi-institutional setting. A total of n=261 lesions with pathologically-confirmed diagnoses in n=189 patients were analyzed. 115 lesions (73 TuR, 42 TrE) from site 1, 86 lesions (38 TuR, 48 TrE) from site 2, and 60 lesions (33 TuR, 27 TrE) from site 3 were used for training and testing the AiRiP-model. Gd-T1w, T2w, FLAIR MRI were preprocessed, and lesions were segmented by experts. Texture features (n=856) were extracted from each lesion. Random-forest classifier was employed for 3-fold crossvalidation. Top-performing AiRiP-features, RANO-BM criteria, perfusion MRI and PET/MRI were evaluated in a sub-group analysis. For n=51 lesions on the test-set (site 3), 14 were classified as stable disease and 37 as TuR using RANO-BM (accuracy=54.1%). AiRiP-model achieved an accuracy of 76.5% on the same test-set and accurately classified 78.6% of the stable lesions as TrE or TuR. For another subset of lesions (n=27) on the same test-set, perfusion MRI and AiRiP-model achieved an accuracy of 59.3% and 70.4%, respectively. Lastly, for a subset of lesions (n=35) on the test-set (site 2), multimodal (perfusion, PET) imaging and AiRiP-model accurately classified 60% and 74.3% of lesions, respectively. 15 lesions were considered indeterminate via multimodal imaging, 73.3% of which AiRiP-model accurately classified as TrE or TuR. Our results suggest AI-driven models on conventional MRI may reliably distinguish TuR from TrE.

Neurosurgery

Walbert T, Cachia D, Hertler C, Sherwood P, Dirven L, Young J, Stockdill M, Almaraz ER, Pill K, and Boele F. ASSESSING CAREGIVER OUTCOMES OF PRIMARY BRAIN TUMOR PATIENTS: A SYSTEMATIC REVIEW OF THE LITERATURE. *Neuro Oncol* 2024; 26:viii226-viii227. Full Text

T. Walbert, Henry Ford Health, Department of Neurosurgery, Detroit, MI, United States

BACKGROUND: Family caregivers in neuro-oncology are known to have high levels of unmet support needs. Intervention trials and effective support options are scarce. The Response Assessment in Neuro-Oncology (RANO-) Cares working group has been established to determine standards of caregiver outcomes (CO) research reporting in neuro-oncology. We present the current state of methodological quality of reporting on neuro-oncology caregiver outcomes in randomized controlled trials (RCTs). METHODS: A systematic literature review (PubMed/Medline, Embase, Web of Science, Emcare, Cochrane Library, PsycINFO; July 2023) was performed to assess to what degree RCTs assessing outcomes of family caregivers of adult primary brain tumor patients adhere to established reporting standards. Using Covidence, screening and data extraction was independently performed by two researchers, with a third guiding consensus. A 33-item checklist (23 applicable to secondary analysis reports) based on the International Society for Quality of Life (ISOQOL) Research criteria for patient-reported outcome reporting was utilized to assess reporting standards. Risk of bias was assessed per RCT. RESULTS: Fifteen publications (12 unique RCTs) included 684 neuro-oncology caregivers, with low overall risk of bias. Ten publications (66%) reported on COs as a primary aim and eight (80%) of these satisfied ≥2/3 of the key methodological criteria. Of the five secondary analysis reports (33%) two met ≥2/3 of applicable key criteria. Criteria often missed are related to sample size calculations, details on statistical approaches, discussion of limitations and clinical significance of studies. Only three of the 12 RCTs were definitive trials aimed at improving COs and five should be considered as pilot or feasibility studies. CONCLUSION: RCTs investigating neuro-oncology COs have high reporting standards and risk of bias was low. Future studies should focus on specific caregiver interventions to reduce high caregiver burden and with that patients' quality of life.

Neurosurgery

Walbert T, **Schultz L**, **Snyder JM**, and **Mohn JD**. ELECTRONIC ASSESSMENT OF QUALITY OF LIFE IN GLIOBLASTOMA PATIENTS USING THE EORTC-QLQ-C30/ EORTC-BN20 AND THE PROMIS SYSTEM IN CLINICAL PRACTICE. *Neuro Oncol* 2024; 26:viii264. Full Text

T. Walbert, Henry Ford Health, Department of Neurosurgery and Neurology, Detroit, MI, United States

BACKGROUND: Patient reported outcomes are essential to guide patient-care and to maintain quality of life. We aim to further assess feasibility of computer adaptations of the Patient-Reported Outcomes Measurement Information System (PROMIS) questionnaire in the clinical setting and compare it with outcomes of the EORTC- QLQ-C30 and EORTC-BN20 questionnaires. METHODS: Newly diagnosed patients with GBM were enrolled to assess feasibility. The PROMIS modules were selected to reflect the HRQoL domains assessed in the EORTC- QLQ-C30 and EORTC-BN20 questionnaires. PROMIS modules selected included anxiety, depression, fatigue, physical function, sleep disturbance, sleep-related impairment, social satisfaction role, applied cognitive ability and global health. EORTC instruments as well as PROMIS was answered to patients in the outpatient setting. Descriptive analysis was performed RESULTS: 43 patients with 124 PROMIS/EORTC responses were included in this analysis. 31 patients completed the survey prior to or within 14 days of start of radiation, 12 patients completed a survey outside of the radiation window, and a total of 60 completed surveys were obtained between both patient groups. The median times to complete the EORTC-QLQ-C30 and the EORTC-BN20 surveys were 4.77 (range=2.05-18.6) and 2.63 (range=1.17- 24.83) minutes respectively. For the PROMIS instruments except global health, the median times to complete different modules ranged from 0.6- 1 minute (range= 0.15- 7.77). For global health, the median time was 2.35 minutes (range= 1.02-21.12). Average time to complete all PROMIS questions was 8.65 minutes (range=3.32-66.01). CONCLUSIONS: Real-time prospective assessment of the EORTC tools is similar to the PROMIS measures. While most response times were short, the ranges suggest that select patients might struggle. Patients were offered to participate online from home for convenience, but low computer literacy, limited internet access and burden of disease might limit participation.

Neurosurgery

Wen P, Ahluwalia M, Odia Y, McKean M, **Snyder J**, Colman H, Lobbous M, Nghiemphu L, Chong R, Yang J, Patel H, Vecchio D, Lokku A, Brail L, and Mellinghoff I. A PHASE 1 STUDY OF ERAS-801, A POTENT, SELECTIVE, AND CENTRAL NERVOUS SYSTEM (CNS)-PENETRANT EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) INHIBITOR, FOR PATIENTS WITH RECURRENT GLIOBLASTOMA MULTIFORME (GBM). *Neuro Oncol* 2024; 26:viii107. Full Text

P. Wen, Dana-Farber Cancer Institute, Methuen, United States

EGFR is among the most common targets for genetic alterations in GBM. Changes in EGFR gene amplification and the extracellular domain result in receptor overexpression or constitutive activation, and enhanced oncogenic signaling. ERAS-801 is a potent, selective, and highly CNSpenetrant EGFR inhibitor being developed for the treatment of GBM, with a focus on tumors harboring EGFR genetic alterations. THUNDERBBOLT-1 is the first-in-human phase 1 dose escalation and expansion trial evaluating ERAS-801 monotherapy for patients with recurrent GBM. ERAS-801 is administered orally once daily for continuous 28-day cycles. As of April 10, 2024, a total of 52 patients were treated across 7 dose cohorts: 20 mg (n=3), 40 mg (n=5), 80 mg (n=3), 160 mg (n=6), 240 mg (n=25), 280 mg (n=4), or 320 mg (n=6). Key patient characteristics were median age of 60 years, 67% male, mostly one prior therapy, and 81% tumors with alterations. The MTD was 240 mg. Dose-limiting toxicities were observed at 320 mg (n=2, Grade 2 QT prolongation, Grade 3 rash and Grade 3 dermatitis acneiform), 280 mg (n=3, Grade 3 QT prolongation), and 240 mg (n=1, Grade 3 QT prolongation) doses. The most common treatment related adverse events (TRAEs), in >10% of patients, were dermatitis acneiform, diarrhea, and nausea. Electrocardiogram QT prolongation occurred in 11.5% of patients and was not associated with clinical findings. ERAS-801 showed rapid absorption; peak plasma concentration was generally achieved within 6 hours post dose. PK exposure increased in a dose-dependent manner over the doses evaluated. Across all doses there was a confirmed partial response (using mRANO) in 1 patient and 6 patients achieved a PFS of 6 months. ERAS-801 shows well behaved PK with substantial CNS penetration, preliminary

safety, and tolerability in patients with recurrent GBM. The TRAEs were reversible, manageable, and consistent with known toxicities of EGFR inhibitors.

Neurosurgery

Zhang Y, **Zhang L**, **Chopp M**, **Zhang ZG**, **Mahmood A**, and **Xiong Y**. N-Acetyl-Seryl-Aspartyl-Lysyl-Proline (AcSDKP) as a Potential Novel Treatment for Experimental Traumatic Brain Injury. *J Neurotrauma* 2024; 41(15-16):A117. Full Text

Y. Zhang, Department of Neurosurgery, Henry Ford Health, Detroit, United States

Objective: N-acetyl-seryl-aspartyl-lysyl-proline (AcSDKP) exhibits multiple functions, such as immunomodulation, anti-inflammation, anti-fibrosis, and pro-angiogenesis. This study was aimed to determine efficacy and mechanism of AcSDKP treatment for traumatic brain injury (TBI). Methods: Young (2-3 months) male Wistar rats were subjected to moderate TBI. Subcutaneous infusion of AcSDKP at a dose of 0.8 mg/kg/day or Vehicle (0.01N acetic acid) was initiated 1h after injury and continued for 3 days. Modified neurological severity score (mNSS), foot-fault, Morris water maze tests were performed. Animals were sacrificed 1 day or 35 days after injury and brain sections processed for histological analyses of neuronal loss, neuroinflammation, BBB damage, angiogenesis, neurogenesis and histone deacetylase 4 (HDAC4). One-way ANOVA followed by post hoc Tukey's tests was used to compare the differences in functional and histological outcomes. P value <0.05 was considered significant. Results: Compared to the Vehicle treatment, AcSDKP treatment led to significant ($p<0.05$): 1) improvements in spatial learning in the Morris water maze test and sensorimotor function in foot-fault and mNSS tests, 2) reductions of lesion volume and hippocampal neuronal cell loss (NeuN), BBB damage (Fibrin deposit), and neuroinflammation (CD68+ microglia/macrophages and GFAP+ astrocytes), 3) enhancement of angiogenesis (BrdU/EBA staining) and neurogenesis (BrdU/NeuN staining), and 4) blockage of neuronal HDAC4 nuclear translocation, which increased histone H3 acetylation in rats after TBI. Conclusions: Our data reveal a novel mechanism that AcSDKPinduced beneficial effects on TBI recovery are associated with its selective inhibition of neuronal HDAC4 nuclear translocation.

Obstetrics, Gynecology and Women's Health Services

Ali-Fehmi R, Krause H, Morris R, Wallbillich J, Wong T, Bandyopadhyay S, Zaeim F, Jain D, Smith W, Alkaram W, Chapel D, **Kheil M**, Abu-Jamea A, Al-saghir M, Lou E, Quddus MR, Winer I, Gogoi R, Ketch P, Herzog T, Toboni MD, Antonarakis E, Thaker P, Braxton D, Swensen J, Hirst J, Karnezis A, Bryant D, and Oberley M. Clinical Outcomes in Endometrial Carcinomas with Overlap in MMRd, POLE, and TP53: Analysis of TCGA/ProMisE "Multiple Classifiers" in a Cohort of > 4500 Endometrial Tumors. *Lab Invest* 2024; 104(3):S1098-S1099. Full Text

[Ali-Fehmi, Rouba; Chapel, David] Univ Michigan, Michigan Med, Ann Arbor, MI USA. [Krause, Harris; Hirst, Jeff] Caris Life Sci, Irving, TX USA. [Morris, Robert; Gogoi, Radhika] Karmanos Canc Inst, Detroit, MI USA. [Wallbillich, John] Wayne State Univ, Sch Med, Detroit, MI USA. [Wong, Terrence] Karmanos Canc Inst, Detroit Med Ctr, Detroit, MI USA. [Bandyopadhyay, Sudeshna] Ascens St John Hosp, Detroit, MI USA. [Zaeim, Fadi; Jain, Deepti; Smith, William; Alkaram, Waed] Wayne State Univ, Detroit Med Ctr, Detroit, MI USA. [Kheil, Mira] Henry Ford Hlth Syst, Detroit, MI USA. [Abu-Jamea, Asem] Marshfield Clin Hlth Syst, Marshfield, WI USA. [Al-saghir, Maya] Oakland Univ, William Beaumont Sch Med, Rochester, MI USA. [Lou, Emil; Antonarakis, Emmanuel] Univ Minnesota, Minneapolis, MN USA. [Quddus, M. Ruhul] Brown Univ, Alpert Med Sch, Women & Infants Hosp, Providence, RI USA. [Winer, Ira] Wayne State Univ, Karmanos Canc Ctr, Detroit, MI USA. [Ketch, Peter] Univ Alabama Birmingham, Birmingham, AL USA. [Herzog, Thomas] Univ Cincinnati, Med Ctr, Cincinnati, OH USA. [Toboni, Michael D.; Thaker, Premal] Washington Univ, Sch Med, St Louis, MO USA. [Braxton, David] Hoag Hosp, Newport Beach, CA USA. [Swensen, Jeffrey; Bryant, David; Oberley, Matthew] Caris Life Sci, Phoenix, AZ USA. [Karnezis, Anthony] UC Davis Med Ctr, Sacramento, CA USA. Karmanos Cancer Institute; Wayne State University; Detroit Medical Center; Barbara Ann Karmanos Cancer Institute; Wayne State University; Detroit Medical Center; Henry Ford Health System; Henry Ford Hospital; Oakland University; University of Minnesota System; University of Minnesota Twin Cities; Brown University; Women & Infants Hospital Rhode Island; Barbara Ann Karmanos Cancer Institute; Wayne State University; University of Alabama System;

University of Alabama Birmingham; University System of Ohio; University of Cincinnati; Washington University (WUSTL); University of California System; University of California Davis

Obstetrics, Gynecology and Women's Health Services
Hadaya O, Chaiworapongsa T, Jacques S, Assudani N, Done B, Chawla S, Impemba J, Chatterton C, Qureshi F, Kaur S, and Tarca A. Impacts of Indicated Preterm Birth and Placental Pathology on Neonatal Outcomes in Early Preterm Births. *Reprod Sci* 2024; 31:210A-211A. Full Text

[Hadaya, Ola; Chaiworapongsa, Tinnakorn; Jacques, Suzanne; Done, Bogdan; Chatterton, Carolyn; Qureshi, Faisal; Kaur, Satinder; Tarca, Adi] Wayne State Univ, Sch Med, Detroit, MI USA. [Hadaya, Ola] Henry Ford Hlth, Detroit, MI USA. [Jacques, Suzanne] Karmanos Canc Inst, Detroit, MI USA. [Assudani, Nupur; Chawla, Sanjay; Impemba, Jenny] Childrens Hosp Michigan, Detroit, MI USA. [Chawla, Sanjay] Cent Michigan Univ, Detroit, MI USA. Cancer Institute; Children's Hospital of Michigan; Central Michigan University

Obstetrics, Gynecology and Women's Health Services
Pezzillo M, **Raffee S**, **Kim S**, **Kheil M**, and **Luck A**. DOES VITAMIN C IMPACT URINARY PHWHEN TAKEN WITH METHENAMINE HIPPURATE? *Urogynecology* 2024; 30(10):S130-S131. Full Text

M. Pezzillo, Henry Ford Health System, United States

OBJECTIVES: Urinary tract infections (UTIs) affect 150 million people worldwide annually and specifically impact the aging female population. Methenamine hippurate (MH) is a non-antibiotic suppressive agent to prevent recurrent UTIs (rUTIs). It is most effective when the urine is acidic (pH < 6) and can be converted to formaldehyde, a bacteriostatic agent. To accomplish this, providers commonly instruct patients to acidify their urine with vitamin C once or twice daily. This can be a cost burden and cause unnecessary side effects to the patient. Weaimto investigate whether vitamin C affects the urinary pHin the clinical setting. We hypothesize that adding daily vitamin C supplements with MH does not affect the urinary pH. METHODS: This is a retrospective, IRB-approved study. Patients diagnosed with RUTI by two urogynecologists between 2014 and 2023 were screened for the study. Patients were excluded with active urinary stone disease, cancer, fistula, bladder mesh erosions, current suprapubic catheter, and lack of urinalysis collected at the initial or follow-up visit. Baseline demographics and data regarding urinary pH, use of vitamin C, and subsequent UTIs were collected. The primary outcome was the change in urinary pH for those taking vitamin C and those who did not. RESULTS: 295 patients were screened, and 78 patients takingMH were included in the final analysis. 40 patients used vitamin C with MH, and 38 did not. The median follow-up time was 3 months for both groups. 14 out of 38 (32.5%) patients using vitamin C experienced a UTI compared to 13 out of 40 (36.8%) with no vitamin C (P = 0.687). The average daily dose of vitamin C was 700 mg. The mean urinary pH was 6.0 for patients taking vitamin C and 6.1 for those who did not (P = 0.513). The mean pH change from the initial visit to the follow-up visit was -0.1 in those who took vitamin C and 0.0 in those who did not (P = 0.442). Patients experiencing one or more UTIs while on MH suppression were found to have a higher urinary pH (pH 6.3) compared to those who did not have a UTI (pH 5.9) (P = 0.002). CONCLUSIONS: The benefit of adding vitamin C when taking MH is unclear. The urinary pH was not affected by adding vitamin C to MH. Those who did and did not take vitamin C had nearly identical urinary pH at follow-up (6.0 versus 6.1), with vitamin C only decreasing the follow-up urinary pH by -0.1. Additionally, there was a similar rate of UTI following MH suppression with or without vitamin C. However, those who did experience a UTI in the follow-up period did have a statistically significantly higher pH than those who did not.

Ophthalmology and Eye Care Services
Qin L, **Kasetty VM**, Davis S, Blodi BA, and Marcus DM. Ultra-Wide Field (UWF) Fluorescein Angiographic Non-Perfusion Status After Endolaserless Vitrectomy and Aflibercept Monotherapy for Eyes with Proliferative Diabetic Retinopathy (PDR)-related Vitreous Hemorrhage (VH). *Invest Ophthalmol Vis Sci* 2024; 65(7):1754. Full Text

L. Qin, Augusta University, Augusta, GA, United States

Purpose : The effect of anti-vascular endothelial growth factor (anti-VEGF) therapy on retinal non-perfusion in PDR remains ill-defined. We report 3-year UWF fluorescein angiogram (FA) gradings of retinal non-perfusion in eyes randomized in the LASERLESS trial. This provides a unique opportunity to determine the effects of intravitreal aflibercept injection (IAI) monotherapy on retinal ischemia in severe PDR eyes. Methods : Eligible eyes with PDR-related VH underwent vitrectomy without panretinal photocoagulation (PRP) endolaser with 1 pre- and 1 intraoperative IAI were randomized to postoperative q8- or q16-week IAI monotherapy. Prospectively planned UWFFA's were performed at 4 weeks (baseline) after vitrectomy and then quarterly throughout the 3- year period. Images were independently graded by the Wisconsin Reading Center for nonperfusion index (NPI), foveal avascular zone integrity, leakage, and neovascularization. Results : A total of 31 eyes (14 and 17 in q8- and q16-week groups, respectively) were randomized. Through 3 years, q8-week and q16-week eyes received 19 and 12 IAI, respectively. Among all patients, NPI increased from 19.1% at baseline to 22.6%, 27.5%, 31.0% at years 1, 2, and 3, respectively (p=0.086, <0.001, <0.001 for change from baseline, respectively). While NPI increased in both the q8-week and q16-week groups at 3 years, NPI progression was less in q8-week eyes with average increase in NPI of 6.3% compared to 10.3% in q16-week eyes (p=0.283). There is an overall trend toward reduced NPI progression with increased aflibercept injection burden over 3 years. Conclusions : More frequent aflibercept dosing resulted in reduced proliferative consequences and reduced NPI progression. Although NPI progression was reduced with more frequent IAI, peripheral retinal non-perfusion continues despite persistent antiVEGF therapy. Our study suggests that anti-VEGF does not reverse retinal ischemia despite a high therapy burden.

Orthopedics/Bone and Joint Center

Chougule AS, **Zhang C**, **Mendez D**, **Vinokurov N**, and **Gardinier JD**. P2Y2 Antagonists Increase Bone Mass and Enhances the Anabolic Response to Exercise in Adult Mice. *J Bone Miner Res* 2024; 39:26-27. Full Text

J.D. Gardinier, Henry Ford Health, United States

Osteocytes' induction of bone formation in response to loading is extremely age dependent, such that exercise is known to be less and less effective with age. Modifying osteocytes' mechanosensitivity may enable adults to better capitalize on the anabolic nature of exercise or daily activities to increase bone mass and reduce fracture risk. Based on previous work, we hypothesize inhibiting P2Y2 activity can enhance the anabolic response to loading of adult mice. To test this hypothesis, 9-month old male C57/Bl6J mice were treated with P2Y2 inhibitor AR-C11892XX (ARC) and exposed to sedentary of treadmill exercise for 5-weeks. Treating sedentary mice with ARC alone significantly increased cortical area by 10% in the tibia and 6.5% in the femur (Fig 1A). The gains in bone mass following ARC treatment in sedentary mice coincided with significant gains in endocortical bone formation rate and a 43% increase in strength based on mechanical testing (Fig 1B). Subjecting mice to treadmill exercise alongside ARC treatment significantly increased cortical area by 40% compared to vehicle mice subjected to same exercise regimen. The gains bone mass were associated with a significant increase in both periosteal and endocortical bone formation rates compared to vehicle treated controls. At the cellular level, ARC treatment in sedentary mice significantly decreased the expression of Sost and Rankl in osteocyte-enriched tibia samples when compared to vehicle treated controls. Exercise further decreased the expression of Sost and Rankl in ARC treated mice when compared to ARC treated sedentary mice or vehicle treated mice subjected to the same exercise regimen. To further understand the effects of ARC, osteoblast and osteoclast function were examined by differentiating bone marrow stromal cells and hemopoietic stem cells in the absence or presence of ARC alongside the respective inducers of ascorbic acid and β-glycerophosphate or Rankl and MCSF. Osteoblast differentiation and function based on alizarin red and gene expression was unaffected by the presence of ARC. Similarly, ARC had no effect on osteoclast differentiation based on the number of multi-nucleated cells stained for tartrate resistant acid phosphatase. These findings demonstrate that ARC has no direct effect on osteoblast or osteoclast function. However, we found osteoclast differentiation was significantly reduced when supplementing the induction media with conditioned media from MLO-Y4 cells treated with ARC when compared to supplementing with condition media from non-treated MLO-Y4 cells (Fig 1C). These findings suggest that ARC indirectly reduces osteoclast activity by decreasing osteocytes' support of osteoclast activity.

Overall, these findings demonstrate that antagonizing P2Y2 function in adults increases bone mass and the sensitivity to loading, namely treadmill exercise.

Orthopedics/Bone and Joint Center
Gaudiani M, **Castle J**, **Elgamy N**, **Gasparro M**, **Wager S**, **Doerr M**, **Moutzouros V**, **Muh S**, and **Makhni E**. Poster 146: Higher Reoperation Rates Following Primary Rotator Cuff Repair in Patients Screening Positive for Depression...American Orthopaedic Society for Sports Medicine (AOSSM) Annual Meeting, July 10-14, 2024, Denver, Colorado. *Orthopaedic J Sports Med* 2024; 12:1-6. Full Text

Henry Ford Health

Objectives: Recent studies have identified an association between preoperative depression and worse outcomes following arthroscopic rotator cuff repair (RCR) surgery, including lower patient-reported outcomes, increased pain and impairment, and higher rates of complications. Patient Health Questionnaire-2 (PHQ-2) is a commonly administered screening tool for measuring depressive symptoms; however, the relationship between PHQ-2 and postoperative outcomes after RCR is not yet established. The purpose of this study is to investigate the association between depression and reoperation rates in patients undergoing primary RCR. Methods: This retrospective chart review evaluated data from all patients who underwent elective primary RCR at 1 health system between March 2016 and December 2021 and had a PHQ-2 score at least 6 months prior to their surgery. The PHQ-2 is a validated tool used to screen for depression with scores ranging from 0-6. Patients were categorized as either depressed (PHQ-2 ≥ 2) or nondepressed (PHQ-2 < 2). Patients <18 years old, history of prior RCR, and patients without PHQ-2 scores within 6 months of surgery were excluded from the study. The primary outcome was to compare reoperation rate, defined as the need for any subsequent surgery related to the primary RCR between depressed and non-depressed patients. The secondary outcome was a comparison of postoperative health care utilization, which included emergency department visits and hospital readmissions within 90 days. Depressed patients were also propensity matched 1:1 to nondepressed patients via age, body mass index (BMI), and tear size for a subanalysis. Results: A total of 238 patients who underwent primary RCR were included with 84 depressed patients and 154 nondepressed patients. Significantly more patients were female (67% versus 46%; P = 0.002) in the depressed cohort compared to nondepressed. There was a significantly increased incidence of comorbid depression (63% vs 28%; P < 0.001), anxiety (52% vs 17%; P < 0.001), and substance use disorder (20% vs 6%; P < 0.001) as well as a lower median household income (MHI) in the depressed cohort versus the nondepressed cohort ($58,451.93 ± $21,024.93 vs. $66,751.93 ± $22,654.45; P < 0.001). Fifteen (17.9%) depressed patients underwent reoperation versus 10 (6.5%) nondepressed patients (P = 0.006). Mean time to reoperation in the depressed cohort was 11.7 months (0.8-35 months). In the subanalysis, 80 patients in the depressed cohort and 80 patients in the nondepressed cohort were matched. Depressed patients had significantly higher rates of comorbid depression (63% vs 18%; P < 0.001), anxiety (52% vs 17%; P < 0.001), and substance use disorder (20% vs 6%; P < 0.001) and a lower MHI ($58,615.20 ± $21,455.12 vs $66,470.73 ± $22,996.49; P = 0.04). Fewer patients were employed full time (22% vs. 44%) and more were disabled (30% vs 8%) amongst the depressed cohort (P = 0.003). Amongst depressed patients, 14 patients (17.5%) versus 4 (5%) underwent reoperation (P = 0.01). No significant differences in postoperative emergency department visits, postoperative complications, or hospital readmissions were found between the depressed and nondepressed cohorts in either analysis. Conclusions: We found patients screening positive for depression preoperatively, as measured by PHQ-2, had a significantly higher reoperation rate following primary RCR compared to nondepressed patients. These patients were more likely to be female, have comorbid mental health diagnoses, no full-time employment, and a lower household income. Screening for depression preoperatively could be a useful adjunct for providers to better identify patients at risk for worse outcomes.

Orthopedics/Bone and Joint Center
Gaudiani M, **Castle J**, **Elgamy N**, **Wager S**, **Bennie J**, **Lynch TS**, **Moutzouros V**, and **Makhni E**. Poster 385: Incidence of Preoperative Depression in Knee and Shoulder Arthroscopy Using Patient Health Questionnaire-2 (PHQ-2)...American Orthopaedic Society for Sports Medicine (AOSSM) Annual Meeting, July 10-14, 2024, Denver, Colorado. *Orthop J Sports Med* 2024; 12:1-3. Full Text

Henry Ford Health

Objectives: Preoperative depression has been associated with worse outcomes following orthopaedic surgery including lower patient-reported outcomes, increased pain and impairment, and a higher rate of complications. Patient Health Questionnaire-2 (PHQ-2) is a commonly administered screening tool for measuring depressive symptoms, however the relationship between PHQ-2 and preoperative characteristics of patients presenting for arthroscopic knee and shoulder surgery have not been established. The purpose of this study was to investigate the association between depression and preoperative demographics and patient recorded outcomes of patients presenting for arthroscopic knee and shoulder surgery. Methods: This retrospective chart review evaluated data from all patients who underwent elective primary arthroscopic shoulder and knee surgery at 1 health system. Current Procedural Terminology codes were used to identify patients undergoing anterior cruciate ligament reconstruction (ACLR) (29888), meniscectomy (29880/29881), meniscus repair (29882/29883), knee chondroplasty (29877), labral repair (29807), rotator cuff repair (29827), and capsulorrhaphy (29806). Patients were included if they had completed Patient-Reported Outcomes Measurement Information System - Pain Interference (PROMIS-PI) and a PHQ-2 score at least 3 months prior to their surgery. The PHQ-2 is a validated tool used to screen for depression with scores ranging from 0-6. Patients were categorized as either depressed (PHQ-2 ≥ 3) or non-depressed (PHQ-2 < 3). Demographic characteristics and PROMIS scores were compared and a univariate and multivariate regression analysis was performed. Results: A total of 979 patients were included with 128 (13%) depressed patients and 851 nondepressed patients. There was no significant differences between the depressed and nondepressed group for age (49.18 ± 16.13 vs. 49.01 ± 15.71; P=0.926), sex (53.1% vs. 47.8% female; P = 0.263), median household income ($65,230 ± $24,684 vs. $66,810 ± $22,414; P=0.463), area deprivation index national percentile (62.48 ± 24.31 vs. 64.12 ± 24.58; P = 0.494), and depression diagnosis (4.7% vs. 3.1%; P = 0.333). Preoperative PROMIS-PI was significantly worse in the depressed cohort versus non-depressed (66.1 ± 5.9 vs. 63.6 ± 6.3; P < 0.001). Preoperative PROMIS-Depression score (R2 = 0.34) was the highest correlated variable to preoperative PHQ2 score in the univariate analysis. In the multivariate regression analysis, higher preoperative PROMIS-PI scores were found to be a risk factor for a PHQ2 score >3 (P < 0.001). Patients undergoing knee chondroplasty were less likely to be in the depressed cohort (odds ratio: 0.092 (0.009-0.914); P = 0.042). No other surgeries were more or less likely to be depressed. There was no difference between groups for age, sex, smoking status, insurance type, Area Deprivation Index, Metabolic Health Index, comorbid depression, and anxiety diagnosis. Conclusions: Overall, a larger number of patients screened positive for depression amongst patients undergoing knee and shoulder arthroscopy than were formally diagnosed. Demographic and socioeconomic variables were similar indicating these patients may be hard to identify without a screening tool like PHQ-2. Preoperative pain scores were higher amongst the depressed patients, indicating higher pain scores may be associated with increased risk of depression. This study highlights the need for further research on preoperative mood screening before arthroscopic surgery.

Orthopedics/Bone and Joint Center
Moutzouros V, **Enweze L**, **Castle J**, **Kasto J**, **Gasparro M**, **Pratt B**, **Abbas M**, **Jiang E**, and **Muh S**. Paper 06: Lower Socioeconomic Status is Associated with Recurrent Shoulder Instability Before Surgical Shoulder Stabilization...American Orthopaedic Society for Sports Medicine (AOSSM) Annual Meeting, July 10-14, 2024, Denver, Colorado. *Orthop J Sports Med* 2024; 12:1-2. Full Text

Henry Ford Health

Objectives: Social determinants of health (SDOH) are comprised of a patient's environmental conditions including social and economic factors, which influence access to health care and resources. Growing evidence in orthopaedic surgery has revealed that SDOH factors lead to differential access to care and ultimately health disparities after surgery. For shoulder instability, previous literature has demonstrated that the number of previous dislocations before a stabilization procedure increases the risk of recurrent instability after the procedure. The purpose of this study was to investigate the impact of SDOH on the number of dislocation events before surgical intervention. Methods: A retrospective review of patients who underwent shoulder stabilization surgery at a health system in a large metropolitan area between

January 1, 2021 and April 13, 2023 were identified. Patients' demographic and social determinants variables were extracted using the electronic medical record. Social Vulnerability Index (SVI) socioeconomic subscore and Area of Deprivation Index (ADI) were collected using online mapping data based on patient zip codes. The number of dislocation events and the time they occurred were determined using clinical charts. Operative variables collected included the date of surgery to determine the time from clinical presentation to surgery and the procedure performed. Univariate linear regression analysis was used to evaluate potential predictors of increasing time to presentation and increasing time to surgery. Univariate logistic regression analysis was also performed of all potential predictors of having >1 dislocation event. A multivariate model was then created using all predictors with a P value < 0.05 in the univariate models. Results: There were 106 patients who underwent shoulder surgery for instability, including arthroscopic and open stabilization, and had complete social determinant data, with 54% (n = 57) identifying as White, 29% (n = 31) as Black/African American, and 17% (n = 18) as other. A total of 38 (35.8%) patients suffered 1 dislocation (single dislocation cohort) before undergoing surgery, and 68 (64.2%) experienced > 1 dislocation (recurrent cohort) before surgery. No significant variables were associated with increasing time to presentation or surgery. Univariate logistic regression revealed that decreasing age (odds ratio [OR] 0.94 [95% confidence interval (CI) 0.89- 0.99]; P = 0.02), decreasing body mass index (BMI) (OR 0.90 [95% CI 0.83-0.98]; P = 0.02), increasing SVI (OR 1.21 [95% CI 1.05-1.38]; P = 0.006), and increasing area deprivation index (ADI) (third tercile compared to first, OR 6.04 [95% CI 2.05-17.8]; P = 0.003) were associated with increased odds of having > 1 instability event before surgical intervention. There was no association with race found in terms of number of dislocations before surgery. Multivariate logistic regression modeling revealed that decreasing BMI (OR 0.87 [95% CI 0.78-0.98]; P = 0.02) and increasing ADI (third tercile compared to first tercile, OR 7.46 [95% CI 1.26-44.2]; P = 0.02) were associated with increased odds of having > 1 instability event before shoulder instability surgery. Conclusions: Lower socioeconomic status, as measured by ADI, is an independent predictor of a higher likelihood of recurrent instability before shoulder stabilization surgery. Recognizing these relationships may motivate surgeons to create pathways to prevent these treatment disparities among shoulder instability patients. Further studies are required to examine if these SDOH variables lead to disparities in postoperative outcomes.

Pathology and Laboratory Medicine

Ahsan B, **Xu ZF**, **Chang Q**, **Husain S**, **Jaratli H**, and **Theisen B**. "Where Does This Specimen Even Go?" An Institutional Experience on the Evaluation of Adequacy and a Model for Tissue Collection and Processing of EUS-Guided Liver Biopsies Collected for the Evaluation of Medical Liver Disease. *Lab Invest* 2024; 104(3):S1636-S1636. Full Text

[Ahsan, Beena; Chang, Qing; Jaratli, Hayan] Henry Ford Hlth Syst, Detroit, MI USA. [Xu, Zhengfan; Husain, Sanam; Theisen, Brian] Henry Ford Hosp, Detroit, MI 48202 USA. Henry Ford Hospital

Pathology and Laboratory Medicine

Ahsan B, **Xu ZF**, **Chang Q**, **Husain S**, and **Theisen B**. Interobserver Agreement in Subclassifying High-grade/Poorly Differentiated Colorectal Carcinomas Among Subspecialty Trained Gastrointestinal Pathologists; Differentiating the Undifferentiated. *Lab Invest* 2024; 104(3):S1981-S1982. Full Text

[Ahsan, Beena; Chang, Qing] Henry Ford Hlth Syst, Detroit, MI USA. [Xu, Zhengfan; Husain, Sanam; Theisen, Brian] Henry Ford Hosp, Detroit, MI USA. Henry Ford Hospital

Pathology and Laboratory Medicine

Aron M, Chandrashekar D, Abdulfatah E, Zein-Sabatto B, Lobo J, Canete-Portillo S, Kunju L, Cox R, Przybycin C, **Al-Obaidy K**, Idrees M, Falzarano S, Harada S, Wu A, and Netto G. Clinical and Molecular Characterization of Clear Cell Adenocarcinoma of the Urinary Tract: A Multi-Institutional Study. *Lab Invest* 2024; 104(3):S903-S904. Full Text

[Aron, Manju] USC, Keck Sch Med, Los Angeles, CA USA. [Chandrashekar, Darshan; Canete-Portillo, Sofia; Harada, Shuko] Univ Alabama Birmingham, Birmingham, AL USA. [Abdulfatah, Eman; Wu, Angela] Univ Michigan, Michigan Med, Ann Arbor, MI USA. [Zein-Sabatto, Bassel; Przybycin, Christopher] Cleveland Clin, Cleveland, OH USA. [Lobo, Joao] Portuguese Oncol Inst Porto, Porto, Portugal. [Kunju,

Lakshmi] Univ Michigan, Ann Arbor, MI USA. [Cox, Roni] PathNet Labs, Little Rock, AR USA. [Al-Obaidy, Khaleel] Henry Ford Hlth Syst, Detroit, MI USA. [Idrees, Muhammad] Indiana Univ Sch Med, Indianapolis, IN USA. [Falzarano, Sara] Univ Florida, Coll Med, Gainesville, FL USA. [Netto, George] Univ Penn, Sch Med, Birmingham, AL USA. Keck Hospital; University of Alabama System; University of Alabama Birmingham; University of Michigan System; University of Michigan; Cleveland Clinic Foundation; Portuguese Institute of Oncology; University of Michigan System; University of Michigan; Henry Ford Health System; Henry Ford Hospital; Indiana University System; Indiana University Bloomington; State University System of Florida; University of Florida

Pathology and Laboratory Medicine
Azordegan N, **Saikia K**, **Theisen B**, **Schultz D**, **Yuan LS**, **Chang Q**, Alruwaii F, Perry K, and **Zhang ZY**. Prevalence of Atypia of Undetermined Significance (AUS) in Thyroid Fine Needle Aspirations; A Three-Year Single Institution Study. *Lab Invest* 2024; 104(3):S380-S381. Full Text

[Azordegan, Nazila; Saikia, Kasturi; Schultz, Daniel; Yuan, Lisi; Chang, Qing; Zhang, Ziying] Henry Ford Hlth Syst, Detroit, MI USA. [Theisen, Brian] Henry Ford Hosp, Detroit, MI USA. [Alruwaii, Fatimah] Cleveland Clin, Cleveland, OH USA. [Perry, Kyle] Univ Michigan, Michigan Med, Detroit, MI USA. Henry Ford Hospital; Cleveland Clinic Foundation; University of Michigan System; University of Michigan

Pathology and Laboratory Medicine
Bava EP, **Abbas O**, **Montecalvo J**, and **Wang ZQ**. Non-Small Cell Lung Carcinomas with MET Exon 2 Skipping Mutations: A Potential Inhibitory Self-Regulatory Mechanism by Tumor Cells. *Lab Invest* 2024; 104(3):S1945-S1945. Full Text

[Bava, Ejas Palathingal; Abbas, Omar; Montecalvo, Joseph; Wang, Zhiqiang] Henry Ford Hlth Syst, Detroit, MI USA.

Pathology and Laboratory Medicine
Bava EP, **Ozcan K**, **Ahsan B**, **Chang Q**, **Husain S**, **Jaratli H**, and **Theisen B**. Assessing the Likeliness of "Unlikely" - An Institutional Analysis of Graft Versus Host Disease (Gvhd) in Solid Organ Transplant Patients Correlating Short Tandem Repeat (Str) Chimerism Testing with Clinical and Available Pathologic Findings. *Lab Invest* 2024; 104(3):S887-S888. Full Text

[Bava, Ejas Palathingal; Ozcan, Kerem; Ahsan, Beena; Chang, Qing; Jaratli, Hayan] Henry Ford Hlth Syst, Detroit, MI USA. [Husain, Sanam; Theisen, Brian] Henry Ford Hosp, Detroit, MI 48202 USA. Henry Ford Hospital

Pathology and Laboratory Medicine
Davis W, **Singh B**, **Kutait A**, and **Abbas O**. Malakoplakia Mimicking Metastatic Colon Cancer. *Am J Gastroenterol* 2024; 119(10):S1934. Full Text

W. Davis, Henry Ford Health, Madison Heights, MI, United States

Introduction: Malakoplakia is a rare, chronic granulomatous inflammatory disease that results from impaired histiocyte clearance of bacteria in immune compromised individuals. We present a case of a postlung transplant patient that was suspected to have diffuse colonic metastatic disease based on computed tomography (computed tomography)that was later deemed to be diffuse malakoplakia related to systemic infection. Case Description/Methods: A 62-year-old woman with history of lung transplant on tacrolimus presented with abdominal distension and diarrhea. Vital signs were stable on arrival. Laboratory results including a complete blood count, liver and chemistry panels were noncontributory. Blood cultures repetitively grew Achromobacter xylosoxidans despite escalation of antibiotic therapy. Abdominal and pelvic computed tomography demonstrated gastric distension, and a colonic filling defect at the hepatic flexure with extensive adenopathy evading the duodenal serosa. At this time there were concerns of metastatic colon cancer with concomitant systemic infection. Interventional radiology performed lymph node biopsy revealing malakoplakia and negative for malignancy. Multidisciplinary discussion between infectious disease and gastroenterology was performed with concerns for the colonic

filling defect as the origin of patient's persistent bacteremia. Colonoscopy was performed showing diffuse nodularity with ulcerations encompassing the right colon without a targetable lesion for source control. Biopsies were obtained redemonstrating malakoplakia. The patient's hospital course was complicated by COVID-19 pneumonia and ultimately expiring due to respiratory failure. Discussion: Malakoplakia is a poorly understood and rare chronic granulomatous inflammatory disease that results from bactericidal defect of histiocytes. This manifests in an accumulation of phagolysosomes most commonly in immune compromised individuals. Symptoms are non-specific ranging from asymptomatic to altered bowel habits, abdominal pain, rectal bleeding, and intestinal obstruction. Endoscopic appearance can range from flat lesions to multiple ulcerated polypoid nodules. Thus, as in this case, the diagnosis can often be delayed and result in unnecessary interventions until a true diagnosis is achieved. Once diagnosed antibiotic therapy is tailored to the culprit organism resulting an accumulation within histiocytes and killing the bacteria. This case serves to educate the reader of this rare disease presentation to limit extensive work up and expedite treatment (see Figure 1).

Pathology and Laboratory Medicine
Din NU, Raza M, **Xu ZF**, Ahmed A, and **Ahsan B**. Clinicopathological Characteristics and Cyclin D1 Immunohistochemical Expression in Extranodal Rosai-Dorfman Disease. *Lab Invest* 2024; 104(3):S889-S891. Full Text

[Din, Nasir Ud; Raza, Muhammad; Ahmed, Arsalan] Aga Khan Univ Hosp, Karachi, Pakistan. [Xu, Zhengfan] Henry Ford Hosp, Detroit, MI 48202 USA. [Ahsan, Beena] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Health System; Henry Ford Hospital

Pathology and Laboratory Medicine
Ghosh SB, **Xu ZF**, **Tawil T**, **Liu W**, **Gomez-Gelvez J**, **Schultz D**, and **Inamdar K**. TP53 Mutated Chronic Myelomonocytic Leukemia is Associated with Complex Genetic Abnormalities and Inferior Outcome. *Lab Invest* 2024; 104(3):S1406-S1407. Full Text

[Ghosh, Sharmila B.; Tawil, Tala; Liu, Wei; Schultz, Daniel; Inamdar, Kedar] Henry Ford Hlth Syst, Detroit, MI USA. [Xu, Zhengfan; Gomez-Gelvez, Juan] Henry Ford Hosp, Detroit, MI USA. Henry Ford Hospital

Pathology and Laboratory Medicine
Gupta A, Zalles N, Sangoi A, Akgul M, **Al-Obaidy K**, Mohanty S, Przybycin C, Myles J, Gallan A, Nguyen J, Alaghehbandan R, and Williamson S. Foamy Macrophages in Clear Cell Renal Cell Carcinoma are Highly Associated with BAP1Deficient Tumors. *Lab Invest* 2024; 104(3):S952-S953. Full Text

[Gupta, Akriti; Zalles, Nicole; Przybycin, Christopher; Myles, Jonathan; Nguyen, Jane; Alaghehbandan, Reza; Williamson, Sean] Cleveland Clin, Cleveland, OH 44106 USA. [Sangoi, Ankur] Stanford Univ, Stanford, CA 94305 USA. [Akgul, Mahmut] Albany Med Ctr, Albany, NY USA. [Al-Obaidy, Khaleel] Henry Ford Hlth Syst, Detroit, MI USA. [Mohanty, Sambit] Adv Med & Res Inst, New Delhi, India. [Gallan, Alexander] Med Coll Wisconsin, Milwaukee, WI 53226 USA. College; Henry Ford Health System; Henry Ford Hospital; Medical College of Wisconsin

Pathology and Laboratory Medicine
Jin M, **Chitale D**, **Theisen B**, **Schultz D**, **Ahsan B**, **Chang Q**, **Azordegan N**, **Shaw B**, and **Zhang ZY**. Comparison of Routine Brush Cytology and Fluorescence in Situ Hybridization (FISH) for Assessment of Biliary Strictures: A Single Teaching Institution Experience. *Lab Invest* 2024; 104(3):S427-S428. Full Text

[Jin, Michelle; Schultz, Daniel; Ahsan, Beena; Chang, Qing; Azordegan, Nazila; Shaw, Brandon; Zhang, Ziying] Henry Ford Hlth Syst, Detroit, MI USA. [Chitale, Dhananjay; Theisen, Brian] Henry Ford Hosp, Detroit, MI USA. Henry Ford Hospital

Pathology and Laboratory Medicine
Kisha S, **Bava EP**, **Ozcan K**, **Chitale D**, **Ahsan B**, **Chang Q**, **Husain S**, **Jaratli H**, and **Theisen B**. An Analysis of Gastrointestinal Graft Versus Host Disease (GVHD) in Bone Marrow Transplant (BMT)

Patients in the Era of Short Tandem Repeat (STR) Chimerism Testing - Is it Time to Stop Hedging? *Lab Invest* 2024; 104(3):S741-S742. Full Text

[Kisha, Sarah; Bava, Ejas Palathingal; Ozcan, Kerem; Ahsan, Beena; Chang, Qing; Jaratli, Hayan] Henry Ford Hlth Syst, Detroit, MI USA. [Chitale, Dhananjay; Husain, Sanam; Theisen, Brian] Henry Ford Hosp, Detroit, MI USA. Henry Ford Hospital

Pathology and Laboratory Medicine
Ohan H, **Tawil T**, **Al-Obaidy K**, **Gupta N**, and **Hassan O**. Do Saturation Prostate Biopsies Provide Additional Clinically Significant Information in Patients with MRI Identified Lesions Sampled at the Same Time: Our Institutional Experience. *Lab Invest* 2024; 104(3):S1029-S1029. Full Text

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Pathology and Laboratory Medicine
Parisi X, Wang W, **Liu W**, Loghavi S, Hu SM, Jelloul FZ, Medeiros LJ, and Fang H. Reactive Intra-sinusoidal Immunoblastic Proliferations in Lymph Nodes: A Diagnostic Pitfall for Diffuse Large B-Cell Lymphoma. *Lab Invest* 2024; 104(3):S1462-S1463. Full Text

[Parisi, Xenia] Univ Texas MD Anderson Canc Ctr, Cypress, TX USA. [Wang, Wei; Loghavi, Sanam; Hu, Shimin; Jelloul, Fatima Zahra; Medeiros, L. Jeffrey; Fang, Hong] Univ Texas MD Anderson Canc Ctr, Houston, TX 77030 USA. [Liu, Wei] Henry Ford Hlth Syst, Detroit, MI USA. Texas System; UTMD Anderson Cancer Center; Henry Ford Health System; Henry Ford Hospital

Pathology and Laboratory Medicine
Patel-Rodrigues P, **Harris K**, **Piraka C**, **Alsheik E**, **Ahsan B**, **Nalamati S**, and **Yudovich A**. A Case of Multiple NSAID-Induced Strictures of the Ascending Colon. *Am J Gastroenterol* 2024; 119(10):S2044. Full Text

P. Patel-Rodrigues, Henry Ford Health, Detroit, MI, United States

Introduction: Nonsteroid anti-inflammatory drugs (NSAID) are one of the most widely used medications in the world. Chronic NSAID use can cause several complications including inflammatory changes to the bowel mucosa that can result in diaphragm-like strictures resulting in abdominal pain, anemia, and small bowel obstructions. NSAID-induced small bowel strictures, although rare, have been well-described in the literature. NSAID-induced colonic strictures are a rarer presentation and are delayed in diagnosis. We describe a case of multiple colonic strictures in the setting of chronic NSAID use. Case Description/Methods: A 72-year-old woman with iron deficiency anemia presented with abdominal pain, weight loss, and fatigue for 3 months and was found to have a hemoglobin of 5.6. She had never undergone an upper endoscopy or colonoscopy. Her daily medications included diclofenac 50 mg twice a day. Computed tomography of her abdomen showed circumferential wall thickening of the terminal ileum and ileocecal valve. Colonoscopy showed a severe stricture with erythema in the ascending colon that could not be traversed. Repeat colonoscopy with interventional gastroenterology 2 weeks later showed 2 strictures. The distal stricture was dilated to 10 mm under fluoroscopic guidance. The upstream colon was examined endoscopically using a direct visualization system, like a cholangioscope, through the colonoscope. A second stricture was seen in the proximal ascending colon which was traversed in a similar fashion. The strictures and surrounding areas were biopsied. Biopsies showed focal erosion, fibrin, architectural disarray, and granulation tissue. Due to ongoing symptoms, she underwent a right hemicolectomy with colorectal surgery 2 months later. The final pathology of the stricture showed submucosal fibrosis and haphazard arrangement of smooth muscle, nerves, and vessels. This constellation of features is associated with NSAID use. She was seen 1 month post-operatively with improved symptoms. Discussion: Colonic diaphragmatic strictures are a rare side effect of chronic NSAID use. This case highlights how important it is for physicians to be mindful of this condition, inquire about NSAID use, and make a prompt and accurate diagnosis. Without awareness of this entity, diclofenac may not have been stopped and a possible incorrect diagnosis of Crohn's disease may have been made.

Many cases improve with use of endoscopic therapies and withdrawal of NSAIDs. In more severe cases, such as this, surgical intervention may be required. (Figure Prresented).

Pathology and Laboratory Medicine
Ren D, Jennings T, Granada CP, Jones A, Nourbakhsh M, Johnson C, Williamson S, **Al-Obaidy K**, Rahmatpanah F, and Giannico G. Molecular Fingerprints in Adult and Pediatric Inflammatory Myofibroblastic Tumors of the Urinary Bladder. *Lab Invest* 2024; 104(3):S1043-S1045. Full Text

[Ren, Dong] UCI Med Ctr, Orange, CA USA. [Jennings, Tara] Univ Calif Irvine, Irvine, CA USA. [Granada, Carlos Prieto; Jones, Angela] Vanderbilt Univ, Med Ctr, Nashville, TN USA. [Nourbakhsh, Mahra; Johnson, Cary] UC Irvine, Med Ctr, Orange, CA USA. [Williamson, Sean] Cleveland Clin, Cleveland, OH USA. [Al-Obaidy, Khaleel] Henry Ford Hlth Syst, Detroit, MI USA. [Rahmatpanah, Farah; Giannico, Giovanna] Univ Calif Irvine, Orange, CA USA. University of California System; University of California Irvine; Vanderbilt University; University of California System; University of California Irvine; Cleveland Clinic Foundation; Henry Ford Health System; Henry Ford Hospital; University of California System; University of California Irvine

Pathology and Laboratory Medicine
Singh B, **Zarrar Khan M**, **Patel-Rodrigues P**, **Ramanan S**, **Ahsan B**, and **Schairer J**. Iron Gut. *Am J Gastroenterol* 2024; 119(10):S3149. Full Text

B. Singh, Henry Ford Jackson Hospital, Jackson, MI, United States

Introduction: Gastric siderosis refers to the abnormal deposition of iron within the gastric mucosa associated withwith unclear etiology. Liver is the primary storage organ and once its capacity is saturated, iron can be deposited in other organs such as the heart, joints, and pancreas, leading to organ mdamage, primarily deposited as hemosiderin. Clinical disorders such as hemochromatosis, gastritis, repeated blood transfusions, and liver diseases are linked to gastric siderosis. Factors like alcohol abuse, iron supplements, NSAIDs, and PPIs also contribute. Studies show oral iron supplementation and NSAIDs can lead to GS. Iron concentration from portocaval shunting may expose stomach cells, particularly in individuals with esophageal varices. Case Description/Methods: A 70-year-old woman with watery diarrhea and rectal urgency for 3 weeks with 7 pounds weight loss. She denied overt bleeding, or recent antibiotic use. Admitted with hemoglobin of 8.8 which was at her baseline, and creatinine 4.6. CT abdomen, Stool studies including Giardia/Cryptococcus, C. difficile toxin, and bacterial PCR were negative. Colonoscopy showed a normal macroscopic appearance with biopsies negative for microscopic colitis. Upper endoscopy showed pitted brown spots mucosa in the gastric body, antrum, duodenal bulb, and second part of duodenum (Figure 1). Biopsies were taken, with antral ones demonstrating antral mucosa with iron deposition in the glands and lamina propria. The iron deposits are highlighted by a Prussian blue stain. The patient had no elevation in transaminases, and further ferritin turned out to be in the 300s limiting our suspicion for hereditary hemochromatosis. In her case, oral iron usage was deemed to be the culprit for the disease. Discussion: Numerous clinical disorders, such as hemochromatosis, gastritis, repeated blood transfusions, and cirrhosis, more so with varices, have been linked to gastric siderosis. Abuse of alcohol, iron supplements, NSAIDs, and PPIs are also implicated. It has diverse endoscopic appearance, characterized as a yellow-brown staining of mucosa. Three primary patterns of iron deposition are as follows: (A) iron deposition in macrophages, stroma, and epithelium, probably linked to stomach irritation, or ulcers, (B) primarily extracellular deposition with some focal deposition in blood vessels, and epithelium; linked to Oral iron supplementation and (C) gastric glandular siderosis and is linked to multiple blood transfusions, cirrhosis, or systemic iron excess caused by hereditary hemochromatosis. (Figure Presented).

Pathology and Laboratory Medicine
Tarcan Z, **Ozcan K**, Xue Y, Raj N, Urganci N, Klimstra D, Adsay NV, and Basturk O. Oncocytic Variant of Pancreatic Neuroendocrine Tumors are Associated with Aggressive Characteristics. *Lab Invest* 2024; 104(3):S1859-S1861. Full Text

[Tarcan, Zeynep; Raj, Nitya; Urganci, Nil; Basturk, Olca] Mem Sloan Kettering Canc Ctr, 1275 York Ave, New York, NY 10021 USA. [Ozcan, Kerem] Henry Ford Hlth Syst, Detroit, MI USA. [Xue, Yue] Case Western Reserve Univ, Univ Hosp Cleveland Med Ctr, Cleveland, OH 44106 USA. [Klimstra, David] Paige AI, New York, NY USA. [Adsay, N. Volkan] Koc Univ Hosp, Istanbul, Turkiye. Ford Hospital; University System of Ohio; Case Western Reserve University; University Hospitals of Cleveland; Koc University

Pathology and Laboratory Medicine
Theisen B, **George M**, **Loveless I**, and **Steele N**. Quantifying Tertiary Lymphoid Structures in Resected Pancreatic Ductal Adenocarcinoma in Clinical Practice - A Feasibility Study Demonstrating a Correlation with Survival. *Lab Invest* 2024; 104(3):S1862-S1863. Full Text

[Theisen, Brian] Henry Ford Hosp, Detroit, MI 48202 USA. [George, Madison; Loveless, Ian] Michigan State Univ, E Lansing, MI 48824 USA. [Steele, Nina] Henry Ford Hlth Syst, Detroit, MI USA. University; Henry Ford Health System; Henry Ford Hospital

Pathology and Laboratory Medicine
Tuthill JM. Validating an AI-based analytic tool for IHC staining QA: precision studies of the digital pathology pipeline. *Virchows Arch* 2024; 485:S398-S398. Full Text

[Tuthill, J. M.] HFHS, Detroit, MI USA.

Background & objectives: Standardization of immunohistochemistry staining quality assessment is critical for diagnostic accuracy. Pathologists currently assess stain quality subjectively, comparing control sections to patient tissue. Qualitopix (Visiopharm, Denmark), a cloud-based artificial intelligence platform for uses quantitative analysis for scoring stained slides. Methods: Glass slides were produced from two 4-core standardized cell-line blocks (Histocyte Laboratories, Newcastle, England) with epitopes for estrogen receptor (ER) and progesterone receptor (PR) of increasing intensities, stained using Ventana Benchmark Ultra and scanned on DP 200 and HT scanners (Roche, Basel, Switzerland). An intra-scanner precision study was performed by comparing Qualitopix-derived H scores of ER and PR slides. Results: Intra-scanner precision studies demonstrated consistent reproducibility using both scanners: %CV for ER cores were 0%, 10.7%, 2.3% and 0.3% for cores 1 [0 +/- 0.003], 2 [0.3 +/- 0.25], 3 [2.4 +/- 1.4] and 4 [79 +/- 0.65] respectively. % CV for PR cores were 0%, 0.6%, 0.4% and 0.1% for cores 1 [0 +/- 0.01], 2 [29 +/-4.5], 3 [65+/-2], and 4 [94+/-2] respectively. Concordance studies revealed tight agreement. ICC for ER cores were 0.64 (moderate), 0.95(excellent), 0.95(excellent) and 0.68 (moderate) for cores 1, 2, 3 and 4 respectively. ICC for PR cores were 0.64 (moderate), 0.87(good), 0.96(excellent) and 0.68 (moderate) for cores 1, 2, 3 and 4 respectively. Conclusion: Quality assurance is essential to the use of digital pathology, particularly to the application of AI. Studies of precision, reproducibility, and accuracy are lacking in the literature. This study demonstrates the precision characteristics of one vendor's digital pathology product line.

Pathology and Laboratory Medicine
Vitale A, **Zhang ZY**, **Azordegan N**, and **Yuan LS**. A Practical Alternative Approach to Rapid Cytological Analysis for Endobronchial UltrasoundGuided Transbronchial Needle Aspiration: A Retrospective Study with Cytologic-Histologic Correlation. *Lab Invest* 2024; 104(3):S487-S488. Full Text

[Vitale, Alyssa] Henry Ford Hosp, Detroit, MI 48202 USA. [Zhang, Ziying; Azordegan, Nazila; Yuan, Lisi] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Hospital

Pathology and Laboratory Medicine
Xu ZF, **Theisen B**, **Chang Q**, **Husain S**, **Jaratli H**, and **Ahsan B**. Poorly Differentiated Variants of Colorectal Carcinoma; Is There a Survival Difference Between WHO-listed Subtypes? A Single Teaching Institute Experience. *Lab Invest* 2024; 104(3):S853-S854. Full Text

[Xu, Zhengfan; Theisen, Brian; Husain, Sanam] Henry Ford Hosp, Detroit, MI USA. [Chang, Qing; Jaratli, Hayan; Ahsan, Beena] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Hospital

Pathology and Laboratory Medicine
Xu ZF, **Theisen B**, **Chang Q**, **Jaratli H**, **Husain S**, and **Ahsan B**. A Comparative Analysis of Endoscopic Ultrasound Guided Fine Needle Liver Biopsy (EUS-FNLB) with Percutaneous and Transjugular Liver Biopsy Specimens; Where Do We Stand? *Lab Invest* 2024; 104(3):S1701-S1702. Full Text

[Xu, Zhengfan; Theisen, Brian; Husain, Sanam] Henry Ford Hosp, Detroit, MI 48202 USA. [Chang, Qing; Jaratli, Hayan; Ahsan, Beena] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Hospital

Pathology and Laboratory Medicine
Xu ZF, **Vitale A**, **Keller C**, **Alkhoory W**, **Zhang ZY**, and **Yuan LS**. Noninvasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP): Prevalence, Molecular and Ultrasonographic Profiles, and Cyto-Histo Correlation. *Lab Invest* 2024; 104(3):S497-S498. Full Text

[Xu, Zhengfan; Vitale, Alyssa; Keller, Christian] Henry Ford Hosp, Detroit, MI 48202 USA. [Alkhoory, Wamidh; Zhang, Ziying; Yuan, Lisi] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Hospital

Public Health Sciences
Kagithala D, **Rademacher A**, **Pawloski J**, **Latack K**, **Fadel H**, **Dallo F**, **Snyder J**, **Lee I**, and **Robin A**. ADJUVANT RADIATION THERAPY IN ATYPICAL MENINGIOMA TREATMENT DOES NOT IMPROVE PROGRESSION FREE SURVIVAL OR OVERALL SURVIVAL: A RETROSPECTIVE COHORT STUDY. *Neuro Oncol* 2024; 26:viii229. Full Text

D. Kagithala, Department of Neurosurgery, Henry Ford Health, Detroit, United States

Treatment of atypical meningiomas (AMs) presents a challenge due to their aggressive nature and tendency to recur. While there is clear evidence for the role of surgical resection of AMs, the use of adjuvant radiation therapy (ART) is a topic of ongoing debate. The aim of this study is to explore the impact of ART following surgical resection of AMs. The primary outcomes of interest are progression free survival (PFS) and overall survival (OS). Records were reviewed for all patients treated for Ams at our institution between January 1, 2014 and January 1, 2024. Patients were grouped into two cohorts, those who were initially treated with surgical resection only and those who also received adjuvant RT. PFS and OS were compared between the two groups using Kaplan Meier curves and Log Rank test. Additionally, multivariable cox proportional hazard models were used to adjust for age, MIB, and resection Simpson grading. There were 76 patients who were initially treated with surgery only and 23 patients who had surgery and ART. No significant difference in PFS or OS was observed between the groups (p=0.3522 and p=0.3636, respectively); including after adjusting for age, MIB, and Simpson grading (HR= 1.55 [0.64-3.76], p= 0.330; and HR = 0.95 [0.31-2.93] p= 0.934, respectively). On multivariate analysis, MIB >10 was associated with a significant difference in PFS (HR=2.76 [1.15-6.59], p=0.023). With ART, PFS was 91% at 12 and 60% at 36 months (versus 89% and 57%, respectively, with surgery only). OS was 95% at 12 and 88% at 36 months (versus 91% and 85%, respectively, with surgery only). In this series, ART was not observed to significantly improve PFS or OS compared to surgery alone. Larger series are needed to determine if there is a subset of patients who benefit from ART.

Public Health Sciences
Rademacher A, **Imran Z**, **Fadel H**, **Pawloski J**, **Anzalone A**, **Latack K**, and **Lee I**. ACCURACY OF THE ROSA ONE BRAIN ROBOTIC PLATFORM FOR THE PLACEMENT OF NEUROBLATE AND VISUALASE LASER INTERSTITIAL THERMAL THERAPY PROBES. *Neuro Oncol* 2024; 26:viii282. Full Text

A. Rademacher, Department of Neurosurgery, Henry Ford Health, Detroit, United States

Laser interstitial thermal therapy (LITT) is a minimally invasive treatment option for patients with intracranial lesions. The success of LITT is dependent on accurate placement of the laser probe in target tissue. Placement can be facilitated by various stereotactic methods, including the Robotic Surgical Assistant (ROSA) ONE Brain robotic platform. The aim of this study is to examine the accuracy of

stereotactic probe placement utilizing the ROSA robot. Primary outcomes were entry distance, target distance, and entry angle error. Accuracy differences between two major LITT platforms, the Neuroblate (Monteris Medical) and Visualase Systems, were compared. A prospective institutional database was used to identify all patients who underwent LITT for intracranial tumors utilizing the ROSA robot between 2013-2023. The sign test was used to compare error values to test their difference from a null value of 0. Spearman correlation was used to assess the relationship between angle of error and trajectory length. Kuskal-Wallis test was used to compare errors and trajectory length between the two companies. Of the 105 patients who underwent LITT during the study period, 337 probes were placed. For Visualase probes, median entry distance (1.1mm, IQR=0.4-2.0), target distance (1.6mm, IQR =0.9-2.4), and entry angle error (1.5°, IQR=0.9-2.5), were significantly different than zero (p=<.0001). For Neuroblate probes, median entry distance (1.5mm, IQR=1.0-2.1), target distance (1.8mm, IQR=1.1-2.4), and entry angle error (1.8°, IQR=1.1-2.5) were significantly different than zero (p=<.0001). When comparing laser systems, there was a significant difference in median entry distance error with Neuroblate having a higher error (1.5mm, IQR=1.0- 2.1) than Visualase (1.1mm IQR=0.4-2.0, p=0.0041). Stereotactic placement of LITT probes utilizing the ROSA robotic system was not able to achieve perfect alignment with the planned trajectory. When comparing the systems, Visualase probes were placed more accurately at the entry point than Neuroblate probes.

Public Health Sciences

Rademacher A, **Kagithala D**, **Pawloski J**, **Latack K**, **Fadel H**, **Dallo F**, **Snyder J**, **Lee I**, and **Robin A**. RADIATION-RELATED MORBIDITY OUTCOMES IN ATYPICAL MENINGIOMA PATIENTS: A RETROSPECTIVE COHORT STUDY. *Neuro Oncol* 2024; 26:viii228-viii229. Full Text

A. Rademacher, Department of Neurosurgery, Henry Ford Health, Detroit, United States

Atypical meningiomas present with unique challenges in management and prognosis. Given their tendency to recur, adjuvant radiation therapy (ART) is frequently utilized, however there are few reports on radiation-related morbidity in this patient population. The study aims to investigate the radiationrelated complications in atypical meningioma patients treated with or without ART. The primary outcomes were the incidence and severity of RT-related morbidity. All patients treated for atypical meningiomas at our institution between January 1, 2014 and January 1, 2024 were retrospectively analyzed. Patients were grouped into two cohorts, those who were initially treated with surgical resection only and those who also received adjuvant RT. Radiation morbidity grading was assigned for all patients that received radiation treatments during their clinical course based on established grading systems. Fisher's Exact and Kruskal-Wallis tests were used to determine associations between the two groups. There were 76 patients who were initially treated with surgery only and 23 patients who had surgery and ART. Mean length of follow-up among all patients was 55.6 months. Significantly lower rates of RT-related morbidity in the surgery only group were observed compared to the surgery and RT cohort (15.8% vs. 60.9%, p < 0.0001). Among patients in the surgery only cohort, 23 patients received RT at recurrence or progression. When comparing this subgroup to those who underwent ART, there was no significant difference in the severity of RT-related morbidity (p=0.2724). In this series, patients receiving ART experienced a higher incidence of radiation-related morbidity. When comparing only those who received RT, there was no difference in the incidence or severity of radiation-related morbidity between the two cohorts.

Public Health Sciences

Ramos-Carpinteyro R, Soputro N, Pedraza A, Calvo RS, Raver M, Manfredi C, **Wang Y**, Chavali JS, Okhawere K, Mikesell C, Ferguson E, Stifelman M, Badani KK, Autorino R, **Rogers C**, Ahmed M, Schwen ZR, Crivellaro S, and Kaouk J. Single-Port Robot-Assisted Simple Prostatectomy: A Multi-Institutional Cohort From the SPARC. *J Endourol* 2024; 38:A372. Full Text

R. Ramos-Carpinteyro, Cleveland Clinic, United States

Introduction: The single-port (SP) robot-assisted simple prostatectomy (RASP) is a viable minimally invasive technique for patients with symptomatic benign prostatic hyperplasia and adenomas > 80 cc. Early SP RASP reports have shown a fast recovery and >90% outpatient cases. This study aims to present updated data from the largest multi-institutional SP cohort. Methods: Retrospective analysis of all

consecutive SP RASP cases done by 11 experienced surgeons from 6 centers from February 2019 to January 2024. In general, a suprapubic incision was performed, and the da Vinci SP access was established through a transvesical, transperitoneal, or extraperitoneal (retropubic) approach. The prostate was excised, and subsequent intraprostatic mucosal reconstruction was performed. Continuous variables were summarized using measures of central tendency based on their distribution, while percentages were employed to depict frequencies. Results: A total of 240 entries were analyzed. All cases were completed successfully, without extra ports or conversion. Three types of approaches were identified: 164 transvesical (68.3%), 51 transperitoneal (21.3%), and 25 extraperitoneal (10.4%). Median age was 70 years. Eighteen percent of patients had previous prostate interventions. Median preoperative International Prostate Symptom Score (IPSS) and prostate volume were 22 and 137 ml, respectively. The most common indication for surgery was urinary retention (43.3%). Median estimated blood loss during surgery and console time were 100 ml and 142 minutes, respectively. One patient required a blood transfusion. There were 5 intraoperative complications, 4 air emboli (during early experience) and 1 accidental posterior cystotomy. The median percentage of tissue removed was 55.5%. Upon discharge, 87.9% of patients did not require narcotics for pain control. Median length of stay was 16 hours and hospitalization was needed for 15.8% of planned outpatient cases. Readmission rate was 0%. Median urinary catheter duration was 6 days. Figure 1 shows the long-term functional outcomes. Conclusions: SP robotic surgery is a feasible technique for transvesical, transperitoneal and extraperitoneal approaches to RASP. Its main advantages are minimal postoperative pain and fast recovery, and long-term functional outcomes show promising results in a multi-institutional setting.

Public Health Sciences

Snyder J, Alford SH, Kumar T, Pindolia K, **Poisson L**, Mahatma S, and **Mikkelsen T**. ONCOPATH: OPTIMIZED TREATMENT GUIDELINE CONCORDANT PATHWAY PRESENTED ON A VISUALINTERACTIVE DASHBOARD FOR CLINICAL DECISION SUPPORT COMPUTED BY OVERLAYING PATIENT LONGITUDINAL DATA ON A KNOWLEDGE GRAPH. *Neuro Oncol* 2024; 26:viii172. Full Text

J. Snyder, Henry Ford Health, Detroit, United States

BACKGROUND: OncoPath provides a visual analysis of a brain tumor patient's longitudinal clinical data overlayed on disease specific pathways with the goal of reducing knowledge discordant care and insurance authorization burden. By ingesting, curating and visually presenting the patient experience on guidelines, OncoPath aims to streamline clinical decision making and related processes. Understanding the patient's journey compared to treatment guidelines is of value in addressing health equity and guideline adoption in real world settings. METHODS: Data from 44 glioma patients diagnosed and treated between 2016-2021 were uploaded to OncoPath using natural language processing and other tools to capture abstractable data elements. The data was overlayed on guidelines using recursive graph modeling. Using the knowledge graph of a patient's history, the model also recommends treatment options in an interactive visual dashboard representing NCCN guidelines. The dashboard includes the guidelines in graphical format with associated references and notation. RESULTS: 28 males and 16 females age 21-38 years at diagnosis were abstracted. Cases represented 4 oligodendrogliomas, 13 astrocytomas, and 27 glioblastomas. Data was available through second line therapy, discharge to hospice or death. Cases were matched to the NCCN 2021 guidelines which was used for treatment decisions until November 2022. The patient data matched OncoPath except in 3 cases where KPS was not available resulting in premature pathway truncation. For these cases we inferred KPS based on subsequent treatment received to optimize the historic data. CONCLUSION: To our knowledge, this is a first-of-a-kind technology in neuro-oncology that may improve time to treatment, reduce health utilization resources and can serve as a benchmarking tool for care delivery. The feasibility of clinically implementing such tools for decision support was demonstrated. This type of tool could be particularly useful in low-resource areas where disease specific expertise may not be available or to illuminate care discrepancies.

Public Health Sciences

Soputro N, Okhawere K, Sauer Calvo R, Ramos-Carpinteyro R, **Wang Y**, Raver M, Snajdar E, Saini I, S Chavali J, D Mikesell C, M Pedraza A, **Rogers C**, Ahmed M, D Stifelman M, Lorentz A, Autorino R, Yuh

B, J Nelson R, Crivellaro S, K Badani K, and Kaouk J. Development of Patient-Specific Nomogram for Clinical Decision-Making Between Single-Port versus Multi-Port Robotic Partial Nephrectomy: A Report from the Single Port Advanced Robotic Consortium(SPARC). *J Endourol* 2024; 38:A53-A54. Full Text

N. Soputro, Department of Urology, Glickman Urological and Kidney Institute, Cleveland Clinic, United States

Introduction: To develop a patient-specific algorithm to better guide clinical decision-making when considering between Single Port (SP) versus Multi Port (MP) robotic partial nephrectomy (RPN). Methods: A retrospective review was performed on the IRBapproved, prospectively maintained multi-institutional database of the Single Port Advanced Research Consortium (SPARC) to identify all consecutive patients who underwent SP and MP-RPN between 2019 and 2023. Baseline clinicodemographic variables were used to identify the significant predictors of SP-RPN. The significant variables were subsequently used to construct a nomogram to predict the likelihood of SP versus MP-RPN. Results: Of the 1021 patients included in our analysis, 189 (18.5%) and 832 (81.5%) underwent SP and MP- RPN, respectively. Statistically significant predictors of SP-RPN included a lower comorbidity profile, a significant abdominal surgical history as characterized by a higher Hostile Abdomen Index (HAI), as well as lower complexity tumors. The nomogram generated using the aforementioned variables demonstrated a reasonable performance with an Area Under the Curve (AUC) of 0.79. An optimal cutoff point was determined, with likelihood ratios above 0.12 indicating a preference for SP-RPN. Of note, all SP-RPN cases that scored above the 0.12 cutoffexhibited improved perioperative outcomes, including shorter ischemia time and less intraoperative blood loss. Conclusions: Herein, we have devised a novel patient selection algorithm aimed at enhancing clinical decision-making within the expanding repertoire of RPN approaches. The findings highlighted in this study offer valuable guidance to facilitate appropriate patient selection and thereby ensuring favorable perioperative outcomes associated with RPN procedures.

Public Health Sciences

Soputro N, Ramos-Carpinteyro R, Calvo RS, Moschovas MC, Manfredi C, Raver M, Okhawere K, **Wang Y**, Snajdar E, Pedraza A, Chavali JS, Mikesell CD, Lorentz A, Yuh B, Nix JW, Joseph J, Kim M, **Rogers C**, Nelson RJ, Stifelman MD, Ahmed M, Crivellaro S, Autorino R, and Kaouk J. Single-Port Robotic Radical Prostatectomy: A Comparison Analysis of Three Common Approaches from the Single-Port Advanced Research Consortium (SPARC). *J Endourol* 2024; 38:A95-A96. Full Text

N. Soputro, Glickman Urological and Kidney Institute, Cleveland Clinic, United States

Introduction: The Single-Port (SP) robotic platform was first introduced in 2018. The distinguishing features of the novel purpose-built platform, especially its narrow profile and doublejointed instruments, offered an improved manoeuvrability and ergonomics, especially when performing procedures in a shallow and smaller surgical working space. In the past few years, several approaches of SP robotic radical prostatectomy (RARP) have been introduced, including the Transperitoneal (TP), Extraperitoneal (EP), and the more regionalized Transvesical (TV) techniques. The aim of this study was to evaluate for the differences in perioperative outcomes between the three most used approaches of SP-RARP, based on a large multi-institutional series. Methods: A retrospective review was performed on the prospectively maintained, IRB-approved database of the Single- Port Advanced Research Consortium (SPARC) to identify all patients who underwent SP-RARP between 2018 to 2023. Baseline clinicodemographic, perioperative, and postoperative data were evaluated and categorized based on the three different approaches of SP-RARP. Statistical analysis was performed using R Packages for Statistical Computing with descriptive statistics as presented. Results: A total of 1867 patients were included, which comprised 568, 994, and 260 cases of TP, EP, and TV SP-RARP. Despite the similarities in age and BMI, history of previous abdominal surgery was more prevalent in the TV cohort (TP 13.2% vs. EP 31.2% vs. TV 49.3%, $p < 0.05$). Patients with higher-grade diseases who required pelvic lymph node dissections were more commonly referred for either TP or EP SPRARP. Intraoperatively, the TV approach was associated with the least amount of intraoperative blood loss and the need for additional ports. All procedures were completed successfully without the need for conversion. Intraoperative complications were identified in 2.2%, 0.7%, and 0.3% of the TP, EP, and TV cases, respectively. TV SP-RARP was associated with the

shortest length of stay and reduced opioid prescription (median length of stay, TP 24 vs. EP 8 vs. TV 5.8 hours, p < 0.05; discharge opioid, TP 31.1% vs. EP 31.9% vs. TV 7.9%, p < 0.05%). The 90-day rates of postoperative complication (p = 0.144) and hospital readmission (p = 0.127) remained comparable across all three approaches. At a median follow-up duration of 12 months, an earlier return of urinary continence was achieved following TV SP-RARP and oncological outcomes remained favorable across the three groups. Conclusions: Herein, we reported the outcomes of three contemporary approaches of SP-RARP, with added values towards enhancing patient comfort and postoperative recovery. Compared with the other techniques, the TV approach was associated with a significantly reduced length of stay, opioid requirements, major postoperative complication, as well as an earlier return of urinary continence.

Public Health Sciences
Theisen B, **George M**, **Loveless I**, and **Steele N**. Quantifying Tertiary Lymphoid Structures in Resected Pancreatic Ductal Adenocarcinoma in Clinical Practice - A Feasibility Study Demonstrating a Correlation with Survival. *Lab Invest* 2024; 104(3):S1862-S1863. Full Text

[Theisen, Brian] Henry Ford Hosp, Detroit, MI 48202 USA. [George, Madison; Loveless, Ian] Michigan State Univ, E Lansing, MI 48824 USA. [Steele, Nina] Henry Ford Hlth Syst, Detroit, MI USA. University; Henry Ford Health System; Henry Ford Hospital

Public Health Sciences
Walbert T, **Schultz L**, **Snyder JM**, and **Mohn JD**. ELECTRONIC ASSESSMENT OF QUALITY OF LIFE IN GLIOBLASTOMA PATIENTS USING THE EORTC-QLQ-C30/ EORTC-BN20 AND THE PROMIS SYSTEM IN CLINICAL PRACTICE. *Neuro Oncol* 2024; 26:viii264. Full Text

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BACKGROUND: Patient reported outcomes are essential to guide patient-care and to maintain quality of life. We aim to further assess feasibility of computer adaptations of the Patient-Reported Outcomes Measurement Information System (PROMIS) questionnaire in the clinical setting and compare it with outcomes of the EORTC- QLQ-C30 and EORTC-BN20 questionnaires. METHODS: Newly diagnosed patients with GBM were enrolled to assess feasibility. The PROMIS modules were selected to reflect the HRQoL domains assessed in the EORTC- QLQ-C30 and EORTC-BN20 questionnaires. PROMIS modules selected included anxiety, depression, fatigue, physical function, sleep disturbance, sleep-related impairment, social satisfaction role, applied cognitive ability and global health. EORTC instruments as well as PROMIS was answered to patients in the outpatient setting. Descriptive analysis was performed RESULTS: 43 patients with 124 PROMIS/EORTC responses were included in this analysis. 31 patients completed the survey prior to or within 14 days of start of radiation, 12 patients completed a survey outside of the radiation window, and a total of 60 completed surveys were obtained between both patient groups. The median times to complete the EORTC-QLQ-C30 and the EORTC-BN20 surveys were 4.77 (range=2.05-18.6) and 2.63 (range=1.17- 24.83) minutes respectively. For the PROMIS instruments except global health, the median times to complete different modules ranged from 0.6- 1 minute (range= 0.15- 7.77). For global health, the median time was 2.35 minutes (range= 1.02-21.12). Average time to complete all PROMIS questions was 8.65 minutes (range=3.32-66.01). CONCLUSIONS: Real-time prospective assessment of the EORTC tools is similar to the PROMIS measures. While most response times were short, the ranges suggest that select patients might struggle. Patients were offered to participate online from home for convenience, but low computer literacy, limited internet access and burden of disease might limit participation.

Public Health Sciences
Yeni YN, **Oravec D**, **Yadav R**, **Drost J**, **Flynn M**, **Divine G**, and **Rao SD**. Textural and geometric measures derived from digital tomosynthesis discriminate patients with vertebral fracture from those without. *J Bone Miner Res* 2024; 39:152. Full Text

Y.N. Yeni, George Divine and Sudhaker D Rao, Henry Ford Health, United States

Digital tomosynthesis (DTS) is a limited-angle tomographic imaging modality providing a stack image of an object at high resolution and low radiation exposure. The purpose of this study was to examine the extent to which DTS derived textural and geometric properties of vertebrae discriminate patients with and without vertebral fracture. Under IRB approval, 93 postmenopausal women (age ≥ 50 years) with no history of bone disease other than osteoporosis were enrolled. The patients with vertebral fracture (Fx, N = 39) and those without (NFx, N = 54) were not different in age (65 ± 8 vs 64 ± 7 years; p > 0.2), BMI (25.1 ± 3.3 vs 25.1 ± 3.7 kg/m2; p > 0.9) or race distribution (9\30 vs 8\46 Black\Nonblack; p > 0.3). Lumbar spine bone mineral density (BMD) and trabecular bone score (TBS) were measured, and vertebral fracture assessment was performed from DXA scans. DTS of the spine was performed using a clinical system (Sonialvision Safire II, Shimadzu Inc) with the participant in supine position and central X-ray tube fixed at the T12-L1 level. DTS images were reconstructed with a voxel spacing of 0.28 x 0.28 x 1 mm. Fractal dimension (FD, a measure of texture complexity) and lacunarity (λ, a measure of texture heterogeneity) were calculated for cancellous bone using FracLac and ImageJ software. Mean intercept length (MIL, a measure of feature size) and line fraction deviation (LFD, a measure of orientation) were measured and degree of anisotropy (DA) was calculated (maximum MIL/minimum MIL). In addition, vertebral width was calculated at the narrowest section of the mid-vertebra using coronal images. DTS values for fractured T12 and L1 vertebrae were imputed from unfractured levels using a mixed model regression of each DTS variable by vertebral level from a superset of 131 patients with no fracture. DTS measurements of the T12 and L1 vertebrae were averaged for each subject. Differences between groups were assessed using t-tests or Wilcoxon tests based on data normality. Logistic regression models were constructed to examine the extent to which DTS predicts vertebral fracture status. BMD and TBS were higher, while DA and width were lower, in NFx than Fx ($p < 0.02$ to $p < 0.003$). Multiple logistic regression identified BMD, FD, λ, DA and width as significant predictors ($p < 0.02$ to $p < 0.001$) with AUC of ROC = 0.79 (compared to 0.67 for BMD alone) (Figure). These results support complementary use of DTS in assessment of bone quality and potentially of fracture risk.

Pulmonary and Critical Care Medicine

McIntosh J, **Abu Sayf A**, **Thavarajah K**, and **Abdul Hameed AM**. Fibrotic Cystic Lung Disease With Pulmonary Interstitial Cholesterol Granulomas (PICG) in Marfan Syndrome Associated Interstitial Lung Disease: A Case Report. *Am J Respir Crit Care Med* 2024; 209. Full Text

J. Mcintosh, Pulmonary and Critical Care, Henry Ford Hospital, Detroit, MI, United States

Introduction Marfan syndrome (MFS) is a common autosomal dominant connective tissue disorder caused by mutation of the FIBRILLIN-1(FBN1) gene located on chromosome 15. Classic manifestations of MFS involve the cardiovascular, skeletal, and ocular systems. However, up to 10 percent of individuals have MFS-associated pulmonary disorders including chronic obstructive pulmonary disease, spontaneous pneumothorax, bronchiectasis, sleep-disordered breathing, chest wall restriction, and interstitial lung disease (ILD). Here we present a case of a young female with MFS-associated ILD. Case Description 24-year-old neversmoker who immigrated from India one year prior with a history of MFS and a positive genetic test for FBN1 gene presented to the ILD clinic for evaluation of abnormal chest imaging and progressively worsening dyspnea. A physical exam revealed clubbing, striae atrophicae, and a positive wrist sign. An autoimmune review of systems and a comprehensive autoimmune workup were negative. No significant occupational or environmental exposures including exposure to Indium compounds was identified. High- Resolution CT (HRCT) Chest demonstrated mid and upper lobe predominant cystic changes, fibrotic changes (reticulation, traction bronchiectasis and honey combing), and ground glass opacity. Surgical lung biopsy showed pulmonary interstitial & interalveolar cholesterol granulomas (PICG), dense collection of chronic inflammatory cells, foamy & pigment-laden macrophages, foreign body giant cells, foci of lymphoid aggregates, and cystically dilated spaces. Pulmonary function testing was significant for combined obstructive and restrictive defect with impaired gas transfer. Echocardiography showed a normal aortic diameter. The case was discussed in the ILD multidisciplinary meeting where a consensus diagnosis of MFS-associated ILD was made and Nintedanib was recommended for progressive pulmonary fibrosis. Discussion The risk of ILD and pulmonary fibrosis in MFS has not been clearly established. Previous case series in patients with MFS-associated ILD have described the presence of upper lung fibrosis, bilateral honeycomb lung disease, and cystic lung disease. PICG on histopathology with or without cystic lung disease has been reported in Indium lung disease

(novel occupational lung disease due to widespread use of indium-tin oxide in the production of electronic devices), juvenile rheumatoid arthritis, lysinuric lung disease, and exposure-related diseases with lipoid pneumonia or cholesterol pneumonitis. Endogenous lipoid pneumonia results from the accumulation of endogenous cholesterol esters in the lungs and has been observed in children whereas exogenous lipoid pneumonia is linked to inhalation of lipid material. Our case highlights a rare ILD manifestation in a patient with MFS with cystic lung disease and PICG on histopathology. (Figure Presented).

Surgery

Hartgerink C, **Todd E**, **Nagai S**, **Muszkat Y**, **Beltran N**, and **Jafri SM**. Safety and Tolerability of Everolimus in Intestinal and Multivisceral Transplantation Patients. *Am J Gastroenterol* 2024; 119(10):S1590. Full Text

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Introduction: Intestinal and multivisceral transplant patients are at high risk for renal dysfunction after transplant. In other solid organ transplants, everolimus has been shown to have renal-sparing benefits, and everolimus may be useful for preserving renal function in intestinal transplantation. However, data are limited regarding the use and tolerance of everolimus in intestinal and multivisceral transplantation patients. Methods: We performed a retrospective analysis of patients who had an intestinal or multivisceral transplant at a single tertiary care center between 2012 and 2022. Patients who were placed on everolimus at any time after transplant were included in the study. Data extracted included length of time on everolimus and reason for discontinuing everolimus. Results: A total of 15 patients, 9 isolated intestinal transplant patients and 6 multivisceral transplant patients, were included in the study. The mean age at time of transplant was (47.0 ± 9.8) years and 53% (8/ 15) patients were women. Everolimuswas started an average of (25.1 ± 25.9) months after transplant, with a range of 1 month to 102 months. Average duration of everolimus therapy was (557.2 ± 751.4) days with a range of 4 to 2437 days. Of the 15 patients placed on everolimus, 60% (9/15) of patients were on everolimus for at least 90 days. Ultimately, 87% (13/15) of the patients were removed from medication due to side effects or complications. 47% (7/15) of patients remained on medication 1 year following initiation and 20% (3/15) of patients remained on medication 3 years following initiation. The most common reason for stopping everolimus was developing diarrhea (5 patients). The other reasons for discontinuing everolimus were to improve wound healing in the setting of surgery (3 patients), severe systemic infection (3 patients), peripheral edema (1 patient), and oral ulcers (1 patient). No patients died while being treated with everolimus. Conclusion: In summary, this retrospective study of 15 patients indicates that tolerability of everolimus in intestinal and multivisceral transplant patients is highly variable. Diarrhea, concern for wound healing, and severe infection were the most common reasons for discontinuing everolimus. These are all labeled adverse reactions of everolimus, as well as common issues faced by intestinal and multivisceral transplant patients at baseline. Clinicians should be aware of the adverse reactions and the high rate of intolerance in these patients when considering everolimus. .

Surgery

Patel-Rodrigues P, **Harris K**, **Piraka C**, **Alsheik E**, **Ahsan B**, **Nalamati S**, and **Yudovich A**. A Case of Multiple NSAID-Induced Strictures of the Ascending Colon. *Am J Gastroenterol* 2024; 119(10):S2044. Full Text

P. Patel-Rodrigues, Henry Ford Health, Detroit, MI, United States

Introduction: Nonsteroid anti-inflammatory drugs (NSAID) are one of the most widely used medications in the world. Chronic NSAID use can cause several complications including inflammatory changes to the bowel mucosa that can result in diaphragm-like strictures resulting in abdominal pain, anemia, and small bowel obstructions. NSAID-induced small bowel strictures, although rare, have been well-described in the literature. NSAID-induced colonic strictures are a rarer presentation and are delayed in diagnosis. We describe a case of multiple colonic strictures in the setting of chronic NSAID use. Case Description/Methods: A 72-year-old woman with iron deficiency anemia presented with abdominal pain, weight loss, and fatigue for 3 months and was found to have a hemoglobin of 5.6. She had never undergone an upper endoscopy or colonoscopy. Her daily medications included diclofenac 50 mg twice a

day. Computed tomography of her abdomen showed circumferential wall thickening of the terminal ileum and ileocecal valve. Colonoscopy showed a severe stricture with erythema in the ascending colon that could not be traversed. Repeat colonoscopy with interventional gastroenterology 2 weeks later showed 2 strictures. The distal stricture was dilated to 10 mm under fluoroscopic guidance. The upstream colon was examined endoscopically using a direct visualization system, like a cholangioscope, through the colonoscope. A second stricture was seen in the proximal ascending colon which was traversed in a similar fashion. The strictures and surrounding areas were biopsied. Biopsies showed focal erosion, fibrin, architectural disarray, and granulation tissue. Due to ongoing symptoms, she underwent a right hemicolectomy with colorectal surgery 2 months later. The final pathology of the stricture showed submucosal fibrosis and haphazard arrangement of smooth muscle, nerves, and vessels. This constellation of features is associated with NSAID use. She was seen 1 month post-operatively with improved symptoms. Discussion: Colonic diaphragmatic strictures are a rare side effect of chronic NSAID use. This case highlights how important it is for physicians to be mindful of this condition, inquire about NSAID use, and make a prompt and accurate diagnosis. Without awareness of this entity, diclofenac may not have been stopped and a possible incorrect diagnosis of Crohn's disease may have been made. Many cases improve with use of endoscopic therapies and withdrawal of NSAIDs. In more severe cases, such as this, surgical intervention may be required. (Figure Prresented).

Surgery

Shamaa O, **Chavarria-Viales M**, **Alhaj Ali S**, **Al Khouly M**, **Varban O**, and **Zuchelli T**. Management of Gastro-Jejunal Anastomotic Strictures: Comparing Endoscopic Outcomes in Primary vs Conversion Roux-en-Y Gastric Bypass Patients. *Am J Gastroenterol* 2024; 119(10):S1118-S1119. Full Text

O. Shamaa, Henry Ford Health, Detroit, MI, United States

Introduction: Conversion surgery from sleeve gastrectomy (SG) to Roux-en-Y gastric bypass (RYGB) is a common intervention for GERD and weight recurrence. There is limited data on post-surgical gastrojejunal anastomotic strictures (GJAS) endoscopic therapy outcomes in patients with sleeve gastrectomy to Roux-en-Y gastric bypass (SG-RYGB) conversion surgeries. Our study aims to compare the outcomes of primary RYGB (P-RYGB) and SG-RYGB GJAS when treated with through-the-scope balloon dilation (TTS BD) and lumen-apposing metal stent (LAMS). Methods: This is a single center retrospective study, that included patients diagnosed with GJAS post P-RYGB and SG-RYGB surgeries who underwent TTS BD or intraluminal LAMS placement. Data was collected between 2/1/2013 - 1/1/2023. Primary outcomes were technical success, clinical success, surgical revision & mortality. Secondary outcomes included immediate clinical success and the number of endoscopic sessions needed to achieve clinical success. Results: A total of 22 patients were identified to have GJAS, 13 post P-RYGB (age 55 67) & 9 post SG-RYGB (age 45.5 66). Among the P-RYGB group, 4 patients were treated with TTS BD (median stricture diameter 5 mm) and 9 with LAMS (median stricture diameter 5.5 mm). Whereas within the 9 SG-RYGB patients, 7 received TTS BD (median stricture diameter 8.5 mm), and 2 underwent LAMS placement (median stricture diameter 7 mm). All 22 patients had a 100% technical success rate with no mortality or need for surgical revision. Half (n=2/4) of the P-RYGB patients had clinical success with TTS BD compared to 89% (n=8/9) of those who received LAMS. In SG-RYGB patients, almost half of those who received TTS BD (n=3/7) & LAMS stents (n=1/2) had immediate clinical success following first intervention. During the duration of the study, 4/7 (57%) TTS BD and 2/2 (100%) LAMS SG-RYGB patients maintained clinical success without symptom recurrence. One P-RYGB case experienced intraprocedural LAMS mis-deployment. Post-procedure adverse event rates were reported in 1 P-RYGB TTS BD patient & 3 P-RYGB LAMS patients (Table 1). Conclusion: This study demonstrates that both TTS BD and LAMS are effective in the management of GJAS following primary as well as conversion bariatric surgery. LAMS generally exhibited higher immediate and maintenance clinical success rates compared to TTS BD, especially in P-RYGB patients. Further multicenter research involving larger patient cohorts is warranted to optimize patient outcomes in this population. (Table Presented).

Surgery

Shamaa O, **Faisal MS**, **Matin T**, **Khoshbin S**, **Cools K**, and **Watson A**. Suprainfected Heterotopic Pancreatic Tissue: A Rare Culprit of Recurrent Gastric Outlet Obstruction. *Am J Gastroenterol* 2024; 119(10):S1743-S1744. Full Text

O. Shamaa, Henry Ford Health, Detroit, MI, United States

Introduction: Pancreatic rest (PR) is an uncommon finding of ectopic pancreatic tissue that can be located throughout the gastrointestinal tract and is commonly asymptomatic. However, when symptoms develop, they can cause severe complications that include pancreatitis and gastrointestinal obstruction. Here we report a rare case of supra-infected pancreatic rest tissue in the gastric antrum, leading to recurrent gastric outlet obstruction. Case Description/Methods: A 30-year-old woman presents with a 6-month history of worsening abdominal pain, nausea and vomiting refractory to proton pump inhibitor therapy. Index upper endoscopy (EGD) showed a subepithelial nodule in the pylorus, with central umbilication and stenosis in the first portion of the duodenum (Figure 1A). The patient developed recurrent symptoms and underwent 2 EGDs, 1 and 7 months later with serial balloon dilations of the duodenal stenosis to 10 mm and 12.5 mm respectively. Due to persistent stenosis and recurrent symptoms, endoscopic ultrasound (EUS) was performed twice, initially showing a well-defined (23 x 12 mm, Figure 1B) subepithelial lesion in the gastric antrum consistent with pancreatic rest and a second (24 x 14 mm, Figure 1C) subepithelial lesion in the pylorus causing stenosis, fine needle aspiration (FNA) consistent with abscess. Repeat EUS 10 months later showed persistent intramural abscess (27 x 23 mm) with extrinsic compression on the pylorus, repeat FNA drainage was performed. Magnetic resonance imaging abdomen 1 month post-EUS FNA showed an 11 mm distal gastric intramural abscess (Figure 1d) and heterotopic pancreatic tissue emanating from the pancreatic head and extending along the stomach inferior to the abscess (Figure 1e). Patient was treated with multiple courses of antibiotics that resulted in symptom improvement, but continued to develop symptom recurrence after antibiotic discontinuation. Given severe symptoms with recurrent episodes refractory to medical therapy, she was referred to surgical oncology to evaluate for resection. Discussion: This case describes the rare development of recurrent gastric outlet obstruction due to a suprainfected PR. It highlights the significance of recognizing the location and pathologic involvement of PR lesions to help predict and appropriately counsel patients about the potential disease course. Our patient had transmural gastric pylorus involvement, contributing to a higher risk for obstruction. Surgical evaluation should be considered in patients with recurrent severe symptoms if refractory to medical and endoscopic treatment.

Urology

Pezzillo M, **Raffee S**, **Kim S**, **Kheil M**, and **Luck A**. DOES VITAMIN C IMPACT URINARY PHWHEN TAKEN WITH METHENAMINE HIPPURATE? *Urogynecology* 2024; 30(10):S130-S131. Full Text

M. Pezzillo, Henry Ford Health System, United States

OBJECTIVES: Urinary tract infections (UTIs) affect 150 million people worldwide annually and specifically impact the aging female population. Methenamine hippurate (MH) is a non-antibiotic suppressive agent to prevent recurrent UTIs (rUTIs). It is most effective when the urine is acidic (pH < 6) and can be converted to formaldehyde, a bacteriostatic agent. To accomplish this, providers commonly instruct patients to acidify their urine with vitamin C once or twice daily. This can be a cost burden and cause unnecessary side effects to the patient. Weaimto investigate whether vitamin C affects the urinary pHin the clinical setting. We hypothesize that adding daily vitamin C supplements with MH does not affect the urinary pH. METHODS: This is a retrospective, IRB-approved study. Patients diagnosed with RUTI by two urogynecologists between 2014 and 2023 were screened for the study. Patients were excluded with active urinary stone disease, cancer, fistula, bladder mesh erosions, current suprapubic catheter, and lack of urinalysis collected at the initial or follow-up visit. Baseline demographics and data regarding urinary pH, use of vitamin C, and subsequent UTIs were collected. The primary outcome was the change in urinary pH for those taking vitamin C and those who did not. RESULTS: 295 patients were screened, and 78 patients takingMH were included in the final analysis. 40 patients used vitamin C with MH, and 38 did not. The median follow-up time was 3 months for both groups. 14 out of 38 (32.5%) patients using vitamin C experienced a UTI compared to 13 out of 40 (36.8%) with no vitamin C (P = 0.687). The

average daily dose of vitamin C was 700 mg. The mean urinary pH was 6.0 for patients taking vitamin C and 6.1 for those who did not (P = 0.513). The mean pH change from the initial visit to the follow-up visit was -0.1 in those who took vitamin C and 0.0 in those who did not (P = 0.442). Patients experiencing one or more UTIs while on MH suppression were found to have a higher urinary pH (pH 6.3) compared to those who did not have a UTI (pH 5.9) (P = 0.002). CONCLUSIONS: The benefit of adding vitamin C when taking MH is unclear. The urinary pH was not affected by adding vitamin C to MH. Those who did and did not take vitamin C had nearly identical urinary pH at follow-up (6.0 versus 6.1), with vitamin C only decreasing the follow-up urinary pH by -0.1. Additionally, there was a similar rate of UTI following MH suppression with or without vitamin C. However, those who did experience a UTI in the follow-up period did have a statistically significantly higher pH than those who did not.

Urology
Ramos-Carpinteyro R, Soputro N, Pedraza A, Calvo RS, Raver M, Manfredi C, **Wang Y**, Chavali JS, Okhawere K, Mikesell C, Ferguson E, Stifelman M, Badani KK, Autorino R, **Rogers C**, Ahmed M, Schwen ZR, Crivellaro S, and Kaouk J. Single-Port Robot-Assisted Simple Prostatectomy: A Multi-Institutional Cohort From the SPARC. *J Endourol* 2024; 38:A372. Full Text

R. Ramos-Carpinteyro, Cleveland Clinic, United States

Introduction: The single-port (SP) robot-assisted simple prostatectomy (RASP) is a viable minimally invasive technique for patients with symptomatic benign prostatic hyperplasia and adenomas > 80 cc. Early SP RASP reports have shown a fast recovery and >90% outpatient cases. This study aims to present updated data from the largest multi-institutional SP cohort. Methods: Retrospective analysis of all consecutive SP RASP cases done by 11 experienced surgeons from 6 centers from February 2019 to January 2024. In general, a suprapubic incision was performed, and the da Vinci SP access was established through a transvesical, transperitoneal, or extraperitoneal (retropubic) approach. The prostate was excised, and subsequent intraprostatic mucosal reconstruction was performed. Continuous variables were summarized using measures of central tendency based on their distribution, while percentages were employed to depict frequencies. Results: A total of 240 entries were analyzed. All cases were completed successfully, without extra ports or conversion. Three types of approaches were identified: 164 transvesical (68.3%), 51 transperitoneal (21.3%), and 25 extraperitoneal (10.4%). Median age was 70 years. Eighteen percent of patients had previous prostate interventions. Median preoperative International Prostate Symptom Score (IPSS) and prostate volume were 22 and 137 ml, respectively. The most common indication for surgery was urinary retention (43.3%). Median estimated blood loss during surgery and console time were 100 ml and 142 minutes, respectively. One patient required a blood transfusion. There were 5 intraoperative complications, 4 air emboli (during early experience) and 1 accidental posterior cystotomy. The median percentage of tissue removed was 55.5%. Upon discharge, 87.9% of patients did not require narcotics for pain control. Median length of stay was 16 hours and hospitalization was needed for 15.8% of planned outpatient cases. Readmission rate was 0%. Median urinary catheter duration was 6 days. Figure 1 shows the long-term functional outcomes. Conclusions: SP robotic surgery is a feasible technique for transvesical, transperitoneal and extraperitoneal approaches to RASP. Its main advantages are minimal postoperative pain and fast recovery, and long-term functional outcomes show promising results in a multi-institutional setting.

Urology
Soputro N, Okhawere K, Sauer Calvo R, Ramos-Carpinteyro R, **Wang Y**, Raver M, Snajdar E, Saini I, S Chavali J, D Mikesell C, M Pedraza A, **Rogers C**, Ahmed M, D Stifelman M, Lorentz A, Autorino R, Yuh B, J Nelson R, Crivellaro S, K Badani K, and Kaouk J. Development of Patient-Specific Nomogram for Clinical Decision-Making Between Single-Port versus Multi-Port Robotic Partial Nephrectomy: A Report from the Single Port Advanced Robotic Consortium(SPARC). *J Endourol* 2024; 38:A53-A54. Full Text

N. Soputro, Department of Urology, Glickman Urological and Kidney Institute, Cleveland Clinic, United States

Introduction: To develop a patient-specific algorithm to better guide clinical decision-making when considering between Single Port (SP) versus Multi Port (MP) robotic partial nephrectomy (RPN).

Methods: A retrospective review was performed on the IRBapproved, prospectively maintained multi-institutional database of the Single Port Advanced Research Consortium (SPARC) to identify all consecutive patients who underwent SP and MP-RPN between 2019 and 2023. Baseline clinicodemographic variables were used to identify the significant predictors of SP-RPN. The significant variables were subsequently used to construct a nomogram to predict the likelihood of SP versus MP-RPN. Results: Of the 1021 patients included in our analysis, 189 (18.5%) and 832 (81.5%) underwent SP and MP- RPN, respectively. Statistically significant predictors of SP-RPN included a lower comorbidity profile, a significant abdominal surgical history as characterized by a higher Hostile Abdomen Index (HAI), as well as lower complexity tumors. The nomogram generated using the aforementioned variables demonstrated a reasonable performance with an Area Under the Curve (AUC) of 0.79. An optimal cutoff point was determined, with likelihood ratios above 0.12 indicating a preference for SP-RPN. Of note, all SP-RPN cases that scored above the 0.12 cutoffexhibited improved perioperative outcomes, including shorter ischemia time and less intraoperative blood loss. Conclusions: Herein, we have devised a novel patient selection algorithm aimed at enhancing clinical decision-making within the expanding repertoire of RPN approaches. The findings highlighted in this study offer valuable guidance to facilitate appropriate patient selection and thereby ensuring favorable perioperative outcomes associated with RPN procedures.

Urology

Soputro N, Ramos-Carpinteyro R, Calvo RS, Moschovas MC, Manfredi C, Raver M, Okhawere K, **Wang Y**, Snajdar E, Pedraza A, Chavali JS, Mikesell CD, Lorentz A, Yuh B, Nix JW, Joseph J, Kim M, **Rogers C**, Nelson RJ, Stifelman MD, Ahmed M, Crivellaro S, Autorino R, and Kaouk J. Single-Port Robotic Radical Prostatectomy: A Comparison Analysis of Three Common Approaches from the Single-Port Advanced Research Consortium (SPARC). *J Endourol* 2024; 38:A95-A96. Full Text

N. Soputro, Glickman Urological and Kidney Institute, Cleveland Clinic, United States

Introduction: The Single-Port (SP) robotic platform was first introduced in 2018. The distinguishing features of the novel purpose-built platform, especially its narrow profile and doublejointed instruments, offered an improved manoeuvrability and ergonomics, especially when performing procedures in a shallow and smaller surgical working space. In the past few years, several approaches of SP robotic radical prostatectomy (RARP) have been introduced, including the Transperitoneal (TP), Extraperitoneal (EP), and the more regionalized Transvesical (TV) techniques. The aim of this study was to evaluate for the differences in perioperative outcomes between the three most used approaches of SP-RARP, based on a large multi-institutional series. Methods: A retrospective review was performed on the prospectively maintained, IRB-approved database of the Single- Port Advanced Research Consortium (SPARC) to identify all patients who underwent SP-RARP between 2018 to 2023. Baseline clinicodemographic, perioperative, and postoperative data were evaluated and categorized based on the three different approaches of SP-RARP. Statistical analysis was performed using R Packages for Statistical Computing with descriptive statistics as presented. Results: A total of 1867 patients were included, which comprised 568, 994, and 260 cases of TP, EP, and TV SP-RARP. Despite the similarities in age and BMI, history of previous abdominal surgery was more prevalent in the TV cohort (TP 13.2% vs. EP 31.2% vs. TV 49.3%, $p < 0.05$). Patients with higher-grade diseases who required pelvic lymph node dissections were more commonly referred for either TP or EP SPRARP. Intraoperatively, the TV approach was associated with the least amount of intraoperative blood loss and the need for additional ports. All procedures were completed successfully without the need for conversion. Intraoperative complications were identified in 2.2%, 0.7%, and 0.3% of the TP, EP, and TV cases, respectively. TV SP-RARP was associated with the shortest length of stay and reduced opioid prescription (median length of stay, TP 24 vs. EP 8 vs. TV 5.8 hours, $p < 0.05$; discharge opioid, TP 31.1% vs. EP 31.9% vs. TV 7.9%, $p < 0.05$%). The 90-day rates of postoperative complication ($p = 0.144$) and hospital readmission ($p = 0.127$) remained comparable across all three approaches. At a median follow-up duration of 12 months, an earlier return of urinary continence was achieved following TV SP-RARP and oncological outcomes remained favorable across the three groups. Conclusions: Herein, we reported the outcomes of three contemporary approaches of SP-RARP, with added values towards enhancing patient comfort and postoperative recovery. Compared with the other techniques, the TV approach was associated with a significantly reduced length of stay, opioid requirements, major postoperative complication, as well as an earlier return of urinary continence.

Books and Book Chapters

Administration
Barach M, **Bennis S**, and **V. B**. C.A.R.E. Program and Family Caregivers. In: Saunders MM, eds. *10 Nursing Interventions for Family Caregivers* 2024**:** 231-244. Full Text

Family caregivers (FCs) are often forgotten patients. Oftentimes, FCs will experience role strain, especially when the patient has a chronic illness or an illness with sudden onset. As a clinical nurse specialist (CNS), I work on a unique inpatient service that focuses on providing patients holistic care and ensuring that patients have the support and resources needed while in the hospital and once they transition to the next phase of care. Our team aims to improve communication, decrease suffering, and increase patient satisfaction. My role as a CNS is to work at the patient and family level, treating both as one when developing plans of care. The plan of care reflects patient and FC treatment preferences, showing shared decision-making. I then work to assist both in reaching goals while integrating and maintaining family values. I assess the FC through active listening and provide necessary resources to the FC. Many times, FCs do not even know what resources are needed until someone asks them to tell their story. This chapter is about a FC's story, a plan of care, and a resource I often collaborate with and refer my patients' families to, the Caregiver Assistance Resources and Education Program (C.A.R.E. Program℠).

Anesthesiology
Guruswamy J, and Angappan S. Effect of Drugs/Anesthetic Technique on Temperature Regulation. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 476-480. Full Text

Anesthesiology
Guruswamy J, and **Epelman M**. Temperature Sensing, Heat Production, and Conservation. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 469. Full Text

Anesthesiology
Guruswamy J, and **Epelman M**. Body Temperature Measurement. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 474-475. Full Text

Anesthesiology
Guruswamy J, and Rao AG. Fluid Warmers and Autotransfusion Devices. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 125-126. Full Text

Anesthesiology
Guruswamy J, and Rao AG. Warming devices and techniques. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 128-129. Full Text

Anesthesiology
Hanna JS, and **Saad R**. Physician Wellness. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 815. Full Text

Anesthesiology
Parker NM, and **Waqar S**. Pharmacokinetics and Pharmacodynamics. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 147-148. Full Text

Anesthesiology
Patel N, and Fayed M. Pharmacokinetics of Neuraxial Anesthesia. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 151-152. Full Text

Anesthesiology
Rossi RM, and C. SL. Relationship to Hormones. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 784-785. Full Text

Anesthesiology
Saad R, and **Hanna JS**. Physician Impairment and Disability. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 813-814. Full Text

Anesthesiology
Saad R, and **Hanna JS**. Professionalism and Licensure. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 816-817. Full Text

Anesthesiology
Saad R, and **Hanna JS**. Ethics. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 818. Full Text

Anesthesiology
Saad R, and **Hanna JS**. Informed Consent. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 819. Full Text

Anesthesiology
Saad R, and **Hanna JS**. Medical Errors. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 821-822. Full Text

Anesthesiology
Saad R, and **Hanna JS**. Shared Decision-Making. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 822. Full Text

Anesthesiology
Saad R, and **Hanna JS**. Disclosure of Errors to Patients. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 823. Full Text

Anesthesiology
Saad R, and **Hanna JS**. Core Competencies. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 824. Full Text

Anesthesiology
V. TF, and **Rossi RM**. Biochemistry of Normal Body Metabolism. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 779-781. Full Text

Anesthesiology
V. TF, and **Rossi RM**. Carbohydrates. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 781-782. Full Text

Anesthesiology
Younger J, and Fayed M. Problems of Term and Delivery. In: Abd-Elsayed A, eds. *Basic Anaesthesia Review* 2024**:** 291-293. Full Text

Behavioral Health Services/Psychiatry
Joseph M, **Cameron-Carter H**, and **E. A**. Major Neurocognitive Disorder Due to Vascular Disease. In: Tampi RR, and Tampi DJ, eds. *Treatment of Psychiatric Disorders Among Older Adults* 2024**:** 17-25. Full Text

Major neurocognitive disorder due to vascular disease, otherwise known as vascular dementia, is a major cause of debility in the elderly. Together with Alzheimer's disease, they both constitute the most common cause of cognitive decline in older adults. The deficits due to vascular disease vary among different individuals, depending on the location of the insult, the magnitude of the insult, and the cumulative effect of the insult over time. Rating scales and neuroimaging are limited in predictive value of the impact of cerebrovascular insults. This necessitates the need for thorough assessments to facilitate appropriate treatments. Vascular dementia is usually caused by modifiable factors and is best prevented, especially as recovery from vascular insults is often incomplete, with recovery of cognitive functions typically lagging

behind functional recovery. In this chapter, we review the epidemiology, risk factors, and treatment options for major neurocognitive disorder due to vascular disease.

Behavioral Health Services/Psychiatry
M. M, **M. F**, and **E. A**. Benzodiazepine Use Disorder. In: Tampi RR, and Tampi DJ, eds. *Treatment of Psychiatric Disorders Among Older Adults* 2024**:** 267-278. Full Text

Benzodiazepine use disorder is a condition characterized by the inappropriate use of benzodiazepine medications. There are special considerations for this disorder in the elderly population, which will be discussed below. A comprehensive assessment of benzodiazepine use disorder includes a thorough history, physical examination, and appropriate laboratory investigations. Treatment of benzodiazepine use disorder consists of assessing the need for continued use of the medication, aggressively treating underlying or comorbid conditions and tapering of the medication. Management may consist of both pharmacological and non-pharmacological interventions. In this chapter, we will review the current recommendations for diagnosing and managing benzodiazepine use disorder in older adults.

Cardiology/Cardiovascular Research
Généreux P, Omar W, and **Wang D**. Staging of cardiac damage for patients with aortic stenosis. In: Cribier A, Grube E, Eltchaninoff Het al, eds. *Transcatheter Aortic Valve Implantation: Current and Future Developments* 2024. Full Text

Aortic stenosis (AS) is the most common valvular disorder and affects ~5% of patients above the age of 65 (1,2). Technological advances in transcatheter aortic valve replacement (TAVR) have led to indication expansion, especially in younger patients considered at low risk for surgical aortic valve replacement (SAVR). The emergence of this new technology generated a renewed interest in the pathophysiology of aortic valve disease, challenging the long-held belief that valve replacement should be delayed until patients are symptomatic. Even in the setting of symptoms, significant AS may be underdiagnosed due to lack of standardization of screening for clinically significant AS (i.e. universal screening of Kansas City Cardiomyopathy Questionnaire [KCCQ] scores and application of 6-minute hall-walk tests).

Dermatology
Lim HW. Foreward. In: Gupta S, Mehta N, and Dudani P, eds. *Critical Thinking in Contemporary Dermatology: Cognitive Essays* 2024**:** V. Full Text
Dermatology
Maghfour J, **Hamzavi I**, and Nguyen B. The Application of High-Resolution Ultrasound in Dermatology. In: Nouri K, eds. *Telemedicine and Technological Advances in Dermatology* 2024**:** 259-271. Full Text

High-resolution ultrasonography (HRUS), also known as high-frequency ultrasonography, is a safe, non-invasive, and rapid method of imaging the epidermis and dermis. HRUS uses high-frequency sound waves, usually in the range of 2–12 MHz, to obtain high resolution images. It is useful for not only diagnosis, but also for monitoring and treating dermatologic conditions. Applications of HRUS include assessing melanoma and non-melanoma skin cancer, inflammatory skin conditions, systemic disorders, and vascular lesions. It is also routinely used to visualize structural landmarks when performing dermatologic procedures such as fillers. In this chapter, we discuss these standard and novel applications of high-resolution ultrasonography in dermatology.

Dermatology
Maghfour J, and Rivis CC. Soft, Subcutaneous Nodule with Central Dark Punctum. In: Chandy RJ, Ghamrawi RI, Emmerich Vet al, eds. *Problem Based Learning in Dermatology* 2024. Full Text

A 21-year-old male presents to the clinic for a nodule on the right side of his neck, which he first noticed several months ago (Figure 4.1). He denies any pruritus, bleeding, pain, or change in the size of the lesion. The lesion is not bothersome; however, the patient has noticed an occasional foul-smelling, thick, white discharge. He has not attempted any treatments and denies any exacerbating or alleviating factors. Family history is positive for malignant melanoma. The patient is otherwise healthy.

Diagnostic Radiology
Ali A, and Sriwastwa A. 3D Printing in Neurosurgery and Neurovascular Intervention. In: Rybicki F, Morris JM, and Grant GT, eds. *3D Printing at Hospitals and Medical Centers: A Practical Guide for Medical Professionals* 2024**:** 227-253. Full Text

This chapter provides a textbook approach to medical 3D printing applied to neurological and neurovascular interventions. Patient-specific simulations for aneurysm repair have been an important use of 3D printed anatomic models. These details will be valuable for surgeons, radiologists, and neurologists who perform these procedures. A majority of brain tumors have been 3D printed to help guide the procedure. For many patients, the patient-specific anatomic model is used to determine the best surgical approach.

Emergency Medicine
J. B, and **Soman S**. Salicylate Toxicity. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 965.e921-965.e923. Full Text

Endocrinology
Bhan A, Rao AD, Bhadad SK, and **Rao SD**. Rickets and Osteomalacia. In: Melmed S, Auchus RJ, Goldfine AB, Rosen CJ, and Kopp PA, eds. *Williams Textbook of Endocrinology* 2024**:** 1276-1295. Full Text

Endocrinology
Shill JE. Diabetic Ketoacidosis. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 374-377.e371. Full Text

Endocrinology
Shill JE. Hyperglycemic Hyperosmolar Syndrome. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 572-573.e571. Full Text

Family Medicine
Dado L. Postthrombotic Syndrome. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 904.e904-904.e905. Full Text

Family Medicine
Singh M, **Workings M**, and Bender AM. Screening for sleep disorders in athletes. In: Grandner MA, and Athey AB, eds. *Sleep and Sport* 2024**:** 103-105. Full Text

Gastroenterology
Schairer J. Endoscopic Management of Diverted or Bypassed Bowel Complications. In: Shen B, and Kiran RP, eds. *Corrective Endoscopy and Surgery in Inflammatory Bowel and Colorectal Diseases: Advanced Management of Complications* 2024. Full Text

Internal Medicine
Molinari J, and **Atchison D**. Salt-Losing Nephropathy. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 965.e932-965.e933. Full Text

Internal Medicine
Singh H, and Khan YS. Pulmonary Arteriovenous Malformation (AVMs) (Archived). *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 32644715. Full Text

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Department of Anatomy, College of Medicine, University of Hail, Saudi Arabia.

Pulmonary arteriovenous malformations (AVMs) are the abnormal connections between a pulmonary artery and a pulmonary vein. Most cases are congenital, and although uncommon, they are a significant part of the differential diagnosis of pulmonary problems like hypoxemia and lung nodules. These

abnormal communications between pulmonary arteries and pulmonary veins usually bypass the capillary bed and lead to right-to-left shunting of blood, which in turn can lead to symptoms depending on the degree of blood shunting. Pulmonary AVMs are also known by other terms such as pulmonary arteriovenous fistulas, pulmonary arterio-venous aneurysms, cavernous hemangiomas, and pulmonary angiomas. In 1897 during an autopsy study, this malformation was recorded for the first time in literature by Churton. Most patients with pulmonary AVMs have the autosomal dominant disease hereditary hemorrhagic telangiectasia (HHT). However, about 15% of patients with pulmonary AVMs do not meet the criteria for the diagnosis of HHT and do not have any other systemic disease. Pulmonary AVMs may also be acquired and found in patients with liver cirrhosis. In these patients, the absence of hepatic 'factor' may lead to the formation of pulmonary AVMs. Pulmonary AVMs may also be acquired secondary to schistosomiasis, tuberculosis, and metastatic thyroid cancer. Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant disorder. The clinical features are secondary to vascular malformations in various organs of the body, most commonly the skin, nasopharynx, GI tract, lungs, and brain. HHT is recognized as a triad of cutaneous telangiectasia, a family history of the disorder, and recurrent epistaxis.

Internal Medicine
Singh H, and Sankari A. Sleep and Neurodegenerative Disorders. eds. *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 39163464. Full Text

Henry Ford Health System
Wayne State University

There is a significant burden of neurodegenerative disorders globally, and it is expected to increase with a rise in the older adult population. Sleep disturbances in these patients are primarily related to the neurodegenerative condition and add to the morbidity caused by the disorder itself. The relationship between sleep and neurodegeneration is bidirectional. Neurodegenerative disorders can impact brain regions that control sleep, while sleep disturbances can accelerate or worsen neurodegeneration by impairing protein clearance and increasing oxidative stress. Along with managing the primary neurodegenerative disorder, managing sleep complaints in affected patients remains challenging. These patients may experience insomnia, hypersomnia, rapid eye movement (REM) sleep behavior disorder (RBD), obstructive sleep apnea (OSA), and restless legs syndrome (RLS), among other disturbances. Management of sleep disorders in patients with neurodegenerative conditions may improve sleep-related symptoms of the disease and overall quality of life. This activity discusses the etiology, epidemiology, clinical manifestations, evaluation, and treatment of sleep disorders in 2 of the most common neurodegenerative diseases: Parkinson disease and Alzheimer disease.

Nephrology
Abu Kar S, and **Soman S**. Calcium-Alkali Syndrome. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 220.e225-220.e227. Full Text

Nephrology
Faber MD. Hyponatremia. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 617-620.e614. Full Text

Nephrology
Faber MD. Syndrome of Inappropriate Antidiuresis. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 1039-1041.e1032. Full Text

Nephrology
Gwinn M, and **Soman S**. Retroperitoneal Fibrosis. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 957.e912-957.e914. Full Text

Nephrology
Hermez KM, and **Reddy ST**. Chronic Kidney Disease. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 264-268.e262. Full Text

Nephrology
J. B, and **Soman S**. Salicylate Toxicity. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 965.e921-965.e923. Full Text

Nephrology
Jalota Sahota R, and Sayad E. Tension Pneumothorax. eds. *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 32644516. Full Text

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Pneumothorax is air collection in the pleural space, resulting in lung collapse from positive pleural pressure. Tension pneumothorax occurs when pleural pressure is transmitted to the mediastinum (see Image. Left-Sided Tension Pneumothorax Radiograph). This uncommon condition has a malignant course and might result in death if left untreated. Tension pneumothorax may arise in the prehospital setting, emergency department, and intensive care unit. The thorax has 3 compartments: the right and left pulmonary cavities and the centrally located mediastinum. The pulmonary cavities are lined internally by the parietal pleura. The visceral or pulmonary pleura wraps around the lungs. The pleural cavity is the potential space between the parietal and visceral pleurae. Serous pleural fluid normally lubricates the pleural surfaces. Diaphragmatic depression and the ribs' outward motion expand the lungs during normal inspiration. The lungs increase in size as the pleural pressure becomes slightly negative. Normal expiration occurs with diaphragmatic elevation and slight inward motion of the ribs. The positive pleural pressure pushes the air out of the lungs. Pleural disruption can introduce air into the pleural cavity. Positive pleural pressure can cause lung contraction, reducing oxygenation and ventilation in the affected lung. High positive pleural pressure can also compress the mediastinum and its structures, notably the heart, great blood vessels, and the trachea. Tension pneumothorax arises, compromising respiration, venous return, and cardiac output. Early recognition and management of tension pneumothorax saves lives. Rapid administration of emergency thoracic decompression is a skill all healthcare professionals must have.

Nephrology
Kumbar L. Contrast-Associated Acute Kidney Injury. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 319.e314-319.e317. Full Text

Nephrology
Kumbar L. Hypernatremia. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 585-588.e581. Full Text

Nephrology
Li J. Bartter Syndrome. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 170.e175-170.e176. Full Text

Nephrology
Li J. Renal Tubular Acidosis. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 952.e956-952.e957. Full Text

Nephrology
Molinari J, and **Atchison D**. Salt-Losing Nephropathy. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 965.e932-965.e933. Full Text

Nephrology
Novak JE, and **Najjar-Mojarrab J**. Hepatorenal Syndrome. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 535.e536-535.e539.
Full Text

Nephrology
Osorio L, and **Shaban H**. Tumor Lysis Syndrome. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 1092.e1037-1092.e1041. Full Text

Nephrology
Prashar R, and **Karthikeyan V**. Graft-Versus-Host Disease. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 478.e472-478.e475. Full Text

Nephrology
Reddy ST. Hypomagnesemia. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 616.e614-616.e617. Full Text

Nephrology
Reddy ST. IgA Nephropathy. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 631.e632-631.e634. Full Text

Nephrology
Roche M. Hypophosphatemia. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 620.e626-620.e629. Full Text

Nephrology
Shaban H. Rhabdomyolysis. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 958-960.e952. Full Text

Nephrology
Sharma Y. Diabetic Nephropathy. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 378-383.e373. Full Text

Nephrology
Soi V, and **Najjar-Mojarrab J**. Diabetes Insipidus. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 352.e356-352.e359. Full Text

Nephrology
Soman S, and Ahmed H. Interstitial Nephritis. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 650-651.e651. Full Text

Nephrology
Soman S, and **Roche M**. Renal Lupus (Lupus Nephritis). In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 952.e952-952.e955. Full Text

Nephrology
Soman S, Subramanian L, and **Thompson S**. Cardiorenal Syndrome. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 239.e233-239.e236. Full Text

Nephrology
Thompson S, and **Soman S**. Hypokalemia. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 613-616.e611. Full Text

Nephrology
Uduman J. Acute Tubular Necrosis. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 59.e54-59.e55. Full Text

Nephrology
Uduman J. Acute Kidney Injury. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 36-41.e32. Full Text

Nephrology
Umanath K. Renal Artery Stenosis. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 950.e918-950.e920. Full Text

Neurology
Bonner K, **Memon BB**, and **Memon AB**. Multiple sclerosis and pregnancy management: From preconception to postpartum. In: Sriwastava SK, and Triantafylou-Bernitsas E, eds. *Clinical Aspects of Multiple Sclerosis: Essentials and Current Updates* 2024**:** 237-265. Full Text

Women with multiple sclerosis (MS) can, indeed, have a healthy pregnancy and postpartum lactation period without fearing postpartum MS relapse. Disease-modifying therapies (DMTs) that halt or slow the progression of MS have improved the lives of women with MS, and while some are contraindicated during and after pregnancy, others may be used judicially before, during, and after pregnancy for managing MS. In particular, a woman's prepregnancy disease state is a critical parameter to consider when developing a therapeutic strategy for women with MS who are planning a pregnancy. Here, we outline what is known about the effect of pregnancy on the MS disease state and highlight key features of DMTs that should be considered when treating women before, during, and after pregnancy to reduce fetal and neonate exposure to drugs while helping women manage their MS and prevent relapse. As new DMTs enter clinical trials and are approved for treating MS, physicians must become acquainted with the possible benefits and risks of each drug for women with MS during each stage of pregnancy.

Neurology
Rout P, Caminero F, **Iqbal Z**, and Tadi P. Histology, Cytotoxic T Cells. In: *StatPearls*. StatPearls Publishing LLC.;2024. PMID: 32644705. Full Text

Wilson Case Western University
LECOM-Bradenton
Henry Ford Hospital
Asram Medical College, Eluru, India

The innate and adaptive immune systems form the basis of immunity in human beings. Innate immunity is a generalized and non-specific response to pathogens, while adaptive immunity induces pathogen-specific, more sophisticated, and long-term responses. Antibody-mediated and cell-mediated responses carry out adaptive immunity. The antibody-mediated response involves the production of immunoglobulin by B lymphocytes. The response generated by T-cells is called a cell-mediated response. There are two classes of T-lymphocytes, helper and cytotoxic T-cells, also called CD4+ and CD8+ T-cells, respectively. Helper T-cells activate macrophages and cytotoxic cells and stimulate antibody synthesis in B lymphocytes. Cytotoxic cells are involved in directly killing intracellular and extracellular pathogens and eliminating mutated and cancerous cells. These immune responses are generated by T-cells when they recognize an antigen, which is exposed to them by antigen-presenting cells. The antigen is a peptide fragment generated by antigen-presenting cells when they degrade the foreign protein. To be recognized by a T-cell, the antigen must bind to a protein called the major histocompatibility complex (MHC). MHC proteins aid in T-cell activation and have a vital role in the maturation of T-cells in the thymus. T-lymphocytes originate from hematopoietic stem cells in the bone marrow and migrate to the thymus for maturation. They enter the thymus at the corticomedullary junction and move towards the cortex while undergoing developmental changes to accumulate in the subcapsular zone. Initially, the newly arrived intrathymic immature T-cells are known as double-negative cells because they lack expression of CD4 or CD8, but during maturation, they develop both CD4 and CD8 receptors and are then called double-positive cells. In the thymus, these immature double-positive cells are presented with various antigens, and a small subset (1%-5%) binds to antigens connected to MHC types 1 or type 2. The rest of the double-positive cells undergo apoptosis. The T-cells that bind to MHC type 1 molecules become CD4-/CD8+ (cytotoxic T-cells), and the T-cells that bind to MHC type 2 molecules become CD4+/CD8- (helper T-cells). This process is called positive selection. Positively selected T-cells enter the medulla, where they undergo negative selection. This process involves eliminating T-cells whose receptors bind strongly to self-antigens or self-MHC proteins (avoiding autoimmunity).

Nursing

Barach M, **Bennis S**, and **V. B**. C.A.R.E. Program and Family Caregivers. In: Saunders MM, eds. *10 Nursing Interventions for Family Caregivers* 2024**:** 231-244. Full Text

Family caregivers (FCs) are often forgotten patients. Oftentimes, FCs will experience role strain, especially when the patient has a chronic illness or an illness with sudden onset. As a clinical nurse specialist (CNS), I work on a unique inpatient service that focuses on providing patients holistic care and ensuring that patients have the support and resources needed while in the hospital and once they transition to the next phase of care. Our team aims to improve communication, decrease suffering, and increase patient satisfaction. My role as a CNS is to work at the patient and family level, treating both as one when developing plans of care. The plan of care reflects patient and FC treatment preferences, showing shared decision-making. I then work to assist both in reaching goals while integrating and maintaining family values. I assess the FC through active listening and provide necessary resources to the FC. Many times, FCs do not even know what resources are needed until someone asks them to tell their story. This chapter is about a FC's story, a plan of care, and a resource I often collaborate with and refer my patients' families to, the Caregiver Assistance Resources and Education Program (C.A.R.E. Program℠).

Ophthalmology and Eye Care Services

Bansal P. Optical coherence tomography in multiple sclerosis: Diagnostic applications. In: Sriwastava SK, and Triantafylou-Bernitsas E, eds. *Clinical Aspects of Multiple Sclerosis: Essentials and Current Updates* 2024**:** 321-340. Full Text

Ocular coherence tomography (OCT) has emerged as a valuable modality in assessing the retinal integrity, structure, and function of optic nerves. Optic neuritis is an inflammatory optic neuropathy commonly seen in demyelinating central nervous system disorders. OCT can be used in the diagnosis of prior episodes of optic neuritis, differentiating multiple sclerosis (MS) optic neuritis from optic neuritis associated with neuromyelitis optica spectrum disorder or chronic relapsing inflammatory optic neuritis. It can be used as a surrogate end point in monitoring of disease activity in multiple sclerosis. Based on various studies, correlations have been seen between OCT parameters and clinical and paraclinical markers, such as imaging and serum biomarkers, disability scales, such as expanded disability status scale and disease phenotype. It might be possible to characterize MS phenotypes based on retinal patterns of disease expression. OCT is an easily accessible, relatively cheap, and reliable marker for determining response to disease-modifying treatment. More recently, ocular coherence tomography angiography (OCTA) has emerged as a noninvasive technique with high-depth resolution, which enables visualization of the ocular microvasculature-retinal blood vessels and retinal blood flow. In comparison to OCT of optic nerve, incorporating OCTA into clinical practice is limited due to poor image quality and lack of standardization in image collection and analysis.

Pulmonary and Critical Care Medicine

Awdish R. Physician as Patient: The 7-Year Consult. In: Tran KM, and Goldstein MA, eds. *Becoming a Better Physician: Insightful and Inspirational Stories from Attending Physicians, Residents, and Medical Students* 2024**:** 70-72. Full Text

Radiation Oncology

Cunningham JM, **Dolan JL**, **Aldridge K**, and E. S. Treatment Planning Considerations for an MR-Linac. In: Das IJ, Alongi F, Yadav P, and Mittal BB, eds. *A Practical Guide to MR-Linac* 2024**:** 123-147. Full Text

This chapter presents a practical guide of treatment planning utilizing MR-Linac delivery platforms and planning systems. Hardware and software requirements for treatment planning systems, as well as the commissioning and quality assurance practices, are described. We provide a general overview of contouring recommendations related to MR-Linac treatment planning, including current contouring initiatives and guidelines, margins, gating, and adaptive considerations. Contouring recommendations are followed by a practical guide to methods for estimating electron density and applications utilizing CT-based planning and MR-based planning. The chapter includes an overview of treatment plan optimization and a review of dose calculation algorithm requirements in MR-Linac treatment planning, as well as their

impact on online adaptive treatment planning. We further discuss adaptive planning considerations including offline, online, and real-time adaptive planning techniques that account for anatomical and functional changes in the patient model. Finally, we conclude with an overview of plan evaluation techniques including the impact of dose calculation accuracy, evaluation metrics, and plan summation techniques related to adaptive planning.

Surgery
Balli S, **Shumway KR**, and Sharan S. Physiology, Fever. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 32966005. Full Text

Ochsner LSU Monroe
Henry Ford Health
LSU Health Sciences, Shreveport, LA

Fever, or pyrexia, is the elevation of an individual's core body temperature above a 'set-point' regulated by the body's thermoregulatory center in the hypothalamus. This increase in the body's 'set-point' temperature is often due to a physiological process brought about by infectious causes or non-infectious causes such as inflammation, malignancy, or autoimmune processes. These processes involve the release of immunological mediators, which trigger the thermoregulatory center of the hypothalamus, leading to an increase in the body's core temperature. The normal temperature of the human body is approximately 37 degrees Celsius (C), or 98.6 degrees Fahrenheit (F), and varies by about 0.5 C throughout the day. This variation in the core body temperature results from normal physiological processes throughout the human body, including metabolic changes, sleep/wake cycles, hormone variability, and changing activity levels. However, in the case of a fever, the increase in the core body temperature is often greater than 0.5 C and is attributed to a fever-inducing substance (pyrogen). While these numbers may vary slightly based on the source, below is a summary of how to categorize fever. Low-grade: 37.3 to 38.0 C (99.1 to 100.4 F). Moderate-grade: 38.1 to 39.0 C (100.6 to 102.2 F). High-grade: 39.1 to 41 C (102.4 to 105.8 F). Hyperthermia: Greater than 41 C (105.8 F). It is essential to understand that the definition of fever is not the same as that of hyperthermia (hyperpyrexia). In fever, there is an increase in the 'set-point' temperature brought about by the hypothalamus, enabling the body to maintain a controlled increase in the core temperature and general functionality of all organ systems. In hyperthermia, however, the rise in the body's core temperature is beyond the confines of the set-point temperature and regulation of the hypothalamus.

Surgery
Campbell M, Sultan A, **Shumway KR**, and Pillarisetty LS. Physiology, Korotkoff Sound. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 30969600. Full Text

Cusom
Tulane School of Medicine
Henry Ford Health
Midland Memorial / Texas Tech University

In 1905, Nikolai Korotkov, a Russian military surgeon, wrote a 281-word report for the imperial medical military academy detailing his auscultatory technique for determining systolic and diastolic blood pressure. This technique requires only a sphygmomanometer (blood pressure cuff) and a stethoscope to listen to what is now known as Korotkoff sounds. Korotkoff sounds are pulsatile circulatory sounds heard upon auscultation of the brachial artery. While advancements in technology have allowed for the use of electronic blood pressure machines, this non-invasive method of acquiring blood pressure measurements has proven accurate and easy to perform, making it the "gold standard" for blood pressure measurement, even today. Understanding the underlying physiology and proper measurement techniques are essential for quality patient care and appropriate medical therapy.

Surgery
Casale J, **Shumway KR**, and Hatcher JD. Physiology, Eustachian Tube Function. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 30335317. Full Text

Campbell University School of Osteopathic Medicine
Henry Ford Health
Mercer University Med. Sch./Coliseum MC

The Eustachian tube (ET), named after Italian anatomist Bartolomeo Eustachio, is a fibrocartilaginous duct connecting the middle ear (posterior to the eardrum) to the nasopharynx. Also known as the pharyngotympanic tube, the Eustachian tube is approximately 36 mm long, 2-3 mm wide, and functions primarily in optimizing middle ear sound transmission and equalizing pressures within the ear. Normally a closed structure, the Eustachian tube opens in response to movement of the mandible and pharynx, such as during chewing or swallowing. Structurally, the Eustachian tube has osseous (anteroinferior) and cartilaginous (posterosuperior) portions, is comprised of cartilage and mucosa, and is supported by surrounding soft tissue, the sphenoid sulcus, and peritubal muscles (tensor veli palatini, levator veli palatini, salpingopharyngeus, and tensor tympani). See Image. Temporal Bone, Coronal View.

Surgery
Dave HD, **Shumway KR**, and Al Obaidi NM. Physiology, Biliary. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 30725792. Full Text

Tver State Medical University, Tver, Russian Federation
Henry Ford Health
Kamc

The biliary system refers to bile production, storage, and secretion via the liver, gallbladder, and bile ducts. Bile ducts are categorized into intrahepatic and extrahepatic bile ducts (see Image. Diagram of the Biliary System). Intrahepatic bile ducts include the left and right hepatic ducts, which join to form the common hepatic duct (CHD), while extrahepatic bile ducts include the common bile duct (CBD), which is formed from the CHD and cystic duct. The CBD and pancreatic duct converge to form the ampulla of Vater, which bile travels through before passing through the sphincter of Oddi and into the second portion of the duodenum. Initially, bile is a unique alkaline (7.5 to 8.1 pH) fluid secreted by hepatocytes (600-1000 mL/day), further altered and refined by the epithelial cells lining the biliary tract, and becoming acidic in the gallbladder (5.2 to 6.0 pH). The gallbladder stores this fluid, where it gets concentrated and subsequently released into the digestive tract via the CBD. After receiving stimulation via the hormone cholecystokinin (CCK) from the intestinal tract due to food in the intestinal lumen, the gallbladder contracts and secretes bile into the duodenum. Bile is predominantly water with multiple dissolved substances, including cholesterol, amino acids, enzymes, vitamins, heavy metals, bile salts, bilirubin, and phospholipids.

Surgery
Derderian C, **Shumway KR**, and Tadi P. Physiology, Withdrawal Response. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 31335012. Full Text

Creighton University School of Medicine
Henry Ford Health
Asram Medical College, Eluru, India

The withdrawal response (reflex), also known as the nociceptive flexion reflex, is an automatic response of the spinal cord that is critical in protecting the body from harmful stimuli. The first known definition of a reflex dates back to 1649 when René Descartes noted that specific bodily movements occurred instantaneously and independent of the process of thought. Modern definitions state that a reflex is an involuntary response of effector tissue caused by the stimulation of specific receptors. The reflex arc is the basic unit of a reflex, which involves neural pathways acting on an impulse before that impulse has reached the brain. Instead of directly traveling to the brain, sensory neurons of a reflex arc synapse in the spinal cord. This is an important evolutionary adaptation for survival, which allows faster actions by activating spinal motor neurons instead of delaying reaction time by signals first having to go to the brain. The withdrawal reflex can occur in either the upper or lower limbs and is a polysynaptic reflex, which

means that interneurons mediate the reflex between the afferent (sensory) and efferent (motor) signals. In contrast, the deep tendon reflex is monosynaptic and does not utilize interneurons to transmit information. Additionally, the withdrawal response is an intersegmental reflex arc, meaning that the outcomes of the reflex are mediated by the stimulation or inhibition of motor neurons from multiple levels of the same spinal cord.

Surgery
Elshazzly M, Anekar AA, **Shumway KR**, and Caban O. Physiology, Newborn. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 29763126. Full Text

Campbell University School of OM
Mysore Medical College
Henry Ford Health
Campbell University

The physiology of a newborn is unique and complex in that it changes over a period of minutes, hours, days, and months. Once a human reaches adulthood, our physiology typically remains stable and predictable, with any deviation potentially leading to pathology and disease. However, a newborn's rapid and ever-changing physiology is essential in adapting to a world outside the womb. This article aims to discuss the important physiology associated with the newborn period to allow a deeper understanding of the complexities of this stage of life.

Surgery
Fish EM, **Shumway KR**, and Burns B. Physiology, Small Bowel. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 30335296. Full Text

Henry Ford Health
East Tennessee State University (ETSU)

The small intestine (small bowel) is a hollow, tubular structure with an average adult length of 22 feet (7 meters), making it the longest portion of the gastrointestinal (GI) tract, where the majority of digestion occurs. The small intestine extends from the stomach pylorus to the ileocecal junction and is subdivided into 3 sections: the duodenum, jejunum, and ileum. Processing a single meal through the complete length of the small intestine takes up to 5 hours, coordinating with the stomach, gallbladder, and pancreas to cue digestive juices to break down and absorb 95% of food nutrients. The small intestine extracts excess water and sends the remaining food waste to the large intestine to form stool. The small intestine is positioned inside the inferior portion of the abdominal cavity, caudal to the stomach, and framed circumferentially by the large intestine. When empty and at rest, the width of the small intestine is about the width of an index finger. This small width gives it the name of the small intestine, not its length. Comparatively, the large intestine is shorter and wider.

Surgery
Gawdi R, **Shumway KR**, and Emmady PD. Physiology, Blood Brain Barrier. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 32491653. Full Text

Wake Forest School of Medicine
Henry Ford Health
UNC school of Medicine, Atrium Health

The blood-brain barrier (BBB), first described by Paul Ehlrich (1885), is a highly selective semi-permeable membrane between the blood and brain interstitium. This unique barrier allows cerebral blood vessels to regulate the movement of molecules and ions between the blood and the brain. The BBB is composed of cerebral capillary wall endothelial cells (ECs) held together via tight junctions (TJs). These TJs, surrounded by pericytes, astrocytes, and the basal lamina, contribute to the highly selective nature of the BBB, limiting the passage of substances from the blood to the brain more so than any other capillaries in the body. See Figure. Blood Brain Barrier.

Surgery
Lacroix AE, Gondal H, **Shumway KR**, and Langaker MD. Physiology, Menarche. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 29261991. Full Text

University of Nebraska Medical Center
Henry Ford Health
Campbell University

Menarche is defined as the first menstrual period in a female adolescent. Menarche typically occurs between the ages of 10 and 16, with the average age of onset being 12.4 years. The determinants of menarcheal age are continuously being researched; socioeconomic conditions, genetics, general health, nutritional status, exercise, seasonality, and family size are thought to play a role. Menarche tends to be painless and occurs without warning. The first cycles are usually anovulatory with varied lengths and flow. Menarche signals the beginning of reproductive abilities and is closely associated with the ongoing development of secondary sexual characteristics.

Surgery
Muse ME, **Shumway KR**, and Crane JS. Physiology, Epithelialization. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 30422572. Full Text

Campbell
Henry Ford Health
Sampson Regional Med Ctr / Campbell Univ

Epithelial tissue comprises sheets of cells bound tightly together found in the skin, GI, urinary, reproductive, and respiratory tracts. The epithelium serves as a barrier to protect the body from pathogens and functions to maintain homeostasis. When epithelial tissue is damaged, the body responds via four phases of wound healing: hemostasis, inflammation, proliferation, and remodeling (maturation). Epithelialization is the process of repairing epithelial surface defects via keratinocytes during the proliferative phase of wound healing.

Surgery
Oberman R, **Shumway KR**, and Bhardwaj A. Physiology, Cardiac. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 30252345. Full Text

Acom
Henry Ford Health
University of California

Clinical personnel must understand how cardiac physiology is intertwined with other organ systems and how pathophysiology relates to simple gross physiology. Cardiac physiology is one of healthcare's most important aspects of medical knowledge. The cardiovascular system constantly adapts to maintain homeostasis in the body, specifically to maintain oxygen perfusion of tissues. The heart will adapt via multiple variables such as heart rate, stroke volume, preload, afterload, diastole, and systole. This article defines these terms and extrapolates them into a working model of cardiac physiology.

Surgery
Ogobuiro I, Gonzales J, **Shumway KR**, and Tuma F. Physiology, Gastrointestinal. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 30725788. Full Text

University of the East Ramon Magsaysay
Henry Ford Health
Central Michigan University

The gastrointestinal (GI) system comprises the GI tract and accessory organs. The GI tract consists of the oral cavity, pharynx, esophagus, stomach, small intestine, large intestine, and anal canal. The accessory organs include the teeth, tongue, and glandular organs such as salivary glands, liver, gallbladder, and pancreas. The main functions of the GI system include ingestion and digestion of food, nutrient absorption, secretion of water and enzymes, and excretion of waste products.

Surgery
Osilla EV, Marsidi JL, **Shumway KR**, and Sharma S. Physiology, Temperature Regulation. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 29939615. Full Text

University of South Alabama, DeBusk COM
Henry Ford Health
Mery Fitzgerald Hospital

Thermoregulation is the maintenance of physiologic core body temperature by balancing heat generation with heat loss. A healthy individual will have a core body temperature of 37 +/- 0.5°C (98.6 +/- 0.9°F), the temperature range needed for the body's metabolic processes to function correctly. The human body's thermostat is the hypothalamic thermoregulatory center, which, more specifically, is located in the preoptic area of the hypothalamus. This center sets the body's set point and regulates temperature homeostasis. The hypothalamus contains temperature sensors, which receive information via nerve cells called thermoreceptors. The body has peripheral and central thermoreceptors. The peripheral thermoreceptors are located in the skin and sense surface temperatures, while central thermoreceptors are found in the viscera, spinal cord, and hypothalamus and sense the core temperature. Variations in body temperature activate these thermoreceptors, which inform the preoptic area of the hypothalamus. This area then activates heat regulation mechanisms to increase or decrease body temperature and return it to baseline.

Surgery
Patel AK, Reddy V, **Shumway KR**, and Araujo JF. Physiology, Sleep Stages. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 30252388. Full Text

NYIT College of Osteopathic Medicine
McKinsey & Company
Henry Ford Health
Ufrn

The human body cycles through 2 phases of sleep, (1) rapid eye movement (REM) and (2) nonrapid eye movement (NREM) sleep, which is further divided into 3 stages—N1 to N3. Each phase and stage of sleep includes variations in muscle tone, brain wave patterns, and eye movements. The body cycles through all stages approximately 4 to 6 times each night, averaging 90 minutes for each cycle.

Surgery
Ripa R, George T, **Shumway KR**, and Sattar Y. Physiology, Cardiac Muscle. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 34283436. Full Text

St. George's University, West Indies, Grenada
Creighton University School of Medicine
Henry Ford Health
Icahn School of Medicine at Mount Sinai

Cardiac muscle also called the myocardium, is one of three major categories of muscles found within the human body, along with smooth muscle and skeletal muscle. Cardiac muscle, like skeletal muscle, is made up of sarcomeres that allow for contractility. However, unlike skeletal muscle, cardiac muscle is under involuntary control. The heart is made up of three layers—pericardium, myocardium, and endocardium. The endocardium is not cardiac muscle and is comprised of simple squamous epithelial cells and forms the inner lining of the heart chambers and valves. The pericardium is a fibrous sac

surrounding the heart, consisting of the epicardium, pericardial space, parietal pericardium, and fibrous pericardium. The cardiac muscle is responsible for the contractility of the heart and, therefore, the pumping action. The cardiac muscle must contract with enough force and enough blood to supply the metabolic demands of the entire body. This concept is termed cardiac output and is defined as heart rate x stroke volume, which is determined by the contractile forces of the cardiac muscle and the frequency at which they are activated. With a change in metabolic demand comes a change in the contractility of the heart.

Surgery
Shaikh FH, **Shumway KR**, and Soni A. Physiology, Taste. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 32491700. Full Text

Dow Medical College
Henry Ford Health
Pandit B.D.Sharma University of Health Science, Rohtak, Haryana, India

The human body is capable of perceiving five traditional senses: hearing, sight, smell, touch, and taste. Also known as gustation, the sense of taste is essential in discerning the characteristics of substances that one ingests. At a basic evolutionary level, taste allows one to assess whether ingested substances are nutritious or potentially hazardous. This sensation is primarily relayed via receptors located on the tongue. However, at a higher cortical level, taste is considered a multisensory experience as smell, texture, and activation of specific receptors (eg, pain receptors from spicy food) all play a role in determining how something "tastes." A fundamental working knowledge of the anatomy of the tongue is important in fully understanding the concept of taste. The human tongue is divided into an anterior two-thirds and a posterior one-third, separated by a v-shaped groove called the sulcus terminalis. The dorsal aspect of the tongue is covered with bumps known as papillae, of which there are four types: circumvallate, fungiform, foliate, and filiform. The circumvallate, fungiform, and foliate papillae contain taste buds known as gustatory papillae. Taste buds are found on the tongue and the pharynx, larynx, soft palate, and epiglottis. The circumvallate papillae are on the distal aspect of the anterior two-thirds of the tongue and are most sensitive to bitter tastes. The fungiform papillae are found on the tip of the tongue and are most sensitive to sweet and savory (umami) tastes. The foliate papillae are found on the sides of the tongue and are most sensitive to salty and sour tastes. Filiform papillae are found throughout the entire surface of the dorsal tongue and do not contain taste buds. The rough texture of the filiform papillae aid in the gripping of food and transfer down to the esophagus, as well as in the cleaning of the mouth and spreading of saliva.

Surgery
Zimmerman B, **Shumway KR**, and Jenzer AC. Physiology, Tooth. In: *StatPearls*. StatPearls Publishing LLC.; 2024. PMID: 30860710. Full Text

Rhode Island Hospital/Brown
Henry Ford Health
Womack Army Hospital

Teeth serve multiple functions beyond mastication, including shaping the kinetics of phonation, breathing, maintaining a patent airway, and serving as a foundation for the vertical dimensions of the face. The maxilla and mandible, which together form the jaw, contain alveolar bone, a thick ridge of bone that forms the sockets of the teeth. Appropriate size and jaw positioning are critical in developing a proper bite (occlusion) and subsequent mastication. As will be discussed later in detail, certain teeth have specialized roles in chewing, with the entire group functioning as a dynamic entity.

Urology
Arora S, and **Leavitt DA**. Acute Urinary Retnetion. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 60-62.e61. Full Text

Urology
Brodowsky EC, and **Leavitt DA**. Hydronephrosis. In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 560-561.e563. Full Text

Urology
Chien M, and **Leavitt DA**. Urolithias (Nephrolithiasis). In: Ferri FF, eds. *Ferri's Clinical Advisor 2025* 2024**:** 1105-1106.e1101. Full Text