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HENRY FORD HEALTH

Henry Ford Health Publication List – May 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, and Google Books during the month, and then imported into EndNote for formatting. There are 163 unique citations listed this month, including 104 articles and 59 conference abstracts.

Articles are listed first, followed by conference abstracts. 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

Articles

Administration

Keener R, Chhetri SB, Connelly CJ, Taub MA, Conomos MP, Weinstock J, Ni B, Strober B, Aslibekyan S, Auer PL, Barwick L, Becker LC, Blangero J, Bleecker ER, Brody JA, Cade BE, Celedon JC, Chang YC, Cupples LA, Custer B, Freedman BI, Gladwin MT, Heckbert SR, Hou L, Irvin MR, Isasi CR, Johnsen JM, Kenny EE, Kooperberg C, Minster RL, Naseri T, Viali S, Nekhai S, Pankratz N, Peyser PA, Taylor KD, Telen MJ, **Wu B**, Yanek LR, Yang IV, Albert C, Arnett DK, Ashley-Koch AE, Barnes KC, Bis JC, Blackwell TW, Boerwinkle E, Burchard EG, Carson AP, Chen Z, Chen YI, Darbar D, de Andrade M, Ellinor PT, Fornage M, Gelb BD, Gilliland FD, He J, Islam T, Kaab S, Kardia SLR, Kelly S, Konkle BA, Kumar R, Loos RJF, Martinez FD, McGarvey ST, Meyers DA, Mitchell BD, Montgomery CG, North KE, Palmer ND, Peralta JM, Raby BA, Redline S, Rich SS, Roden D, Rotter JI, Ruczinski I, Schwartz D, Sciurba F, Shoemaker MB, Silverman EK, Sinner MF, Smith NL, Smith AV, Tiwari HK, Vasan RS, Weiss ST, **Williams LK**, Zhang Y, Ziv E, Raffield LM, Reiner AP, Arvanitis M, Greider CW, Mathias RA, and Battle A. Validation of human telomere length multi-ancestry meta-analysis association signals identifies POP5 and KBTBD6 as human telomere length regulation genes. *Nat Commun* 2024; 15(1):4417. PMID: 38789417. Full Text

Genome-wide association studies (GWAS) have become well-powered to detect loci associated with telomere length. However, no prior work has validated genes nominated by GWAS to examine their role in telomere length regulation. We conducted a multi-ancestry meta-analysis of 211,369 individuals and identified five novel association signals. Enrichment analyses of chromatin state and cell-type heritability suggested that blood/immune cells are the most relevant cell type to examine telomere length association signals. We validated specific GWAS associations by overexpressing KBTBD6 or POP5 and demonstrated that both lengthened telomeres. CRISPR/Cas9 deletion of the predicted causal regions in K562 blood cells reduced expression of these genes, demonstrating that these loci are related to transcriptional regulation of KBTBD6 and POP5. Our results demonstrate the utility of telomere length GWAS in the identification of telomere length regulation mechanisms and validate KBTBD6 and POP5 as genes affecting telomere length regulation.

Allergy and Immunology

Hall AL, Movva P, Dailey R, Gibson-Scipio W, **Baptist AP**, and MacDonell KK. COVID-19 vaccine intentions and attitudes in Black American emerging adults with asthma. *BMC Public Health* 2024; 24(1):1356. PMID: 38769561. Full Text

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Department of Behavioral Sciences and Social Medicine, Center for Translational Behavioral Science, Florida State University College of Medicine, Tallahassee, FL, USA.

BACKGROUND: Emerging adults (aged 18-29) are less likely to receive the COVID-19 vaccine than any other adult age group. Black Americans are less likely than non-Hispanic white Americans to be fully vaccinated against COVID-19. This study explored factors which affect vaccine intention and attitudes in Black American emerging adults with asthma. METHODS: Participants were recruited from an NHLBI-funded clinical trial to improve asthma control. Fifty-nine Black American emerging adults completed a Qualtrics survey that assessed asthma control, intention to vaccinate, and factors which may affect the decision to vaccinate. Twenty-five participants also completed a semi-structured interview via Zoom. Bivariate correlations and descriptive statistics, including Chi Square analyses, were run using SPSS. Interview thematic analyses were conducted via QDA Miner. RESULTS: Of the 59 Black American emerging adults with asthma who completed surveys, 32.2% responded that they were highly unlikely to receive the COVID-19 vaccine, while 50.8% responded that they were highly likely to receive it. Increased

asthma control was significantly correlated with a higher likelihood to discuss the COVID-19 vaccine with their healthcare provider (ρ = 0.339, α = 0.011). Concerns about immediate (ρ= -0.261, α = 0.050) and long-term (ρ= -0.280, α = 0.035) side effects were inversely correlated with intention to vaccinate. Only 17% of the participants who were unemployed stated that they were highly likely to receive the vaccines compared to 65% of the participants who were employed; however, interview participants who were unemployed stated not needing the vaccine because they were protecting themselves by social distancing. When deciding whether to receive the vaccine, safety, efficacy, and immediate side effects were the top three factors for 91%, 54%, and 49% of the participants, respectively. Beliefs about the vaccines' safety and efficacy, information gathering, personal factors, and societal factors emerged as important themes from the interviews. CONCLUSION: Only half of the surveyed Black American emerging adults with asthma were highly likely to receive the COVID-19 vaccine. Safety and efficacy were important for the majority of the participants, regardless of vaccine intention. Greater asthma control, but not access to asthma-related healthcare, was correlated with intention to discuss the vaccine with their healthcare provider.

Allergy and Immunology

Hauk M, **Todter E**, **Sitarik A**, **Lin CH**, **Joseph C**, **Kim H**, **Eapen A**, **Johnson C**, Ownby D, **Wegienka G**, and **Zoratti E**. Associations between FeNO and clinical characteristics of asthma and allergy among Black and White children. *J Allergy Clin Immunol Pract* 2024; Epub ahead of print. PMID: 38821439. Full Text

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Allergy and Immunology

Zoratti E, Wood R, Pomés A, Da Silva Antunes R, Altman MC, Benson B, Wheatley LM, Cho K, Calatroni A, Little FF, Pongracic J, Makhija M, Khurana Hershey GK, Sherenian MG, Rivera-Spoljaric K, Stokes JR, Gill MA, Gruchalla RS, Chambliss J, Liu AH, Kattan M, Busse PJ, Bacharier LB, Sheehan W, **Kim H**, Glesner J, Gergen PJ, Togias A, Baucom JL, Visness CM, Sette A, Busse WW, and Jackson DJ. A pediatric randomized, controlled trial of German cockroach subcutaneous immunotherapy. *J Allergy Clin Immunol* 2024; Epub ahead of print. PMID: 38718950. Full Text

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University of Texas Southwest Medical Center, Dallas TX.
Children's Hospital of Colorado, Aurora, CO.
Columbia University Medical Center, New York, NY.
Icahn School of Medicine at Mount Sinai, New York NY.
Monroe Carell Children's Hospital at Vanderbilt University, Nashville, TN.
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BACKGROUND: Cockroach allergy contributes to morbidity among urban children with asthma. Few trials address the effect of subcutaneous immunotherapy (SCIT) with cockroach allergen among these at-risk children. OBJECTIVE: To determine if nasal allergen challenge (NAC) responses to cockroach allergen would improve following one year of SCIT. METHODS: Urban children with asthma, that were cockroach-sensitized and reactive on NAC, participated in a yearlong randomized double-blind placebo-controlled SCIT trial using German cockroach extract. The primary endpoint was the change in mean total nasal symptoms scores (TNSS) during NAC after 12 months of SCIT. Changes in nasal transcriptomic responses during NAC, skin prick test (SPT) wheal size, serum allergen-specific antibody production and T-cell responses to cockroach allergen were assessed. RESULTS: Changes in mean NAC TNSS did not differ between SCIT-assigned (n=28) versus placebo-assigned (n=29) participants (p=0.63). Nasal transcriptomic responses correlated with TNSS, but a treatment effect was not observed. Cockroach serum specific IgE (sIgE) decreased to a similar extent in both groups, while decreased cockroach SPT wheal size was greater among SCIT participants (p=0.04). A 200-fold increase in cockroach sIgG4 was observed among subjects receiving SCIT (p<0.001) but was unchanged in the placebo group. T-cell interleukin-4 responses following cockroach allergen stimulation decreased to a greater extent among SCIT versus placebo (p=0.002), while no effect was observed for interleukin-10 or interferon-gamma. CONCLUSION: A year of SCIT failed to alter NAC TNSS and nasal transcriptome responses to cockroach allergen challenge despite systemic effects on allergen-specific skin tests, induction of serum sIgG4 production and down-modulation of allergen stimulated T-cell responses.

Anesthesiology
Guruswamy J, **Chhina A**, **Mitchell JD**, **Shah S**, and **Uribe-Marquez S**. Virtual Reality and Augmented Reality in Anesthesiology Education. *Int Anesthesiol Clin* 2024; Epub ahead of print. PMID: 38798152. Full Text

Department of Anesthesiology, Pain Management, and Perioperative Medicine, Henry Ford Health, Michigan State University, Detroit, Michigan.

Anesthesiology
Mahmood S, **Sallowm Y**, Affan M, **Schultz L**, **Cerghet M**, and **Ali A**. Radiological features of patients with headache as a presenting symptom of neurosarcoidosis. *Headache* 2024; Epub ahead of print. PMID: 38780214. Full Text

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OBJECTIVE: To describe the radiological features of patients with headache as a presenting symptom of neurosarcoidosis. BACKGROUND: Neurologic complications occur in approximately 5%-10% of patients with sarcoidosis, and approximately 50% of these patients have neurologic deficits at the time sarcoidosis is first diagnosed. A wide spectrum of central and peripheral nervous system clinical manifestations may be observed, including cranial nerve palsies, sensory and/or motor deficits, and headache. Magnetic resonance imaging (MRI) results in patients with neurosarcoidosis may include abnormal contrast enhancement, structural masses, and demyelinating lesions. METHODS: This single-center retrospective cohort study assessed patients who were diagnosed with neurosarcoidosis in an urban tertiary care center between 1995 and 2016. We included patients who had MRI results at the time of diagnosis. Patients were divided into two groups based on the presence or absence of headache as a presenting symptom. The MRI result of meningeal contrast enhancement was reviewed. RESULTS: Of the 110 patients analyzed, 30 (27.3%) had an initial presenting symptom of headache while 80 (72.7%) did not. Patients with headache had a higher proportion of meningeal contrast enhancement on MRI (66.7% [20/30] vs. 25.0% [20/80]; $p < 0.001$) and leptomeningeal involvement (53.3% [16/30] vs. 7.5% [6/80], $p < 0.001$) compared to patients with no headache. However, those with headache had a lower proportion of spinal cord localization (13.8% [4/29] vs. 34.2% [26/76], $p = 0.038$) and intraparenchymal central nervous system involvement (16.7% [5/30] vs. 51.3% [41/80], $p = 0.001$) compared to patients with no headache. CONCLUSION: Patients with neurosarcoidosis who presented with headache as an initial symptom had a higher proportion of meningeal contrast enhancement seen by MRI than patients who presented with other neurological symptoms. This suggests a clinico-radiologic link between headache and meningeal disruption in patients with neurosarcoidosis.

Anesthesiology

Patel N, **Nowak K**, **Vaidyanathan A**, **Milad H**, **Adlaka K**, **Rubino C**, **Vasquez ET**, Nerusu L, Rahavard B, **Fayed M**, **Forrest P**, **Money S**, **Dwivedi S**, **Zador L**, **Haddad R**, **Khaja D**, **Sibai N**, and Aiyer R. The Effect of Sedation on Diagnostic Lumbar Medial Branch Blocks for Facetogenic Low Back Pain: An Observational Study. *Pain Physician* 2024; 27(4):E407-e418. PMID: 38805536. Full Text

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BACKGROUND: Lumbar medial branch blocks (MBB) are some of the most commonly performed pain procedures in the United States. Diagnostic MBBs are performed to confirm if the generator of low back pain is the facet joint. However, with diagnostic injections, false positive blocks may occur. OBJECTIVES: Our prospective observational study aims to investigate the effects of midazolam sedation on patients' perceived intensity of pain relief following lumbar MBB. STUDY DESIGN: This is a single-center multi-site prospective observational study registered on clinicaltrials.gov (NCT04453449). SETTING: The study was approved by the Henry Ford Health System Institutional Review Board (IRB) in June 2020 (IRB# 14010) and registered on clinicaltrials.gov in July 2020 (NCT04453449). This manuscript adheres to the applicable EQUATOR STROBE guidelines for an observational cohort study. METHODS: Patients that underwent MBB without sedation were compared to sedated patients. Patients were asked to complete the Numeric Rating Scale (NRS) at baseline, one day after their diagnostic blocks, as well as 4 weeks and 8 weeks after their lumbar radiofrequency ablation (RFA). The primary outcome is the difference between baseline NRS pain scores and the lowest reported score in the 8 hours following MBB. For patients who proceed to RFA, the frequency of false positive blocks was evaluated. A patient was considered to have a false positive block when they failed to achieve 50% pain relief from RFA after 2 successful sequential MBBs. RESULTS: There was no significant difference in the NRS pain score change between the sedated and non-sedated groups for diagnostic block one (P =

0.167) and diagnostic block 2 (P = 0.6145). There was no significant difference of false positive rates between non-sedation and sedation patients at 4-weeks post-RFA (P = 0.7178) and at 8-weeks post-RFA (P = 1.000). LIMITATIONS: Some of the limitations of this study include its nonrandomized design, patient self-reported pain scores, as well as the small variability in the injection technique of proceduralists and in the anatomical location of the injection site. CONCLUSIONS: This study showed that midazolam did not change patients' perceived intensity of pain following MBB, as well as false positive rates after RFA. Larger studies are required to draw definitive conclusions.

Behavioral Health Services/Psychiatry/Neuropsychology
Fedson S, Lavee J, **Bryce K**, Egan T, Olland A, Kanwar M, Courtwright A, and Holm AM. Ethical considerations in xenotransplantation of thoracic organs - a call for a debate on value based decisions. *J Heart Lung Transplant* 2024; 43(7):1033-1038. PMID: 38775760. Full Text

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Xenotransplant covers a broad ethical territory and there are several ethical questions that have arisen in parallel with the technological advances that have allowed the first porcine transplants to occur. This brief communication highlights ethical considerations regarding heart and lung xenotransplantation, with an emphasis on unresolved value-based concerns in the field. The aim of this text is therefore to encourage the readers to consider the vast potential of this emerging technique to do good, but also the risk of doing harm, and to participate in a discussion. The list of questions presented here is not exhaustive but hopefully represents some of the questions that appear to be most pressing as the field advances. The focus is on the value-based, or ethical questions, not the questions related to the practical medical procedures.

Behavioral Health Services/Psychiatry/Neuropsychology
Simiola V, **Miller-Matero LR**, Erickson C, Nie S, **Kazan R**, **Gootee J**, and Simon GE. Patient perspectives for improving treatment initiation for new episodes of depression in historically minoritized racial and ethnic groups. *Gen Hosp Psychiatry* 2024; 89:69-74. PMID: 38815506. Full Text

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OBJECTIVE: Depression is one of the costliest and most prevalent health conditions in the U.S. with 21 million adults having experienced at least one major depressive episode. Despite the availability of evidence-based treatments for depression, a large proportion of people with new diagnoses fail to initiate

formal mental health treatment. Although individuals across all racial and ethnic groups fail to initiate treatment for depression, historically minoritized racial/ethnic groups are at even greater risk. METHOD: Thirty-four participants representing historically underserved racial and ethnic populations from two large health care systems in the U.S. participated in qualitative interviews or focus group to identify factors that impede and facilitate depression treatment initiation in primary care settings. RESULTS: Participants identified individual and systemic barriers and facilitators of treatment initiation for depression and suggested several ideas for increasing treatment engagement (i.e., increased communication and education from providers, community events, information on social media). CONCLUSION: Novel interventions are needed to improve treatment initiation following initial diagnosis of depression in primary care settings. Findings from this study offer suggestions for improving treatment initiation in traditionally underserved communities.

Cardiology/Cardiovascular Research

Alameh A, Anaya F, **Jabri A**, Sukhon F, Alhuneafat L, Khader S, **Villablanca P**, **Aggrawal V**, Siraj A, Balakumaran K, and **Alqarqaz M**. Hypertrophic cardiomyopathy in pregnancy: Nationwide analysis of patients characteristics and outcomes. *Curr Probl Cardiol* 2024; 49(8):102638. PMID: 38734121. Full Text

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INTRODUCTION: Hypertrophic cardiomyopathy (HCM) poses unique challenges in the management of pregnant patients due to the complex interplay of physiological changes of pregnancy. Despite its relatively low prevalence among pregnant women, HCM can significantly impact maternal and fetal outcomes. This study aims to enhance understanding of pregnant patients with HCM and the associated outcomes through a nationwide analysis of patient characteristics and outcomes. METHODS: A retrospective analysis was conducted using data obtained from the Agency for Healthcare Research in Quality (AHRQ) Nationwide Inpatient Sample (NIS) database from January 2016 to December 2020. 3,599,855 pregnant patients without HCM and 187 pregnant patients with HCM were identified using International Classification of Disease (ICD) codes, and baseline characteristics, medical comorbidities, and outcomes were compared between the two groups. RESULTS: Significant differences were observed in baseline characteristics, including age distribution, racial composition, and prevalence of systemic organ disease, between pregnant women with and without HCM. Women with HCM had higher odds of experiencing maternal complications, such as acute heart failure and peripartum cardiomyopathy, as well as higher rates of fetal distress and obstetric interventions, including preterm delivery and caesarean section. CONCLUSION: Comprehensive cardiovascular assessment and risk stratification are essential in pregnant women with HCM to optimize maternal and fetal outcomes. Moreover, disparities in baseline characteristics and outcomes among black pregnant women with HCM highlight the need for a multifactorial approach to addressing pregnancy-related complications.

Cardiology/Cardiovascular Research

Alexandrou M, Rempakos A, Mutlu D, Al Ogaili A, Choi JW, Poommipanit P, **Alaswad K**, **Basir MB**, Davies R, Jaffer FA, Chandwaney RH, Azzalini L, Aygul N, ElGuindy AM, Jefferson BK, Gorgulu S, Khatri JJ, Krestyaninov O, Khelimskii D, Frizzell J, Elbarouni B, Goktekin O, McEntegart MB, Rangan BV, Mastrodemos OC, Burke MN, Sandoval Y, and Brilakis ES. Geographic diversity in chronic total occlusion percutaneous coronary intervention: insights from the PROGRESS-CTO registry. *J Invasive Cardiol* 2024; Epub ahead of print. PMID: 38776473. Request Article

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BACKGROUND: There is variability in clinical and lesion characteristics as well as techniques in chronic total occlusion (CTO) percutaneous coronary intervention (PCI). METHODS: We analyzed patient and lesion characteristics, techniques, and outcomes in 11 503 CTO-PCI procedures performed in North America (NA) and in the combined regions of Europe, Asia, and Africa from 2017 to 2023 as documented in the PROGRESS-CTO registry. RESULTS: Eight thousand four hundred seventy-nine (74%) procedures were performed in NA. Compared with non-NA patients, NA patients were older, with higher body mass index and higher prevalence of diabetes, hypertension, dyslipidemia, family history of coronary artery disease, prior history of PCI, coronary artery bypass graft surgery and heart failure, cerebrovascular disease, and peripheral arterial disease. Their CTOs were more complex, with higher J-CTO (2.56 ± 1.22 vs 1.81 ± 1.24; P less than .001) and PROGRESS-CTO (1.29 ± 1.01 vs 1.07 ± 0.95; P less than .001) scores, longer length, and higher prevalence of proximal cap ambiguity, blunt/no stump, moderate to severe calcification, and proximal tortuosity. Retrograde (31.0% vs 22.1%; P less than .001) and antegrade dissection and re-entry (ADR) (21.2% vs 9.2%; P less than .001) were more commonly used in NA centers, along with intravascular ultrasound (69.0% vs 10.1%; P less than .001). Procedure and fluoroscopy times were longer in NA, while contrast volume and radiation dose were lower. Technical (86.7% vs 86.8%; P > .90) and procedural (85.4% vs 85.8%; P = .70) success and in-hospital major adverse cardiovascular events (MACE) (1.9% vs 1.7%; P = .40) were similar in NA and non-NA centers. CONCLUSIONS: Compared with non-NA patients, NA patients undergoing CTO PCI have more comorbidities, higher CTO lesion complexity, are more likely to undergo treatment with retrograde and ADR, and have similar technical success and MACE.

Cardiology/Cardiovascular Research

Arora S, Vallabhajosyula S, **Aggarwal V**, **Basir MB**, **Kelly B**, and Atreya AR. Novel Risk Stratification and Hemodynamic Profiling in Acute Pulmonary Embolism: A Proposed Classification Inspired by Society for Cardiovascular Angiography and Intervention Shock Staging. *Interv Cardiol Clin* 2024. Epub ahead of print. PMID: Not assigned. Full Text

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Cardiology/Cardiovascular Research

Bharadwaj AS, Abu-Much A, Maini AS, Zhou Z, Li Y, Batchelor WB, Grines CL, Baron SJ, Redfors B, Lansky AJ, **Basir MB**, and **O'Neill WW**. Angiographic Characteristics and Clinical Outcomes in Patients With Chronic Kidney Disease Undergoing Impella-Supported High-Risk Percutaneous Coronary Intervention: Insights From the cVAD PROTECT III Study. *Circ Cardiovasc Interv* 2024; Epub ahead of print. PMID: 38708609. Full Text

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BACKGROUND: Prior studies have found that patients with chronic kidney disease (CKD) have worse outcomes following percutaneous coronary intervention (PCI). There are no data about patients with advanced CKD undergoing Impella-supported high-risk PCI. We, therefore, aimed to evaluate angiographic characteristics and clinical outcomes in patients with CKD who received Impella-supported high-risk PCI as part of the catheter-based ventricular assist device PROTECT III study (A Prospective, Multi-Center, Randomized Controlled Trial of the IMPELLA RECOVER LP 2.5 System Versus Intra Aortic Balloon Pump [IABP] in Patients Undergoing Non Emergent High Risk PCI). METHODS: Patients enrolled in the PROTECT III study were analyzed according to their baseline estimated glomerular filtration rate (eGFR). The primary outcome was 90-day major adverse cardiovascular and cerebrovascular events (the composite of all-cause death, myocardial infarction, stroke/transient ischemic attack, and repeat revascularization). RESULTS: Of 1237 enrolled patients, 1052 patients with complete eGFR baseline assessment were evaluated: 586 with eGFR ≥60 mL/min per 1.73 m(2), 190 with eGFR ≥45 to <60, 105 with eGFR ≥30 to <45, and 171 with eGFR <30 or on dialysis. Patients with lower eGFR (all groups with eGFR <60) were more frequently females and had a higher prevalence of hypertension, diabetes, anemia, and peripheral artery disease. The baseline Synergy Between PCI With Taxus and Cardiac Surgery score was similar between groups (28.2±12.6 for all groups). Patients with lower eGFR were more likely to have severe coronary calcifications and higher usage of atherectomy. There were no differences in individual PCI-related coronary complications between groups, but the rates of overall PCI complications were less frequent among patients with lower eGFR. Major adverse cardiovascular and cerebrovascular events at 90 days and 1-year mortality were significantly higher among patients with eGFR <30 mL/min per 1.73 m(2) or on dialysis. CONCLUSIONS: Patients with advanced CKD undergoing Impella-assisted high-risk PCI tend to have higher baseline comorbidities, severe coronary calcification, and higher atherectomy usage, yet CKD was not associated with a higher rate of immediate PCI-related complications. However, 90-day major adverse cardiovascular and cerebrovascular events and 1-year mortality were significantly higher among patients with eGFR<30 mL/min per 1.73 m(2) or on dialysis. Future studies of strategies to improve intermediate and long-term outcomes of these high-risk patients are warranted. REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT04136392.

Cardiology/Cardiovascular Research

Buchwald CLV, **Jabri A**, **Fadel R**, Alhuneafat L, **Wang DD**, **Mariscal E**, **Alqarqaz M**, **Engel P**, **O'Neill B**, **Frisoli T**, **Lee J**, Abbas A, **O'Neill WW**, and **Villablanca PA**. The various perioperative issues of structural heart diseases and cardiogenic shock. *Curr Probl Cardiol* 2024; 49(8):102646. PMID: 38820919. Full Text

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Up to 20 % of patients presenting with acute heart failure and cardiogenic shock have a structural etiology. Despite efforts in timely management, mortality rates remain alarmingly high, ranging from 50 % to 80 %. Surgical intervention is often the definitive treatment for structural heart disease; however, many patients are considered high risk or unsuitable candidates for such procedures. Consequently, there has been a paradigm shift towards the development of novel percutaneous management strategies and

temporizing interventions. This article aims to provide a comprehensive review of the pathophysiology of valvular and structural heart conditions presenting in cardiogenic shock, focusing on the evolving landscape of mechanical circulatory support devices and other management modalities.

Cardiology/Cardiovascular Research
Earle WB, Li S, Yang S, Krawisz A, **Aronow HD**, Parikh SA, Juraschek SP, Cluett JL, Schermerhorn ML, Carroll BJ, and Secemsky EA. Procedural trends and event rates in severe renovascular hypertension. *EuroIntervention* 2024; 20(9):616-618. PMID: 38726717. Request Article

Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA.
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Cardiology/Cardiovascular Research
Elhage Hassan M, Vinales J, Perkins S, Sandesara P, **Aggarwal V**, and Jaber WA. Pathogenesis, Diagnosis, and Management of Chronic Thromboembolic Pulmonary Hypertension. *Interv Cardiol Clin* 2024. Full Text

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Cardiology/Cardiovascular Research
Gupta K, Rawlley B, Meloche C, Minhas AMK, Hermel M, Slipczuk L, Sheikh S, Khoja A, Vaughan EM, Dalakoti M, and Virani SS. Highlights of Cardiovascular Disease Prevention Studies Presented at the 2024 American College of Cardiology Conference. *Curr Atheroscler Rep* 2024; Epub ahead of print. PMID: 38829515. Full Text

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PURPOSE OF REVIEW: To summarize selected late-breaking science on cardiovascular (CV) disease prevention presented at the 2024 Scientific Session of the American College of Cardiology (ACC) conference. RECENT FINDINGS: The LIBerate-HR trial showed the efficacy and safety of lerodalcibep, a subcutaneous injection that prevents binding of Pro-Protein Convertase Subtilisin/Kexin (PCSK) 9 to low-

density lipoprotein (LDL)-receptors resulting in LDL-cholesterol (LDL-C) lowering in patients at very high risk or high risk of atherosclerotic CV disease (ASCVD). The AEGIS-II randomized patients with type 1 myocardial infarction (MI) with multivessel coronary artery disease and additional CV risk factors and found no benefit in major adverse CV events (MACE) with CSL112, an apolipoprotein A1 infusion shown to increase cholesterol efflux capacity. The Bridge-TIMI 73a trial showed a significant reduction in triglyceride (TG) levels with olezarsen, an antisense mRNA, in patients with moderate hyperTG with elevated CV risk. The BE ACTIVE trial showed significant improvement in step counts in patients given behavioral and financial incentives. The DRIVE study showed a significant increase in the prescription of either sodium-glucose co-transporter-2 inhibitors or glucagon-like peptide-1 receptor agonists in patients with type 2 diabetes mellitus (T2DM) at elevated CV or renal risk with a remote team-based, non-licensed navigator and clinical pharmacist approach. The TACTiC trial showed increased and sustained use of statin therapy by patient-driven use of a web-based portal that calculated the ASCVD risk score and gave prompts. The VICTORIAN-INITIATE trial showed efficacy and safety in early use of inclisiran in patients with ASCVD who did not reach target LDL-C < 70 mg/dL despite maximally tolerated statin therapy. The ARISE-HF trial showed no difference in change of peak oxygen consumption with the use of an oral aldose reductase inhibitor, AT-001, in patients with well-controlled T2DM and diabetic cardiomyopathy with high-risk features compared to placebo. The PREVENT trial showed a significant reduction in target vessel failure at 2 years in patients with non-flow limiting vulnerable plaques with percutaneous coronary intervention and optimal medical therapy (OMT) compared to OMT alone. The late-breaking clinical science presented at the 2024 Scientific Session of the ACC paves the way for an evidence-based alternative to statin therapy and provides data on several common clinical scenarios encountered in daily practice.

Cardiology/Cardiovascular Research

Krittanawong C, Ang SP, **Qadeer YK**, Wang Z, Alam M, Jneid H, and Sharma S. National Trends, Mortality and Outcomes in Intravascular Imaging-Guided Versus Angiography-Guided Percutaneous Coronary Intervention in the United States. *Crit Pathw Cardiol* 2024; Epub ahead of print. PMID: 38768049. Full Text

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Intravascular ultrasound (IVUS) and optical coherence tomography (OCT) have become increasingly utilized in patients undergoing percutaneous coronary intervention (PCI). Despite these purported advantages, prior reports regarding the use of IVUS and OCT have indicated that contemporary use of intravascular imaging remains low with significant regional variation. Here, we present the findings of an updated contemporary analysis regarding the use of IVUS/OCT guided PCI vs. angiography-guided PCI in the United States. We also evaluated in-hospital mortality and clinical outcomes between IVUS/OCT-guided PCI versus angiography-guided PCI-only over million patients in the United States. There has been a significant decrease in the number of PCIs performed, while there has been increasing in trend of IVUS/OCT-guided PCI over this period. Most importantly, we found that IVUS/OCT guided PCI were associated with better clinical outcomes in terms of in-hospital mortality, compare with angiography guided PCI.

Cardiology/Cardiovascular Research
Rawlley B, **Gupta K**, Khalid SN, Vaishnav PP, Sanchez AC, Somerville A, Anuforo A, Pruthi S, and Chaudhuri D. Memantine and Incident Atrial Fibrillation or Flutter in Alzheimer's Disease: A Propensity Score-Matched Analysis. *JACC Clin Electrophysiol* 2024; Epub ahead of print. PMID: 38727659. Full Text

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Cardiology/Cardiovascular Research
Smati H, Sellke FW, Bourque JM, **Qadeer YK**, Niccoli G, Montone RA, and Krittanawong C. Coronary Microvascular Dysfunction: A Guide for Clinicians. *Am J Med* 2024; Epub ahead of print. PMID: 38723930. Full Text

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Dysfunction of the coronary microvasculature has become increasingly recognized as an important mechanism of myocardial ischemia in patients without obstructive coronary artery disease. The causes and management of coronary microvascular dysfunction remain poorly understood and is still largely based on extrapolation of epicardial coronary artery disease data. Quantification of myocardial blood flow and flow reserve have improved diagnosis, though important questions remain In this review, we explain current understanding of the spectrum of pathophysiology of coronary microvascular dysfunction, summarize current diagnostic techniques to assess for coronary microvascular dysfunction, and appraise the limited data on management options specifically for patients with coronary microvascular dysfunction.

Cardiology/Cardiovascular Research
Yin MY, Maneta E, Kyriakopoulos CP, **Michaels AT**, Genovese LD, Indaram MB, Wever-Pinzon O, Singh R, Tseliou E, Taleb I, **Nemeh HW**, Alharethi R, Tang DG, Goldstein J, Hanff TC, Selzman CH, **Cowger J**, Kanwar M, Shah P, and Drakos SG. Cardiac Reverse Remodeling Mediated by HeartMate 3 Left Ventricular Assist Device: Comparison to Older Generation Devices. *ASAIO J* 2024; Epub ahead of print. PMID: 38810218. Full Text

From the Utah Cardiac Recovery (UCAR) Program (Divisions of Cardiology and Cardiothoracic Surgery at University of Utah Health & School of Medicine, Intermountain Medical Center, and George E. Wahlen Department of Veterans Affairs Medical Center), Salt Lake City, Utah.
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Currently, the fully magnetically levitated left ventricular assist device (LVAD) HeartMate 3 (HM3) is the only commercially available device for advanced heart failure (HF) patients. However, the left ventricular

(LV) functional and structural changes following mechanical unloading and circulatory support (MCS) with the HM3 have not been investigated. We compared the reverse remodeling induced by the HM3 to older generation continuous-flow LVADs. Chronic HF patients (n = 405) undergoing MCS with HeartWare Ventricular Assist Device (HVAD, n = 115), HM3 (n = 186), and HeartMate II (HM2, n = 104) at four programs were included. Echocardiograms were obtained preimplant and at 1, 3, 6, and 12 months following LVAD implantation. There were no differences in the postimplant serial LV ejection fraction (LVEF) between the devices. The postimplant LV internal diastolic diameter (LVIDd) was significantly lower for HM2 at 3 and 6 months compared with HVAD and HM3. The proportion of patients achieving "cardiac reverse remodeling responder" status (defined as LVEF improvement to ≥40% and LVIDD ≤5.9 cm) was 11.9%, and was similar between devices. HeartMate 3 appears to result in similar cardiac reverse remodeling as older generation CF-LVADs, suggesting that the fully magnetically levitated device technology could provide an effective platform to further study and promote cardiac reverse remodeling.

Center for Health Policy and Health Services Research
Amodei N, Nixon E, **Zhang S**, **Hu Y**, **Vance A**, and **Maye M**. Associations between sociodemographic characteristics and neonatal length of the stay. *J Perinatol* 2024; Epub ahead of print. PMID: 38773215. Full Text

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BACKGROUND: Infants with past NICU admission have a significantly higher risk of developing neurodevelopmental disorders. Studies have demonstrated an iatrogenic effect of the NICU environment on neurodevelopmental outcomes, even while accounting for physical factors. It is, therefore, critical that an infant's LOS is driven by physical needs versus sociodemographic barriers. METHODS: We leveraged electronic health records and a backward selection regression model to explore physical and sociodemographic predictors of infant LOS. RESULTS: Our results demonstrated that physical predictors (birthweight and ventilator use) accounted for the majority of variance in our model but that a sociodemographic predictor, mean visits per day, was also significant. CONCLUSIONS: Infants who were visited more frequently experienced a shorter LOS, possibly due to increased parental involvement resulting in more individualized care and directly impacting infant stability and morbidity. By supporting visitation, we can reduce the costs of lengthy NICU hospitalizations while improving infant and parent health and well-being.

Center for Health Policy and Health Services Research
D'Agostino SR, Pinkelman SE, and **Maye M**. Implementation of Naturalistic Developmental Behavioral Intervention Strategies: An Examination of Preschool Teachers' Perceptions. *Journal of Early Intervention* 2024; 46(2):299-320. PMID: Not assigned. Request Article

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Naturalistic developmental behavioral intervention (NDBI) strategies appear to be well-suited for implementation by preschool teachers of young children ages 3 through 5, yet research exploring NDBI implementation within this specific context is extremely limited. We applied an implementation science framework to examine reported knowledge, frequency of use, and social validity perceptions of NDBI to support implementation within preschool classrooms. We surveyed 152 preschool teachers and compared ratings of general and special educators to understand their knowledge and use of NDBI strategies. We also compared ratings of preschool teachers with and without higher education training in

applied behavior analysis. Findings indicate that NDBI strategies are a usable innovation for preschool teachers, yet targeted preservice and inservice training is warranted along with improved organizational factors to support NDBI uptake. Furthermore, open-ended survey responses provided a deeper understanding of social validity ratings and suggestions for NDBI-focused professional development.

Center for Health Policy and Health Services Research

Miller TR, Weinstock LM, **Ahmedani BK**, Carlson NN, Sperber K, Cook BL, Taxman FS, Arias SA, Kubiak S, Dearing JW, Waehrer GM, Barrett JG, Hulsey J, and Johnson JE. Share of Adult Suicides After Recent Jail Release. *JAMA Netw Open* 2024; 7(5):e249965. PMID: 38728036. Full Text

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IMPORTANCE: Although people released from jail have an elevated suicide risk, the potentially large proportion of this population in all adult suicides is unknown. OBJECTIVE: To estimate what percentage of adults who died by suicide within 1 year or 2 years after jail release could be reached if the jail release triggered community suicide risk screening and prevention efforts. DESIGN, SETTING, AND PARTICIPANTS: This cohort modeling study used estimates from meta-analyses and jail census counts instead of unit record data. The cohort included all adults who were released from US jails in 2019. Data analysis and calculations were performed between June 2021 and February 2024. MAIN OUTCOMES AND MEASURES: The outcomes were percentage of total adult suicides within years 1 and 2 after jail release and associated crude mortality rates (CMRs), standardized mortality ratios (SMRs), and relative risks (RRs) of suicide in incarcerated vs not recently incarcerated adults. Taylor expansion formulas were used to calculate the variances of CMRs, SMRs, and other ratios. Random-effects restricted maximum likelihood meta-analyses were used to estimate suicide SMRs in postrelease years 1 and 2 from 10 jurisdictions. Alternate estimate was computed using the ratio of suicides after release to suicides while incarcerated. RESULTS: Included in the analysis were 2019 estimates for 7 091 897 adults (2.8% of US adult population; 76.7% males and 23.3% females) who were released from incarceration at least once, typically after brief pretrial stays. The RR of suicide was 8.95 (95% CI, 7.21-10.69) within 1 year after jail release and 6.98 (95% CI, 4.21-9.76) across 2 years after release. A total of 27.2% (95% CI, 18.0%-41.7%) of all adult suicide deaths occurred in formerly incarcerated individuals within 2 years of jail release, and 19.9% (95% CI, 16.2%-24.1%) of all adult suicides occurred within 1 year of release (males: 23.3% [95% CI, 20.8%-25.6%]; females: 24.0% [95% CI, 19.7%-36.8%]). The alternate method yielded slightly larger estimates. Another 0.8% of adult suicide deaths occurred during jail stays. CONCLUSIONS AND RELEVANCE: This cohort modeling study found that adults who were released from incarceration at least once make up a large, concentrated population at greatly elevated risk for death by suicide; therefore, suicide prevention efforts focused on return to the community after jail release could reach many adults within 1 to 2 years of jail release, when suicide is likely to occur. Health systems could develop infrastructure to identify these high-risk adults and provide community-based suicide screening and prevention.

Center for Health Policy and Health Services Research

Saulnier KG, King CA, Ilgen MA, Ganoczy D, Jagusch J, Garlick J, Abraham KM, Lapidos A, Kim HM, Vega E, **Ahmedani BK**, and Pfeiffer PN. Do measures of social support and social distress share general factors associated with suicidal ideation and attempts? *Suicide Life Threat Behav* 2024; Epub ahead of print. PMID: 38813963. Full Text

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INTRODUCTION: Aspects of social relationships have variably been associated with suicidal ideation (SI) and suicide attempts (SAs). This study assessed whether social support and social distress measures have general factors versus measure-specific factors that are associated with suicide risk. METHODS: Adults (N = 455, 60.0% female), admitted to psychiatric inpatient units following a recent suicide attempt or active SI, completed assessments of social support (emotional support, instrumental support, friendship, perceived support from significant others, friends, family) and social distress (loneliness, perceived rejection, perceived burdensomeness, thwarted belongingness). Bifactor modeling examined general and specific factors of social support and distress in relation to SI (week prior to hospitalization, via the Beck Scale for SI) and SAs (past 30 days, via the Columbia Suicide Severity Rating Scale). RESULTS: SI was significantly associated with the general social support (B = -1.51), the general social distress (B = 1.67), and the specific perceived burdensomeness (B = 1.57) factors. SAs were significantly associated with the specific Perceived Rejection (OR = 1.05) and Thwarted Belongingness (OR = 0.91) factors. CONCLUSION: General social support and social distress were associated with SI but not recent SAs. Specific social distress factors were also related to SI and SAs controlling for general social distress, suggesting areas for future interventions.

Center for Health Policy and Health Services Research

Simiola V, **Miller-Matero LR**, Erickson C, Nie S, **Kazan R**, **Gootee J**, and Simon GE. Patient perspectives for improving treatment initiation for new episodes of depression in historically minoritized racial and ethnic groups. *Gen Hosp Psychiatry* 2024; 89:69-74. PMID: 38815506. Full Text

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OBJECTIVE: Depression is one of the costliest and most prevalent health conditions in the U.S. with 21 million adults having experienced at least one major depressive episode. Despite the availability of evidence-based treatments for depression, a large proportion of people with new diagnoses fail to initiate formal mental health treatment. Although individuals across all racial and ethnic groups fail to initiate treatment for depression, historically minoritized racial/ethnic groups are at even greater risk. METHOD: Thirty-four participants representing historically underserved racial and ethnic populations from two large health care systems in the U.S. participated in qualitative interviews or focus group to identify factors that impede and facilitate depression treatment initiation in primary care settings. RESULTS: Participants identified individual and systemic barriers and facilitators of treatment initiation for depression and

suggested several ideas for increasing treatment engagement (i.e., increased communication and education from providers, community events, information on social media). CONCLUSION: Novel interventions are needed to improve treatment initiation following initial diagnosis of depression in primary care settings. Findings from this study offer suggestions for improving treatment initiation in traditionally underserved communities.

Center for Individualized and Genomic Medicine Research

Keener R, Chhetri SB, Connelly CJ, Taub MA, Conomos MP, Weinstock J, Ni B, Strober B, Aslibekyan S, Auer PL, Barwick L, Becker LC, Blangero J, Bleecker ER, Brody JA, Cade BE, Celedon JC, Chang YC, Cupples LA, Custer B, Freedman BI, Gladwin MT, Heckbert SR, Hou L, Irvin MR, Isasi CR, Johnsen JM, Kenny EE, Kooperberg C, Minster RL, Naseri T, Viali S, Nekhai S, Pankratz N, Peyser PA, Taylor KD, Telen MJ, **Wu B**, Yanek LR, Yang IV, Albert C, Arnett DK, Ashley-Koch AE, Barnes KC, Bis JC, Blackwell TW, Boerwinkle E, Burchard EG, Carson AP, Chen Z, Chen YI, Darbar D, de Andrade M, Ellinor PT, Fornage M, Gelb BD, Gilliland FD, He J, Islam T, Kaab S, Kardia SLR, Kelly S, Konkle BA, Kumar R, Loos RJF, Martinez FD, McGarvey ST, Meyers DA, Mitchell BD, Montgomery CG, North KE, Palmer ND, Peralta JM, Raby BA, Redline S, Rich SS, Roden D, Rotter JI, Ruczinski I, Schwartz D, Sciurba F, Shoemaker MB, Silverman EK, Sinner MF, Smith NL, Smith AV, Tiwari HK, Vasan RS, Weiss ST, **Williams LK**, Zhang Y, Ziv E, Raffield LM, Reiner AP, Arvanitis M, Greider CW, Mathias RA, and Battle A. Validation of human telomere length multi-ancestry meta-analysis association signals identifies POP5 and KBTBD6 as human telomere length regulation genes. *Nat Commun* 2024; 15(1):4417. PMID: 38789417. Full Text

Genome-wide association studies (GWAS) have become well-powered to detect loci associated with telomere length. However, no prior work has validated genes nominated by GWAS to examine their role in telomere length regulation. We conducted a multi-ancestry meta-analysis of 211,369 individuals and identified five novel association signals. Enrichment analyses of chromatin state and cell-type heritability suggested that blood/immune cells are the most relevant cell type to examine telomere length association signals. We validated specific GWAS associations by overexpressing KBTBD6 or POP5 and demonstrated that both lengthened telomeres. CRISPR/Cas9 deletion of the predicted causal regions in K562 blood cells reduced expression of these genes, demonstrating that these loci are related to transcriptional regulation of KBTBD6 and POP5. Our results demonstrate the utility of telomere length GWAS in the identification of telomere length regulation mechanisms and validate KBTBD6 and POP5 as genes affecting telomere length regulation.

Clinical Quality and Safety

Musgrove H, **Morales P**, **Ruby A**, **Thompson Y**, **Chami E**, and **Gupta A**. Improving Early Detection of Clostridioides difficile Infections Through Electronic Reports. *J Nurs Care Qual* 2024; Epub ahead of print. PMID: 38768430. Full Text

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Dermatology

Fu C, **Wang J**, Ma T, **Yin C**, **Zhou L**, Clausen BE, **Mi QS**, and **Jiang A**. β-Catenin in Dendritic Cells Negatively Regulates CD8 T Cell Immune Responses through the Immune Checkpoint Molecule Tim-3. *Vaccines (Basel)* 2024; 12(5). PMID: 38793711. Full Text

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Recent studies have demonstrated that β-catenin in dendritic cells (DCs) serves as a key mediator in promoting both CD4 and CD8 T cell tolerance, although the mechanisms underlying how β-catenin exerts its functions remain incompletely understood. Here, we report that activation of β-catenin leads to the up-regulation of inhibitory molecule T-cell immunoglobulin and mucin domain 3 (Tim-3) in type 1 conventional DCs (cDC1s). Using a cDC1-targeted vaccine model with anti-DEC-205 engineered to express the melanoma antigen human gp100 (anti-DEC-205-hgp100), we demonstrated that CD11c-β-catenin(active) mice exhibited impaired cross-priming and memory responses of gp100-specific CD8 T (Pmel-1) cells upon immunization with anti-DEC-205-hgp100. Single-cell RNA sequencing (scRNA-seq) analysis revealed that β-catenin in DCs negatively regulated transcription programs for effector function and proliferation of primed Pmel-1 cells, correlating with suppressed CD8 T cell immunity in CD11c-β-catenin(active) mice. Further experiments showed that treating CD11c-β-catenin(active) mice with an anti-Tim-3 antibody upon anti-DEC-205-hgp100 vaccination led to restored cross-priming and memory responses of gp100-specific CD8 T cells, suggesting that anti-Tim-3 treatment likely synergizes with DC vaccines to improve their efficacy. Indeed, treating B16F10-bearing mice with DC vaccines using anti-DEC-205-hgp100 in combination with anti-Tim-3 treatment resulted in significantly reduced tumor growth compared with treatment with the DC vaccine alone. Taken together, we identified the β-catenin/Tim-3 axis as a potentially novel mechanism to inhibit anti-tumor CD8 T cell immunity and that combination immunotherapy of a DC-targeted vaccine with anti-Tim-3 treatment leads to improved anti-tumor efficacy.

Dermatology

Gilaberte Y, Piquero-Casals J, Schalka S, Leone G, Brown A, Trullàs C, Jourdan E, **Lim HW**, Krutmann J, and Passeron T. Exploring the impact of solar radiation on skin microbiome to develop improved photoprotection strategies. *Photochem Photobiol* 2024; Epub ahead of print. PMID: 38767119. Full Text

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The skin microbiome undergoes constant exposure to solar radiation (SR), with its effects on health well-documented. However, understanding SR's influence on host-associated skin commensals remains nascent. This review surveys existing knowledge on SR's impact on the skin microbiome and proposes innovative sun protection methods that safeguard both skin integrity and microbiome balance. A team of skin photodamage specialists conducted a comprehensive review of 122 articles sourced from PubMed and Research Gateway. Key terms included skin microbiome, photoprotection, photodamage, skin cancer, ultraviolet radiation, solar radiation, skin commensals, skin protection, and pre/probiotics. Experts offered insights into novel sun protection products designed not only to shield the skin but also to mitigate SR's effects on the skin microbiome. Existing literature on SR's influence on the skin microbiome is limited. SR exposure can alter microbiome composition, potentially leading to dysbiosis, compromised skin barrier function, and immune system activation. Current sun protection methods generally overlook microbiome considerations. Tailored sun protection products that prioritize both skin and microbiome health may offer enhanced defense against SR-induced skin conditions. By safeguarding both skin and microbiota, these specialized products could mitigate dysbiosis risks associated with SR exposure, bolstering skin defense mechanisms and reducing the likelihood of SR-mediated skin issues.

Dermatology

Kircik LH, **Stein Gold L**, Gold M, Weiss JS, Harper JC, Del Rosso JQ, Bunick CG, Bhatia N, Tanghetti EA, Eichenfield LF, Baldwin H, Draelos ZD, Callender VD, Han G, Gooderham MJ, Sadick N, Lupo MP, Lain ET, and Werschler WP. Triple Combination Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% for Acne: Efficacy and Safety from a Pooled Phase 3 Analysis. *Dermatol Ther (Heidelb)* 2024; 14(5):1211-1227. PMID: 38724841. Full Text

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INTRODUCTION: A three-pronged approach to acne treatment combining an antibiotic, antimicrobial, and retinoid may be more efficacious than single/double treatments while potentially reducing antibiotic resistance. This study evaluated the efficacy and safety of the first fixed-dose, triple-combination topical acne product, clindamycin 1.2%/adapalene 0.15%/benzoyl peroxide (BPO) 3.1% gel (CAB) using pooled phase 3 data. METHODS: In two identical phase 3 (N = 183; N = 180), double-blind, 12-week studies, participants aged ≥ 9 years with moderate-to-severe acne were randomized 2:1 to receive once-daily CAB or vehicle gel. Endpoints included ≥ 2-grade reduction from baseline in Evaluator's Global Severity Score and clear/almost clear skin (treatment success) and least-squares mean percent change from baseline in acne lesion counts. Treatment-emergent adverse events (TEAEs) and cutaneous safety/tolerability were evaluated. RESULTS: At week 12, 50.0% of participants achieved treatment success with CAB versus 22.6% with vehicle gel ($P < 0.001$). CAB resulted in > 70% reductions in inflammatory and noninflammatory lesions at week 12 (77.9% and 73.0%, respectively), which were significantly greater than vehicle (57.9% and 48.2%; $P < 0.001$, both). Most TEAEs were of mild-moderate severity, and < 3% of CAB-treated participants discontinued study/treatment because of AEs. Transient increases from

baseline in scaling, erythema, itching, burning, and stinging were observed with CAB, but resolved back to or near baseline values by week 12. CONCLUSIONS: The innovative fixed-dose, triple-combination clindamycin phosphate 1.2%/adapalene 0.15%/BPO 3.1% gel was efficacious and well tolerated in children, adolescents, and adults with moderate-to-severe acne. Half of participants achieved clear/almost clear skin by 12 weeks, rates not previously seen in clinical studies of other topical acne products. TRIAL REGISTRATION: ClinicalTrials.gov identifier NCT04214639 and NCT04214652.

Dermatology

Lim HW, Saint Aroman M, Skayem C, Halioua B, Perez Cullell N, Ben Hayoun Y, Baissac C, Bergqvist C, Taieb C, Richard MA, and Ezzedine K. Sun exposure and protection habits: Self-reported attitudes, knowledge and behaviours. *J Eur Acad Dermatol Venereol* 2024; Epub ahead of print. PMID: 38738687. Full Text

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BACKGROUND: As exposure to UV radiation is the primary modifiable environmental risk factor associated with skin cancer, it remains the principal focus of most prevention strategies. Numerous sun protection campaigns have been implemented worldwide; however, their impact on the actual incidence and mortality rates of skin cancer seems to be limited. To create successful skin cancer prevention campaigns, it is important to have a comprehensive understanding of individuals' attitudes and behaviours regarding sun protection. The aim of the current study was to determine and report on the prevalence of self-reported attitudes, knowledge and behaviours regarding two of the major sun protection recommendations-avoidance of sun exposure and use of sunscreens-in an international representative sample across five continents. METHODS: This cross-sectional study was conducted in 20 countries using a web-based online survey. FINDINGS: A total of 50,552 individuals, comprising 25,388 men (50.22%) and 25,164 women (49.78%), participated in the survey. Among them, 83.2% reported having been voluntarily exposed to the sun (for sun-basking reasons) at least once in the last 12 months, and 47.96% acknowledged being exposed to the sun between the hours of 10 AM and 4 PM. The primary reason for non-adherence was that these hours were the most convenient times (32.28%). Only 24.05% reported applying sunscreen every 2 h when outdoors. Forgetfulness was the primary reason as provided by 27.79% of participants. Males and older age groups were less likely to adopt sun-protective behaviours around the world. Forgetfulness and the challenges posed by time constraints seem to be the biggest barriers to proper adherence. INTERPRETATION: These findings should prompt the collaboration with health authorities and the manufacturers to enhance adherence by setting reasonable sunscreen prices and creating formulations that make their application less burdensome.

Dermatology

Mansour MR, **Abushukur Y**, and **Mohammad TF**. Navigating the changing landscape of reef-safe/reef-friendly sunscreens: current bans and accessibility. *Arch Dermatol Res* 2024; 316(6):310. PMID: 38822830. Full Text

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Dermatology

Morita A, **Lim HW**, Passeron T, Goh CL, Kang HY, Ly F, Ocampo-Candiani J, Puig S, Schalka S, Wei L, Demessant AL, Le Floc'h C, Kerob D, Dreno B, and Krutmann J. Attitudes and behaviors regarding sun exposure in Japan compared to Europe and North America. *J Dermatol* 2024; Epub ahead of print. PMID: 38700256. Full Text

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The objective of our study was to assess the attitudes and behaviors in Japan regarding sun exposure and compare them to those in Europe and North America. The study population was a representative sample of individuals aged >18 years from Ipsos panels in Japan (N = 1000), North America (N = 1000), and Europe (N = 6000) using the quota method. Questionnaires covered habits, practices, and perceptions regarding sun exposure. Results revealed that the majority of people (80.1%) believed that the sun gives them energy, and 61.1% considered that being tanned made them look healthier. However, there was a significant difference between men and women regarding the appeal of tanned skin, with 54.95% of men versus 34.67% ($p < 0.001$) of women seeing a tan as an aesthetic asset. People aged <40 years were less likely to find a tan attractive (30.3%) compared to those aged ≥40 years (48.9%) ($p < 0.001$). Of those questioned, 45.70% of used sunscreen with a much higher use among women (70.10%) than men (18.74%) ($p < 0.001$). Almost 54% of people said they stayed in the shade to protect themselves from the sun with this behavior being more prevalent among women (67.05%) and fair-skinned individuals (56.13%). Fear of the risks of sun exposure was more common among women, with 84.8% fearing premature skin aging, compared to 71.8% of men ($p < 0.001$). In Japan, 44.30% of those questioned said tanned skin was attractive ($p < 0.001$); for Europeans and North Americans the proportions were 81.1% and 77.6%, respectively. Only a quarter (25.80%) thought it essential to return from vacation with a tan. On the other hand, Europeans showed a strong recognition of the energy the sun brings (83.18%), and widely believed that tanned skin is attractive (82.32%) and healthy (73.15%). In North America, attitudes were similar to those in Europe regarding the attractiveness of tanned skin (77.65%) and the importance of returning tanned from vacation (48.15%). Compared to Europeans and North Americans, the Japanese seemed to be more cautious about sun-induced hazards and considered lighter skin to be more attractive.

Dermatology

Rose L, Novice M, Kobayashi S, Minta A, **Novice T**, Sicco KL, and Dulmage B. Characterization of the role of Facebook groups for patients who use scalp cooling therapy: a survey study. *Support Care Cancer* 2024; 32(6):351. PMID: 38748328. Full Text

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Since the emergence of scalp cooling therapy (SCT) for the prevention of chemotherapy-induced alopecia (CIA), support groups on social media platforms for interested patients have surfaced. Though there are over 20,000 active members across SCT Facebook groups, little is known about how members use this platform. A 23-question survey was posted in five scalp cooling Facebook groups, reaching 219 women. Results indicated that these Facebook groups play clear roles in providing the following: (1) a supportive community for patients, (2) instructions for SCT use, (3) advice regarding insurance coverage and reimbursement, and (4) recommendations for over-the-counter products for hair loss. Despite reported interest in hair loss products, only 5% of patients sought medical treatment from dermatologists. Due to group-specific access restrictions, private Facebook groups provide patients with a protected platform to learn more about SCT from both those with personal experience and SCT company specialists. Providers may consider recommending these online groups to interested patients during the scalp cooling counseling process. As patients with CIA express a growing interest in over-the-counter hair, eyebrow, and eyelash products, it is important for dermatologists to be aware of where their patients obtain recommendations, and further, if these recommendations have clinical evidence of efficacy.

Dermatology

Silverberg JI, Eichenfield LF, Hebert AA, Simpson EL, **Stein Gold L**, Bissonnette R, Papp KA, Browning J, Kwong P, Korman NJ, Brown PM, Rubenstein DS, Piscitelli SC, Somerville MC, Tallman AM, and Kircik L. Tapinarof Cream 1% Once Daily: Significant Efficacy in the Treatment of Moderate to Severe Atopic Dermatitis in Adults and Children Down to 2 Years of Age in the Pivotal Phase 3 ADORING Trials. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 38777187. Full Text

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BACKGROUND: Tapinarof cream 1% once daily (QD), a topical aryl hydrocarbon receptor agonist, downregulates pro-inflammatory Th2 cytokines, upregulates skin-barrier components, and reduces oxidative stress. OBJECTIVE: To assess tapinarof efficacy and safety in adults and children down to 2 years of age with atopic dermatitis (AD). METHODS: 813 patients were randomized to tapinarof or vehicle QD in two 8-week phase 3 trials. RESULTS: The primary efficacy endpoint, Validated Investigator Global

Assessment for Atopic Dermatitis(TM) score of 0 or 1 and ≥2-grade improvement from baseline at Week 8, was met with statistical significance in both trials: 45.4% vs 13.9% and 46.4% vs 18.0% (tapinarof versus vehicle; both P<0.0001). Significantly superior EASI75 responses were also observed with tapinarof versus vehicle at Week 8: 55.8% vs 22.9% and 59.1% vs 21.2% (both P<0.0001). Rapid improvements in patient-reported pruritus were also significant with tapinarof versus vehicle. Common adverse events (≥5%) of folliculitis, headache, and nasopharyngitis were mostly mild or moderate, with lower discontinuations due to adverse events in the tapinarof groups than with vehicle. LIMITATIONS: Long-term efficacy was not assessed. CONCLUSION: Tapinarof demonstrated highly significant efficacy and favorable safety and tolerability in a diverse population of patients with AD down to 2 years of age.

Dermatology

Szeto MD, Sivesind TE, Kim LS, O'Connell KA, Sprague KA, Nong Y, Strock DM, Cao AL, Wu J, Toledo LM, Wolfe SM, **Boothby-Shoemaker W**, and Dellavalle RP. Gender Parity Analysis of the Editorial Boards of Influential Dermatology Journals: Cross-Sectional Study. *JMIR Dermatol* 2024; 7:e40819. PMID: 38772024. Full Text

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This study underscores the persistent underrepresentation of women in academic dermatology leadership positions by examining the gender composition of editorial boards across top dermatology journals, emphasizing the urgent need for proactive strategies to promote diversity, equity, and inclusion.

Dermatology

Veenstra J, and **Ozog D**. Benzoyl peroxide use in acne therapy: Evaluating the association with acute myeloid leukemia risk. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 38704034. Full Text

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Dermatology

Yang QB, **Zhang MY**, Yang L, **Wang J**, **Mi QS**, and Zhou JG. Deficiency of histone deacetylases 3 in macrophage alleviates monosodium urate crystals-induced gouty inflammation in mice. *Arthritis Res Ther* 2024; 26(1):96. PMID: 38711064. Full Text

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BACKGROUND: Gout is caused by monosodium urate (MSU) crystals deposition to trigger immune response. A recent study suggested that inhibition of Class I Histone deacetylases (HDACs) can significantly reduce MSU crystals-induced inflammation. However, which one of HDACs members in response to MSU crystals was still unknown. Here, we investigated the roles of HDAC3 in MSU crystals-induced gouty inflammation. METHODS: Macrophage specific HDAC3 knockout (KO) mice were used to investigate inflammatory profiles of gout in mouse models in vivo, including ankle arthritis, foot pad arthritis and subcutaneous air pouch model. In the in vitro experiments, bone marrow-derived macrophages (BMDMs) from mice were treated with MSU crystals to assess cytokines, potential target gene and protein. RESULTS: Deficiency of HDAC3 in macrophage not only reduced MSU-induced foot pad and ankle joint swelling but also decreased neutrophils trafficking and IL-1β release in air pouch models. In addition, the levels of inflammatory genes related to TLR2/4/NF-κB/IL-6/STAT3 signaling pathway were significantly decreased in BMDMs from HDAC3 KO mice after MSU treatment. Moreover, RGFP966, selective inhibitor of HDAC3, inhibited IL-6 and TNF-α production in BMDMs treated with MSU crystals. Besides, HDAC3 deficiency shifted gene expression from pro-inflammatory macrophage (M1) to anti-inflammatory macrophage (M2) in BMDMs after MSU challenge. CONCLUSIONS: Deficiency of HDAC3 in macrophage alleviates MSU crystals-induced gouty inflammation through inhibition of TLR2/4 driven IL-6/STAT3 signaling pathway, suggesting that HDAC3 could contribute to a potential therapeutic target of gout.

Diagnostic Radiology
Eghbali N, **Klochko C**, **Razoky P**, **Chintalapati P**, **Jawad E**, **Mahdi Z**, **Craig J**, and Ghassemi MM. Improving Automating Quality Control in Radiology: Leveraging Large Language Models to Extract Correlative Findings in Radiology and Operative Reports. *AMIA Jt Summits Transl Sci Proc* 2024; 2024:135-144. PMID: 38827099. Request Article

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Radiology Imaging plays a pivotal role in medical diagnostics, providing clinicians with insights into patient health and guiding the next steps in treatment. The true value of a radiological image lies in the accuracy of its accompanying report. To ensure the reliability of these reports, they are often cross-referenced with operative findings. The conventional method of manually comparing radiology and operative reports is labor-intensive and demands specialized knowledge. This study explores the potential of a Large Language Model (LLM) to simplify the radiology evaluation process by automatically extracting pertinent details from these reports, focusing especially on the shoulder's primary anatomical structures. A fine-tuned LLM identifies mentions of the supraspinatus tendon, infraspinatus tendon, subscapularis tendon, biceps tendon, and glenoid labrum in lengthy radiology and operative documents. Initial findings emphasize the model's capability to pinpoint relevant data, suggesting a transformative approach to the typical evaluation methods in radiology.

Diagnostic Radiology
Moradiya K, and **Patel S**. Cerebral Amyloid Angiopathy-related Inflammation. *Appl Radiol* 2024; 53(3):44-46. PMID: Not assigned. Request Article

Emergency Medicine
Haering S, Seligowski AV, Linnstaedt SD, Michopoulos V, House SL, Beaudoin FL, An X, Neylan TC, Clifford GD, Germine LT, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Swor RA, Gentile NT, Hudak LA, Pascual JL, Seamon MJ, Pearson C, Peak DA, Merchant RC, Domeier RM, Rathlev NK, O'Neil BJ, Sanchez LD, Bruce SE, Harte SE, McLean SA, Kessler RC, Koenen KC, Stevens JS, and Powers A. Sex-dependent differences in

vulnerability to early risk factors for posttraumatic stress disorder: results from the AURORA study. *Psychol Med* 2024; Epub ahead of print.:1-11. PMID: 38775091. Full Text

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BACKGROUND: Knowledge of sex differences in risk factors for posttraumatic stress disorder (PTSD) can contribute to the development of refined preventive interventions. Therefore, the aim of this study was to examine if women and men differ in their vulnerability to risk factors for PTSD. METHODS: As part of the longitudinal AURORA study, 2924 patients seeking emergency department (ED) treatment in the acute aftermath of trauma provided self-report assessments of pre- peri- and post-traumatic risk factors, as well as 3-month PTSD severity. We systematically examined sex-dependent effects of 16 risk factors that have previously been hypothesized to show different associations with PTSD severity in women and men. RESULTS: Women reported higher PTSD severity at 3-months post-trauma. Z-score comparisons indicated that for five of the 16 examined risk factors the association with 3-month PTSD severity was stronger in men than in women. In multivariable models, interaction effects with sex were observed for pre-traumatic anxiety symptoms, and acute dissociative symptoms; both showed stronger associations with PTSD in men than in women. Subgroup analyses suggested trauma type-conditional effects. CONCLUSIONS: Our findings indicate mechanisms to which men might be particularly vulnerable, demonstrating that known PTSD risk factors might behave differently in women and men. Analyses did not identify any risk factors to which women were more vulnerable than men, pointing toward further mechanisms to explain women's higher PTSD risk. Our study illustrates the need for a more systematic examination of sex differences in contributors to PTSD severity after trauma, which may inform refined preventive interventions.

Emergency Medicine
Horwitz A, McCarthy K, House SL, Beaudoin FL, An X, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Swor RA, Hudak LA, Pascual JL, Seamon MJ, Harris E, Pearson C, Peak DA, Domeier RM, Rathlev NK, Sergot P, Sanchez LD, Bruce SE, Joormann J, Harte SE, Koenen KC, McLean SA, and Sen S. Intensive longitudinal assessment following index trauma to predict development of PTSD using machine learning. *J Anxiety Disord* 2024; 104:102876. PMID: 38723405. Full Text

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There are significant challenges to identifying which individuals require intervention following exposure to trauma, and a need for strategies to identify and provide individuals at risk for developing PTSD with timely interventions. The present study seeks to identify a minimal set of trauma-related symptoms, assessed during the weeks following traumatic exposure, that can accurately predict PTSD. Participants were 2185 adults (Mean age=36.4 years; 64% women; 50% Black) presenting for emergency care following traumatic exposure. Participants received a 'flash survey' with 6-8 varying symptoms (from a pool of 26 trauma symptoms) several times per week for eight weeks following the trauma exposure (each symptom assessed ~6 times). Features (mean, sd, last, worst, peak-end scores) from the repeatedly assessed symptoms were included as candidate variables in a CART machine learning analysis to develop a pragmatic predictive algorithm. PTSD (PCL-5 ≥38) was present for 669 (31%) participants at the 8-week follow-up. A classification tree with three splits, based on mean scores of nervousness, rehashing, and fatigue, predicted PTSD with an Area Under the Curve of 0.836. Findings suggest feasibility for a 3-item assessment protocol, delivered once per week, following traumatic exposure to assess and potentially facilitate follow-up care for those at risk.

Emergency Medicine

Nelson BD, McLaughlin CJ, Rivera OE, Kaul K, Ferdock AJ, Matuzsan ZM, Yazdanyar AR, Gopal JV, Patel AY, **Chaska RM**, Feldman BA, and Jacoby JL. Implementation of a Novel Prehospital Clinical Decision Tool and ECG Transmission for STEMI Significantly Reduces Door-to-Balloon Time and Sex-Based Disparities. *Prehosp Emerg Care* 2024; 1-10. Epub ahead of print. PMID: 38771723. Full Text

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Background: An important method employed to reduce door to balloon time (DTBT) for ST segment elevation Myocardial Infarctions (STEMIs) is a prehospital MI alert. The purpose of this retrospective study was to examine the effects of an educational intervention using a novel decision support method of STEMI notification and prehospital electrocardiogram (ECG) transmission on DTBT.Methods: An ongoing database (4/4/2000 - present) is maintained to track STEMI alerts. In 2007, an MI alert program began; emergency medicine physicians could activate a "prehospital MI alert". In October 2015, modems were purchased for Emergency Medical Services personnel to transmit ECGs. There was concurrent implementation of a decision support tool for identifying STEMI. Sex was assigned as indicated in the medical record. Data were analyzed in two groups: Pre-2016 (PRE) and 2016-2022 (POST).Results: In total, 3,153 patients (1,301 PRE; 1,852 POST) were assessed; the average age was 65.2 years, 32.6% female, 87.7% white with significant differences in age and race between the two cohorts. Of the total 3,153 MI alerts, 239 were false activations, leaving 2,914 for analysis. 2,115 (72.6%) had cardiac catheterization while 16 (6.7%) of the 239 had a cardiac catheterization. There was an overall decrease in DTBT of 27.5% PRE to POST of prehospital ECG transmission ($p < 0.001$); PRE median time was 74.5 minutes vs. 55 minutes POST. There was no significant difference between rates of cardiac catheterization PRE and POST for all patients. After accounting for age, race, and mode of arrival, DTBT was 12.2% longer in women, as compared to men ($p < 0.001$) PRE vs. POST. DTBT among women was significantly shorter when comparing PRE to POST periods (median 77 minutes vs. 60 minutes; $p = 0.0001$). There was no significant sex difference in the proportion of those with cardiac catheterization between the two cohorts (62.5% vs. 63.5%; $p = 0.73$).Conclusion: Introduction of a decision support tool with prehospital ECG transmission with prehospital ECG transmission decreased overall DTBT by 20 minutes (27.5%). Women in the study had a 17-minute decrease in DTBT (22%), but their DTBT remained 12.2% longer than men for reasons that remain unclear.

Endocrinology and Metabolism

Demay MB, Pittas AG, Bikle DD, Diab DL, Kiely ME, Lazaretti-Castro M, Lips P, Mitchell DM, Murad MH, Powers S, **Rao SD**, Scragg R, Tayek JA, Valent AM, Walsh JME, and McCartney CR. Vitamin D for the Prevention of Disease: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2024; Epub ahead of print. PMID: 38828931. Full Text

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BACKGROUND: Numerous studies demonstrate associations between serum concentrations of 25-hydroxyvitamin D (25[OH]D) and a variety of common disorders, including musculoskeletal, metabolic, cardiovascular, malignant, autoimmune, and infectious diseases. Although a causal link between serum 25(OH)D concentrations and many disorders has not been clearly established, these associations have led to widespread supplementation with vitamin D and increased laboratory testing for 25(OH)D in the general population. The benefit-risk ratio of this increase in vitamin D use is not clear, and the optimal vitamin D intake and the role of testing for 25(OH)D for disease prevention remain uncertain.
OBJECTIVE: To develop clinical guidelines for the use of vitamin D (cholecalciferol [vitamin D3] or ergocalciferol [vitamin D2]) to lower the risk of disease in individuals without established indications for vitamin D treatment or 25(OH)D testing. METHODS: A multidisciplinary panel of clinical experts, along with experts in guideline methodology and systematic literature review, identified and prioritized 14 clinically relevant questions related to the use of vitamin D and 25(OH)D testing to lower the risk of disease. The panel prioritized randomized placebo-controlled trials in general populations (without an established indication for vitamin D treatment or 25[OH]D testing), evaluating the effects of empiric vitamin D administration throughout the lifespan, as well as in select conditions (pregnancy and prediabetes). The panel defined "empiric supplementation" as vitamin D intake that (a) exceeds the Dietary Reference Intakes (DRI) and (b) is implemented without testing for 25(OH)D. Systematic reviews queried electronic databases for publications related to these 14 clinical questions. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology was used to assess the certainty of evidence and guide recommendations. The approach incorporated perspectives from a patient representative and considered patient values, costs and resources required, acceptability and feasibility, and impact on health equity of the proposed recommendations. The process to develop this clinical guideline did not use a risk assessment framework and was not designed to replace current DRI for vitamin D. RESULTS: The panel suggests empiric vitamin D supplementation for children and adolescents aged 1 to 18 years to prevent nutritional rickets and because of its potential to lower the risk of respiratory tract infections; for those aged 75 years and older because of its potential to lower the risk of mortality; for those who are pregnant because of its potential to lower the risk of preeclampsia, intra-uterine mortality, preterm birth, small-for-gestational-age birth, and neonatal mortality; and for those with high-risk prediabetes because of its potential to reduce progression to diabetes. Because the vitamin D doses in the included clinical trials varied considerably and many trial participants were allowed to

continue their own vitamin D-containing supplements, the optimal doses for empiric vitamin D supplementation remain unclear for the populations considered. For nonpregnant people older than 50 years for whom vitamin D is indicated, the panel suggests supplementation via daily administration of vitamin D, rather than intermittent use of high doses. The panel suggests against empiric vitamin D supplementation above the current DRI to lower the risk of disease in healthy adults younger than 75 years. No clinical trial evidence was found to support routine screening for 25(OH)D in the general population, nor in those with obesity or dark complexion, and there was no clear evidence defining the optimal target level of 25(OH)D required for disease prevention in the populations considered; thus, the panel suggests against routine 25(OH)D testing in all populations considered. The panel judged that, in most situations, empiric vitamin D supplementation is inexpensive, feasible, acceptable to both healthy individuals and health care professionals, and has no negative effect on health equity. CONCLUSION: The panel suggests empiric vitamin D for those aged 1 to 18 years and adults over 75 years of age, those who are pregnant, and those with high-risk prediabetes. Due to the scarcity of natural food sources rich in vitamin D, empiric supplementation can be achieved through a combination of fortified foods and supplements that contain vitamin D. Based on the absence of supportive clinical trial evidence, the panel suggests against routine 25(OH)D testing in the absence of established indications. These recommendations are not meant to replace the current DRIs for vitamin D, nor do they apply to people with established indications for vitamin D treatment or 25(OH)D testing. Further research is needed to determine optimal 25(OH)D levels for specific health benefits.

Endocrinology and Metabolism

Simonson GD, Criego A, Battelino T, Carlson AL, Choudhary P, Franc S, Gershenoff D, Grunberger G, Hirsch IB, Isaacs D, Johnson M, Kerr D, **Kruger D**, Mathieu C, Martens T, Nimri R, Oser S, Peters A, Weinstock RS, Wright EE, Jr., Wysham CH, and Bergenstal RM. Expert Panel Recommendations for a Standardized Ambulatory Glucose Profile Report for Connected Insulin Pens. *Diabetes Technol Ther* 2024; Epub ahead of print. PMID: 38758213. Request Article

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BACKGROUND: Connected insulin pens capture data on insulin dosing/timing and can integrate with continuous glucose monitoring (CGM) devices with essential insulin and glucose metrics into a single platform. Standardization of connected insulin pen reports is desirable to enhance clinical utility with a single report. METHODS: An international expert panel was convened to develop a standardized connected insulin pen report incorporating insulin and glucose metrics into a single, clinically useful report. An extensive literature review and identification of examples of current connected insulin pen reports was performed serving as the basis for creation of a draft of a standardized connected insulin pen report. The expert panel participated in three virtual standardization meetings and online surveys. RESULTS: The AGP Report: Connected Insulin Pen brings all clinically relevant CGM-derived glucose and connected insulin pen metrics into a single simplified two-page report. The first page contains the time in ranges bar, summary of key insulin and glucose metrics, the ambulatory glucose profile (AGP) curve, and detailed basal (long-acting) insulin assessment. The second page contains the bolus (mealtime and correction) insulin assessment periods with information on meal timing, insulin-to-carbohydrate ratio (ICR), average bolus insulin dose and number of days with bolus doses recorded. The report's second page contains daily glucose profiles with an overlay of the timing and amount of basal and bolus insulin administered. CONCLUSION: The AGP Report: Connected Insulin Pen is a standardized clinically useful report that should be considered by companies developing connected pen technology as part of their system reporting/output.

Gastroenterology

Amjad W, Hamaad Rahman S, Schiano TD, and **Jafri SM**. Epidemiology and Management of Infections in Liver Transplant Recipients. *Surg Infect (Larchmt)* 2024; 25(4):272-290. PMID: 38700753. Request Article

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Background: Improvements in liver transplant (LT) outcomes are attributed to advances in surgical techniques, use of potent immunosuppressants, and rigorous pre-LT testing. Despite these improvements, post-LT infections remain the most common complication in this population. Bacteria constitute the most common infectious agents, while fungal and viral infections are also frequently encountered. Multi-drug-resistant bacterial infections develop because of polymicrobial overuse and prolonged hospital stays. Immediate post-LT infections are commonly caused by viruses. Conclusions: Appropriate vaccination, screening of both donor and recipients before LT and antiviral prophylaxis in high-risk individuals are recommended. Antimicrobial drug resistance is common in high-risk LT and

associated with poor outcomes; epidemiology and management of these cases is discussed. Additionally, we also discuss the effect of coronavirus disease 2019 (COVID-19) infection and monkeypox in the LT population.

Gastroenterology
Bhatnagar AR, **Siddiqui F**, **Khan G**, **Pompa R**, **Kwon D**, and **Nyati S**. Long-Term Follow-Up of Phase I Trial of Oncolytic Adenovirus-Mediated Cytotoxic and Interleukin-12 Gene Therapy for Treatment of Metastatic Pancreatic Cancer. *Biomedicines* 2024; 12(5). PMID: 38791027. Full Text

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The long-term follow-up findings of the phase I trial evaluating the efficacy of oncolytic adenovirus-mediated cytotoxic and interleukin-12 gene therapy in metastatic pancreatic cancer (mPC) seem very promising. The study employed a replication-competent Adenovector in combination with chemotherapy in a dose-escalation format. The trial demonstrated a clinically meaningful median overall survival (OS) benefit, with patients in the highest dose cohort exhibiting an impressive median OS of 18.4 months. This contrasts starkly with patients receiving lower doses who experienced a median OS of 4.8 and 3.5 months, respectively. Remarkably, subject number 10, who received the highest dose, demonstrated an extraordinary survival of 59.1 months, presenting a compelling case for further exploration. Additionally, this patient displayed complete responses in lung and liver metastases, a rare occurrence in mPC treatment. Statistical analyses supported the observed survival benefit. The unprecedented OS results emphasize the potential of this treatment strategy and pave the way for future investigations into this promising gene therapy approach.

Gastroenterology
Maraj D, **Singh B**, **Fuller R**, and **Bern M**. A Rare Case of Transient Mesenteric Ischemia After Atrial Fibrillation With Rapid Ventricular Response Rate. *Cureus* 2024; 16(4):e58210. PMID: 38741839. Full Text

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Mesenteric ischemia is an urgent event and requires prompt recognition and treatment, in order to reduce the risk of mortality. It results from the sudden onset of small intestinal hypoperfusion, from a reduction or cessation of arterial perfusion, which can occur from an embolic obstruction at the superior mesenteric artery. We present a case of transient mesenteric ischemia from an episode of atrial fibrillation with a rapid ventricular response rate. Despite being on chronic anticoagulation therapy, the patient developed transient mesenteric ischemia from an embolic clot. The patient's heart rate was controlled and no surgical intervention was required, a rare finding; however, it is very important to recognize and treat promptly.

Gastroenterology
Tetali B, and **Suresh S**. Management of irritable bowel syndrome: a narrative review. *Transl Gastroenterol Hepatol* 2024; 9:26. PMID: 38716216. Full Text

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BACKGROUND AND OBJECTIVE: As our understanding of the pathophysiology of irritable bowel syndrome (IBS) has advanced, so too has the therapeutic landscape, offering a myriad of approaches to alleviate symptoms and enhance the well-being of patients. This review paper is dedicated to a

comprehensive exploration of the diverse therapeutic modalities available for managing IBS. By delving into the complexities of IBS therapeutics, our aim is to contribute to the enhancement of patient care and the overall quality of life for patients grappling with this complex condition. METHODS: This review utilized information from PubMed/MEDLINE using the key search term "irritable bowel syndrome" as well as the 2020 American College of Gastroenterology (ACG) and 2022 American Gastroenterological Association (AGA) society guidelines on IBS. The search was restricted to articles in the English language only and included peer-reviewed observational studies and randomized controlled trials (RCTs) in adult patients from April 22, 2020 to October 16, 2023. KEY CONTENT AND FINDINGS: This review will start with an overview of the current guidelines for pharmacologic therapies for IBS as recommended by the ACG and the AGA, with an emphasis on clinical trials published after the most recent guidelines. It will then delve into the literature on dietary modifications, probiotics, fecal microbiota transplant, behavioral therapy, and complementary and alternative medicine approaches to IBS. CONCLUSIONS: It is evident that the management of IBS has transcended a one-size-fits-all approach. As the field of IBS management continues to evolve, it is imperative for physicians to stay informed and receptive to the array of therapeutic options available, ultimately providing patients with the most effective and personalized care.

Global Health Initiative

Rid A, Aguilera B, Banda C, Divi R, Harris M, Kim A, Ossandon M, **Zervos J**, and Rowthorn V. Global health reciprocal innovation: ethical, legal and regulatory considerations. *BMJ Glob Health* 2024; 8(Suppl 7). PMID: 38821558. Full Text

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Global health reciprocal innovation (GHRI) is a recent and more formalised approach to conducting research that recognises and develops innovations (eg, medicines, devices, methodologies) from low- and middle-income countries (LMICs). At present, studies using GHRI most commonly adapt innovations from LMICs for use in high-income countries (HICs), although some develop innovations in LMICs and HICs. In this paper, we propose that GHRI implicitly makes two ethical commitments: (1) to promote health innovations from LMICs, especially in HICs, and (2) to conduct studies on health innovations from LMICs in equitable partnerships between investigators in LMICs and HICs. We argue that these commitments take a significant step towards a more equal global health research enterprise while helping to ensure that populations and investigators in LMICs receive equitable benefits from studies using GHRI. However, studies using GHRI can raise potential ethical concerns and face legal and regulatory barriers. We propose ethical, legal and regulatory considerations to help address these concerns and barriers. We hope our recommendations will allow GHRI to move the global health research enterprise forward into an era where all people are treated equally as knowers and learners, while populations in both LMICs and HICs benefit equitably from studies using GHRI.

Graduate Medical Education

Hoffert MM, **Newman J**, **Mortimore A**, **Passalacqua KD**, and **Abreu Lanfranco O**. Explicit Training in Systematic Communication Strategies: A Pilot Study Exploring the Incorporation of Communication Tools by First-Year Residents in Simulation and in Clinical Practice. *J Med Educ Curric Dev* 2024; 11:23821205241256042. PMID: 38765320. Full Text

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OBJECTIVES: Educational approaches for training physicians in clinical communications vary, and whether physicians apply the communication skills they learn or find them useful in the clinic is not well known. The aim of this study was to determine how first-year residents who received explicit instruction in 7 communication strategies would apply them in a simulation exercise and in clinical practice. METHODS: First-year Internal Medicine residents at an urban teaching hospital received instruction in 7 systematic communication strategies: Ask-Tell-Ask, Teach-back, open-ended questioning, NURSE, open body language, pausing, and plain language. Residents were evaluated on their use of specific communication behaviors associated with the 7 strategies during a simulation exercise of disclosing a medical error to a standardized patient. Control group residents who did the simulation before attending the training program and training group residents who did the simulation after the training were compared. Residents were queried 6 months after the training program on their use of communication strategies during clinical practice. RESULTS: A total of 27 residents participated (n = 13 control group; n = 14 training group). The training group performed behaviors for "establishing patient understanding" significantly more often than the control group. Both groups used non-verbal communication and behaviors for addressing patient emotions at similar levels. Of the 24 residents who responded to the 6-month follow-up questionnaire, 24 (100%) reported using Ask-Tell-Ask, open-ended questioning, and Teach-back, and 22 (92%) reported using NURSE statements and non-verbal communication. Most respondents reported using the strategies in clinical practice often or very often (79%) and found the strategies useful or very useful (96%). CONCLUSION: Providing explicit instruction in systematic communication strategies, particularly those focused on establishing patient understanding, may be an efficient approach for helping early career physicians develop effective communication skills that can be readily implemented during clinical training and practice.

Hematology-Oncology
Bhatnagar AR, **Siddiqui F**, **Khan G**, **Pompa R**, **Kwon D**, and **Nyati S**. Long-Term Follow-Up of Phase I Trial of Oncolytic Adenovirus-Mediated Cytotoxic and Interleukin-12 Gene Therapy for Treatment of Metastatic Pancreatic Cancer. *Biomedicines* 2024; 12(5). PMID: 38791027. Full Text

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The long-term follow-up findings of the phase I trial evaluating the efficacy of oncolytic adenovirus-mediated cytotoxic and interleukin-12 gene therapy in metastatic pancreatic cancer (mPC) seem very promising. The study employed a replication-competent Adenovector in combination with chemotherapy in a dose-escalation format. The trial demonstrated a clinically meaningful median overall survival (OS) benefit, with patients in the highest dose cohort exhibiting an impressive median OS of 18.4 months. This contrasts starkly with patients receiving lower doses who experienced a median OS of 4.8 and 3.5 months, respectively. Remarkably, subject number 10, who received the highest dose, demonstrated an extraordinary survival of 59.1 months, presenting a compelling case for further exploration. Additionally, this patient displayed complete responses in lung and liver metastases, a rare occurrence in mPC treatment. Statistical analyses supported the observed survival benefit. The unprecedented OS results emphasize the potential of this treatment strategy and pave the way for future investigations into this promising gene therapy approach.

Hematology-Oncology
Deshpande A, Munoz J, **Dabak V**, Hanbali A, and Kurzrock R. Images in Immunotherapy and Precision Oncology: A Case Report of Neurofibromatosis-1. *J Immunother Precis Oncol* 2024; 7(2):122-125. PMID: 38721407. Full Text

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Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder that primarily causes the growth of tumors along nerves. Additionally, the germline mutations involved in NF1 predispose patients to develop further malignancies. The mainstay initial treatment for these malignancies is surgical removal at diagnosis, although targeted therapies are under evaluation in the relapsed setting. We report a case of malignant peripheral nerve sheath tumor (MPNST), gastrointestinal stromal tumor (GIST), and pheochromocytoma in a patient with NF1 who presented with an infected right shoulder lesion that was confirmed to be spindle cell sarcoma via biopsy. She was treated with antibiotics; however, she rapidly deteriorated and opted for hospice care. NF1 germline mutations increase the risk of patients developing various types of cancer. Recent studies have shown that there is a role for using MEK inhibitors such as selumetinib for treating patients with NF1.

Hematology-Oncology
Krishnan J, and **Thanikachalam K**. Sezary Syndrome: A Case Report and Review of Current Therapeutics. *Cureus* 2024; 16(4):e58570. PMID: 38765439. Full Text

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Sezary syndrome (SS) is a rare but aggressive type of cutaneous T-cell lymphoma (CTCL). Patients with SS have characteristic skin lesions (erythroderma) and a leukemic phase. The rash associated with CTCLs can often mimic common benign skin conditions such as psoriasis, atopic dermatitis, etc. and therefore can go undiagnosed until later stages. We present a case of a patient with SS who managed eczema for over one year with topical steroids before receiving a skin biopsy. Workup confirmed leukemic involvement, and the patient was started on systemic therapy with bexarotene. The patient continues to have a good response to systemic therapy. When treating patients with persistent rash of uncertain etiology and/or unresponsive to treatment, primary care physicians and internists need to consider SS/Mycosis fungoides as a possible differential and should have a low threshold to initiate early referral to dermatology for definitive diagnosis.

Hematology-Oncology
Kulkarni AA, Hennessy C, Wilson G, Ramesh V, **Hwang C**, Awosika J, Bakouny Z, Khan H, Vilar-Compte D, McKay R, Jani C, Weissmann L, Griffiths E, Batist G, Bouganim N, Mavromatis B, Bashir B, Nguyen RH, Riess JW, Puc M, Kasi A, Berg S, Castillo DR, Hayes-Lattin B, Hosmer W, Flora D, Mishra S, French B, Warner JL, Lopes G, Peters S, and Florez N. Brief Report: Impact of Anti-Cancer Treatments on Outcomes of COVID-19 in Patients With Thoracic Cancers: A CCC19 Registry Analysis. *Clin Lung Cancer* 2024; Epub ahead of print. PMID: 38744613. Full Text

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Instituto Nacional de Cancerologia, Mexico City, Mexico.
University of California, San Diego, CA.
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Rosewell Park Comprehensive Cancer Center, Buffalo, NY.

Segal Cancer Centre, Jewish General Hospital, McGill University, Montreal, Canada.
UPMC Western Maryland, Cumberland, MD.
Sidney Kimmel Cancer Center at Thomas Jefferson University, Philadelphia, PA.
University of Illinois Hospital & Health Sciences System, Chicago, IL.
University of California Davis Comprehensive Cancer Center, Sacramento, CA.
Virtua Health, Marlton, NJ.
University of Kansas, Kansas City, KS.
Loyola University, Chicago, IL.
Loma Linda University, Loma Linda, CA.
Oregon Health and Science University, Portland, OR.
Hartford HealthCare Cancer Institute, Southington, CT.
St. Elizabeth Healthcare, Edgewood, KY.
University of Miami, Miami, FL.
Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland.
Dana-Farber Brigham Cancer Center, Boston, MA.

Hematology-Oncology
Malla R, Srilatha M, Muppala V, **Farran B**, Chauhan VS, and Nagaraju GP. Neoantigens and cancer-testis antigens as promising vaccine candidates for triple-negative breast cancer: Delivery strategies and clinical trials. *J Control Release* 2024; 370:707-720. PMID: 38744346. Request Article

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Immunotherapy is gaining prominence as a promising strategy for treating triple-negative breast cancer (TNBC). Neoantigens (neoAgs) and cancer-testis antigens (CTAs) are tumor-specific targets originating from somatic mutations and epigenetic changes in cancer cells. These antigens hold great promise for personalized cancer vaccines, as supported by preclinical and early clinical evidence in TNBC. This review delves into the potential of neoAgs and CTAs as vaccine candidates, emphasizing diverse strategies and delivery approaches. It also highlights the current status of vaccination modalities undergoing clinical trials in TNBC therapy. A comprehensive understanding of neoAgs, CTAs, vaccination strategies, and innovative delivery methods is crucial for optimizing neoAg-based immunotherapies in clinical practice.

Hematology-Oncology
Monga J, **Ghosh R**, **Guddeti R**, **Chitale D**, **Khan G**, and **Ghosh J**. MK591 (Quiflapon), a 5-lipoxygenase inhibitor, kills pancreatic cancer cells via downregulation of protein kinase C-epsilon. *Front Oncol* 2024; 14:1387535. PMID: 38746674. Full Text

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INTRODUCTION: Pancreatic tumors and cell lines derived from them exhibit elevated expression of 5-lipoxygenase (5-Lox), whereas non-tumor glands or normal cells do not exhibit this overexpression. Arachidonic acid stimulates pancreatic cancer cell growth via metabolic conversion through the 5-Lox pathway, and inhibition of 5-Lox activity decreases the viability of pancreatic cancer cells. However, the downstream signaling mechanisms through which 5-Lox exerts its effects on the survival of pancreatic

cancer cells remain to be elucidated. METHODS: The effects of 5-Lox inhibition on cell proliferation, apoptosis, and invasive potential were investigated in pancreatic cancer cells. The protein expression was analyzed by Western blot. Apoptosis was analyzed by Annexin-V binding assay and by detecting the degradation of chromatin-DNA to nucleosomal fragments. The protein kinase C-epsilon (PKCε) activity was measured by an immunoprecipitation-kinase assay. The in vivo effects of MK591 were evaluated in pancreatic tumor xenograft model. RESULTS: MK591, a specific inhibitor of 5-Lox activity, killed pancreatic cancer cells via induction of apoptosis, involving externalization of phosphatidylserine, cleavage of PARP (poly-ADP ribose polymerase) and degradation of chromatin DNA to nucleosomes. MK591 effectively blocked in vitro invasion and soft-agar colony formation by pancreatic cancer cells and decreased pancreatic tumor growth in nude mice xenografts. Furthermore, inhibition of 5-Lox downregulated K-Ras and inhibited phosphorylation of c-Raf and ERKs. Interestingly, 5-Lox inhibition induced apoptosis in pancreatic cancer cells without the inhibition of Akt but the protein level of PKCε was dramatically downregulated. Furthermore, inhibition of 5-Lox decreased the phosphorylation of Stat3 at Serine-727. Pre-treatment of pancreatic cancer cells with peptide activators of PKCε prevented apoptosis induced by 5-Lox inhibition, suggesting that the mechanism by which 5-Lox inhibition causes cell death in pancreatic cancer involves downregulation of PKCε. The combination of low doses of MK591 and gemcitabine synergistically reduced the oncogenic phenotype and killed pancreatic cancer cells by inducing apoptosis. DISCUSSION: These findings indicate that inhibition of 5-Lox interrupts an Akt-independent, PKCε-dependent survival mechanism in pancreatic cancer cells and suggest that metabolism of arachidonic acid through the 5-Lox pathway plays an integral part in the survival of pancreatic cancer cells via signaling through PKCε, an oncogenic, pro-survival serine/threonine kinase.

Infectious Diseases

Arena CJ, **Kenney RM**, **Eriksson E**, **Brar I**, and **Veve MP**. Prescribing Practices of Recommended Treatment for Trichomonas vaginalis and Chlamydia trachomatis after 2021 STI Treatment Guideline Update. *Sex Transm Dis* 2024; Epub ahead of print. PMID: 38709026. Full Text

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We evaluated the proportion of patients with trichomoniasis and chlamydial infections who received recommended versus non-recommended antibiotic therapy after the updated 2021 Sexually Transmitted Infections Guideline. Of 712 patients, 473 (66%) received recommended therapy. Receipt of emergency department care was independently associated with recommended therapy (adjOR, 2.1; 95% CI 1.5-2.9).

Infectious Diseases

Hoffert MM, **Newman J**, **Mortimore A**, **Passalacqua KD**, and **Abreu Lanfranco O**. Explicit Training in Systematic Communication Strategies: A Pilot Study Exploring the Incorporation of Communication Tools by First-Year Residents in Simulation and in Clinical Practice. *J Med Educ Curric Dev* 2024; 11:23821205241256042. PMID: 38765320. Full Text

Henry Ford Health, Detroit, MI, USA.
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OBJECTIVES: Educational approaches for training physicians in clinical communications vary, and whether physicians apply the communication skills they learn or find them useful in the clinic is not well known. The aim of this study was to determine how first-year residents who received explicit instruction in 7 communication strategies would apply them in a simulation exercise and in clinical practice. METHODS: First-year Internal Medicine residents at an urban teaching hospital received instruction in 7 systematic communication strategies: Ask-Tell-Ask, Teach-back, open-ended questioning, NURSE, open body language, pausing, and plain language. Residents were evaluated on their use of specific communication behaviors associated with the 7 strategies during a simulation exercise of disclosing a medical error to a standardized patient. Control group residents who did the simulation before attending the training program and training group residents who did the simulation after the training were compared. Residents were queried 6 months after the training program on their use of communication strategies during clinical

practice. RESULTS: A total of 27 residents participated (n = 13 control group; n = 14 training group). The training group performed behaviors for "establishing patient understanding" significantly more often than the control group. Both groups used non-verbal communication and behaviors for addressing patient emotions at similar levels. Of the 24 residents who responded to the 6-month follow-up questionnaire, 24 (100%) reported using Ask-Tell-Ask, open-ended questioning, and Teach-back, and 22 (92%) reported using NURSE statements and non-verbal communication. Most respondents reported using the strategies in clinical practice often or very often (79%) and found the strategies useful or very useful (96%). CONCLUSION: Providing explicit instruction in systematic communication strategies, particularly those focused on establishing patient understanding, may be an efficient approach for helping early career physicians develop effective communication skills that can be readily implemented during clinical training and practice.

Internal Medicine
Jamal FE, Vey JA, Proctor T, **Ishak A**, Schmitt FC, and Nikas IP. The International System for Reporting Serous Fluid Cytopathology: A Systematic Review and Meta-Analysis of Diagnostic Test Accuracy Studies. *Adv Anat Pathol* 2024; Epub ahead of print. PMID: 38695284. Full Text

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This is the first systematic review and meta-analysis of The International System (TIS) for reporting serous fluid cytopathology. Our aims were to present the pooled malignancy rate of each TIS reporting category and the diagnostic accuracy of cytology using this system. Database search using a predefined strategy was followed by study selection, data extraction, study quality assessment, and statistical analysis. Data derived from 16 eligible studies were pooled. The pooled rates of malignancy were as follows: 27% (95% CI; 16%-41%) for "nondiagnostic" (ND), 11% (95% CI; 7%-18%) for negative for malignancy" (NFM), 49% (95% CI; 37%-61%) for "atypia of undetermined significance" (AUS), 90% (95% CI; 81%-95%) for "suspicious for malignancy" (SFM), and 100% (95% CI; 98%-100%) for "positive for malignancy" (MAL). Studies performed exclusively in cancer hospitals showed higher pooled malignancy rates, compared with academic and community hospitals serving the general population, in the ND [40% (95% CI; 21%-62%) vs. 22% (95% CI; 11%-39%)], NFM [20% (95% CI; 13%-30%) vs. 9% (95% CI; 5%-17%)], and AUS categories [55% (95% CI; 47%-63%) vs. 46% (95% CI; 31%-62%)]. Notably, the difference was significant in the NFM category (P=0.04). When both SFM and MAL cytology interpretations were considered as malignant outcomes, the pooled sensitivity and specificity were 68.74% (95% CI; 59.90%-76.39%) and 98.81% (95% CI; 98.18%-99.22%), respectively. In addition, the diagnostic odds ratio (DOR) was found to be 170.7 (95% CI; 96.2-303.3). Despite its strengths, our study also had some limitations. Therefore, future large-scale longitudinal studies could strengthen the findings of this review.

Internal Medicine
Kalsi J, Suffredini JM, Koh S, Liu J, Khalid MU, Denktas A, Alam M, Kayani W, and Jia X. Intravascular Ultrasound-Guided versus Angiography-Guided Percutaneous Coronary Intervention for Stent Thrombosis Elevation Myocardial Infarction: An Updated Systematic Review and Meta-Analysis. *Cardiology* 2024; 149(3):196-204. PMID: 38350431. Request Article

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INTRODUCTION: Intravascular ultrasound (IVUS) provides intra-procedural guidance in optimizing percutaneous coronary interventions (PCI) and has been shown to improve clinical outcomes in stent

implantation. However, current data on the benefit of IVUS during PCI in ST-elevation myocardial infarction (STEMI) patients is mixed. We performed meta-analysis pooling available data assessing IVUS-guided versus angiography-guided PCI in STEMI patients. METHODS: We conducted a systematic search on PubMed and Embase for studies comparing IVUS versus angiography-guided PCI in STEMI. Mantel-Haenszel random effects model was used to calculate risk ratios (RRs) with 95% confidence intervals (CIs) for outcomes of major adverse cardiovascular events (MACEs), death, myocardial infarction (MI), target vessel revascularization (TVR), stent thrombosis (ST) and in-hospital mortality. RESULTS: A total of 8 studies including 336,649 individuals presenting with STEMI were included for the meta-analysis. Follow-up ranged from 11 to 60 months. We found significant association between IVUS-guided PCI with lower risk for MACE (RR 0.82, 95% CI 0.76-0.90) compared with angiography-guided PCI. We also found significant association between IVUS-guided PCI with lower risk for death, MI, TVR, and in-hospital mortality but not ST. CONCLUSION: In our meta-analysis, IVUS-guided compared with angiography-guided PCI was associated with improved long-term and short-term clinical outcomes in STEMI patients.

Internal Medicine
Maraj D, **Singh B**, **Fuller R**, and **Bern M**. A Rare Case of Transient Mesenteric Ischemia After Atrial Fibrillation With Rapid Ventricular Response Rate. *Cureus* 2024; 16(4):e58210. PMID: 38741839. Full Text

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Mesenteric ischemia is an urgent event and requires prompt recognition and treatment, in order to reduce the risk of mortality. It results from the sudden onset of small intestinal hypoperfusion, from a reduction or cessation of arterial perfusion, which can occur from an embolic obstruction at the superior mesenteric artery. We present a case of transient mesenteric ischemia from an episode of atrial fibrillation with a rapid ventricular response rate. Despite being on chronic anticoagulation therapy, the patient developed transient mesenteric ischemia from an embolic clot. The patient's heart rate was controlled and no surgical intervention was required, a rare finding; however, it is very important to recognize and treat promptly.

Internal Medicine
Ramanan SP, **Singh B**, Gandhamaneni SH, and Sange I. Eosinophilic Esophagitis: The Role of Steroids and the Dose, Duration, and Delivery of Steroid Therapy. *Cureus* 2024; 16(4):e58343. PMID: 38756322. Full Text

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Eosinophilic esophagitis (EoE) is a chronic immune-mediated condition characterized by the eosinophil infiltration of the esophagus (>15 per high power field). Recently, there has been an increase in both the incidence and prevalence of the disease. The common modalities of treatment are dietary modification, proton pump inhibitors, and steroids. However, the United States Food and Drug Administration has not approved any drugs for the treatment of EoE. This review has discussed the role of steroids in the treatment of EoE, focusing on the various formulations of the drug, its dosage, drug delivery, and duration of therapy. The study also covers the common outcomes of steroid therapy and its side effects.

Internal Medicine

Robinson C, Minhas JS, **Kisule A**, and **Zebda H**. Eosinophilic Granulomatosis With Polyangiitis: A Case Report. *Cureus* 2024; 16(4):e58211. PMID: 38741799. Full Text

Internal Medicine, Henry Ford Health System, Jackson, USA.
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Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare form of necrotizing small-to-medium vessel vasculitis that can be associated with antineutrophil cytoplasmic antibody (ANCA) positivity, asthma, and eosinophilia. We present the case of a 65-year-old male with a past medical history of asthma who presented to the emergency department with bilateral upper and lower extremity paresthesias, as well as right foot drop, persisting for a two-week duration. His lab work revealed leukocytosis of 20.6 K/uL with 12.36 K/uL of absolute eosinophils as well as elevated inflammatory markers with an erythrocyte sedimentation rate of 32 mm/hr and CRP of 7.3 mg/dL. Both c-ANCA and p-ANCA titers were also elevated at 1:320. An eventual MRI of the entire spine did not reveal any neurologic or anatomic lesions to explain the patient's symptoms. CT imaging was also remarkable for airspace opacities involving the anterior right and bilateral lower posterior lung regions, as well as pansinusitis. A nerve biopsy showed axonopathy as well as evidence of healed vasculitis. Pulse dose steroids were started, which conferred benefits to the patient after other forms of treatment were unsuccessful. Given the rarity of EGPA, we think it is important to add new cases to the literature with a thorough discussion of the steps leading up to how the diagnosis was made.

Nephrology

Malinzak L, **Gartrelle K**, **Sragi Z**, **Segal A**, **Prashar R**, and **Jesse MT**. Access to robotic assisted kidney transplant for recipients: a systematic review and call for reporting standards. *J Robot Surg* 2024; 18(1):239. PMID: 38833043. Full Text

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Robot-assisted kidney transplantation (RAKT) is a relatively novel, minimally invasive option for kidney transplantation. However, clarity on recipient selection in the published literature is lacking thereby significantly limiting interpretation of safety and other outcomes. This systematic review aimed to identify and synthesize the data on selection of RAKT recipients, compare the synthesized data to kidney transplant recipients across the USA, and explore geographical clusters of availability of RAKT. Systematic literature review, in accordance with PRISMA, via OVID MEDLINE, Embase, and Web of science from inception to March 5, 2023. All data entry double blinded and quality via Newcastle Ottawa Scale. 44 full-text articles included, encompassing approximately 2402 kidney transplant recipients at baseline but with considerable suspicion for overlap across publications. There were significant omissions of information across studies on patient selection for RAKT and/or analysis. Overall, the quality of studies was very low. Given suspicion of overlap across studies, it is difficult to determine how many RAKT recipients received living (LD) versus deceased donor (DD) organs, but a rough estimate suggests 89% received LD. While the current RAKT literature provides preliminary evidence on safety, there are significant omissions in reporting on patient selection for RAKT which limits interpretation of findings. Two recommendations: (1) international consensus is needed for reporting guidelines when publishing RAKT data and (2) larger controlled trials consistently reporting recipient characteristics are needed to clearly determine selection, safety, and outcomes across both LD and DD recipients.

Neurology

Jumah A, **Fu S**, **Albanna AJ**, **Agarwal U**, **Fana M**, **Choudhury O**, **Idris A**, **Elfaham A**, **Iqbal Z**, **Schultz L**, **Latack K**, **Brady M**, **Scozzari D**, and **Ramadan AR**. Early vs late anticoagulation in acute ischemic stroke with indications outside atrial fibrillation. *J Stroke Cerebrovasc Dis* 2024; 33(7):107757. PMID: 38705498. Full Text

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BACKGROUND: Current literature lacks guidance on the safety of administering anticoagulation in acute ischemic stroke with emergent indications that require anticoagulation other than atrial fibrillation. Therefore, we tend to rely on studies investigating acute ischemic stroke in atrial fibrillation for anticoagulation recommendations. METHODS: We retrospectively reviewed data for patients with acute ischemic stroke who had a non-atrial fibrillation emergent indication for anticoagulation (e.g., intra-arterial thrombus, intracardiac thrombus, acute coronary syndrome, acute limb ischemia, deep vein thrombosis and pulmonary embolism) diagnosed within 3 days of acute ischemic stroke. Patients who received anticoagulation ≤ 3 days of stroke onset (Group A) were compared to those who either received it afterwards or did not receive it at all (Group B). RESULTS: Out of the 558 patients, only 88 patients met our inclusion criteria. Of the total cohort, 55.7 % patients were males, and basic demographics were similar in both groups except for milder strokes in Group A (national institute of health stroke scale 6 vs. 12.5, p = 0.03). Only 2 patients in Group A and 1 patient in Group B developed intracranial hemorrhage, which was not statistically significant. Group A patients had a lower incidence of both new diagnosis (2 % vs. 34.2 % %, p < 0.001) and propagation of an established venous thromboembolism. They also had a lower rate of any thromboembolic complication (2 % vs. 42 %, p < 0.001). CONCLUSION: Early anticoagulation (i.e., ≤ 3 days) in non-atrial fibrillation ischemic stroke patients with an emergent indication may be safe and carry a lower risk of thromboembolic complications than later anticoagulation.

Neurology

Mahmood S, **Sallowm Y**, Affan M, **Schultz L**, **Cerghet M**, and **Ali A**. Radiological features of patients with headache as a presenting symptom of neurosarcoidosis. *Headache* 2024; Epub ahead of print. PMID: 38780214. Full Text

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OBJECTIVE: To describe the radiological features of patients with headache as a presenting symptom of neurosarcoidosis. BACKGROUND: Neurologic complications occur in approximately 5%-10% of patients with sarcoidosis, and approximately 50% of these patients have neurologic deficits at the time sarcoidosis is first diagnosed. A wide spectrum of central and peripheral nervous system clinical manifestations may be observed, including cranial nerve palsies, sensory and/or motor deficits, and headache. Magnetic resonance imaging (MRI) results in patients with neurosarcoidosis may include abnormal contrast enhancement, structural masses, and demyelinating lesions. METHODS: This single-center retrospective cohort study assessed patients who were diagnosed with neurosarcoidosis in an urban tertiary care center between 1995 and 2016. We included patients who had MRI results at the time of diagnosis. Patients were divided into two groups based on the presence or absence of headache as a presenting symptom. The MRI result of meningeal contrast enhancement was reviewed. RESULTS: Of the 110 patients analyzed, 30 (27.3%) had an initial presenting symptom of headache while 80 (72.7%) did not. Patients with headache had a higher proportion of meningeal contrast enhancement on MRI (66.7% [20/30] vs. 25.0% [20/80]; p < 0.001) and leptomeningeal involvement (53.3% [16/30] vs. 7.5% [6/80],

p < 0.001) compared to patients with no headache. However, those with headache had a lower proportion of spinal cord localization (13.8% [4/29] vs. 34.2% [26/76], p = 0.038) and intraparenchymal central nervous system involvement (16.7% [5/30] vs. 51.3% [41/80], p = 0.001) compared to patients with no headache. CONCLUSION: Patients with neurosarcoidosis who presented with headache as an initial symptom had a higher proportion of meningeal contrast enhancement seen by MRI than patients who presented with other neurological symptoms. This suggests a clinico-radiologic link between headache and meningeal disruption in patients with neurosarcoidosis.

Neurology
Zeidman LA. Effectiveness of IVIG on Non-Length-Dependent Skin Biopsies in Small Fiber Neuropathy With Plexin D1, Trisulfated Heparin Disaccharide, and Fibroblast Growth Factor Receptor 3 Autoantibodies. *J Clin Neuromuscul Dis* 2024; 25(4):184-196. PMID: 38771228. Full Text

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OBJECTIVES: To demonstrate treatment efficacy on composite and non-length-dependent (NLD) punch biopsy specimens from intravenous immunoglobulin (IVIG) in pure small-fiber neuropathy (SFN) with trisulfated heparin disaccharide (TS-HDS), fibroblast growth factor-3 (FGFR-3), or Plexin D1 antibodies. SFN has an increasing prevalence, and over 30% of cases may be immune-mediated. TS-HDS, FGFR-3, and Plexin D1 autoantibodies have been shown to be present in 44%-55% of cryptogenic SFN cases, suggesting an immune mechanism. Reports have shown IVIG to be effective for this condition, but some controversy exists based on length-dependent (LD) post-IVIG treatment data in a recent trial. METHODS: In a retrospective review, all pure SFN cases tested for the 3 antibodies from January 2021 to May 2022 were tabulated, and patients who underwent IVIG treatment were separated and analyzed for changes in epidermal nerve fiber density (ENFD) on skin biopsy, as well as SFN-specific questionnaire and pain scores. RESULTS: Ninety-one patients with pure SFN had antibody testing. Sixty of these (66%) were seropositive, and 31 (34%) were seronegative. Seventeen seropositive patients (13 female patients, 4 male patients, 6 FGFR-3, 2 TS-HDS, 4 Plexin D1, 2 with all 3 antibodies, 1 with FGFR-3 and Plexin D1, 1 with FGFR-3 and TS-HDS, and 1 with TS-HDS and Plexin D1) underwent IVIG treatment. Of these, 2 patients stopped treatment due to side effects, and the remaining 15 completed at least 6 months of IVIG. Of these, 12 had a post-IVIG skin biopsy, and of these, 11 (92%) had a 55.1% improved mean composite ENFD (P = 0.01). NLD-ENFD specimens improved by 42.3% (P = 0.02), and LD-ENFD specimens improved by 99.7% (P = 0.01). Composite ENFD in Plexin D1-SFN patients improved by 139% (P = 0.04). In addition, 14 patients had questionnaires pre-IVIG/post-IVIG, and average pain decreased by 2.7 (P = 0.002). CONCLUSIONS: IVIG shows disease-modifying effect in immune SFN with novel antibodies, especially Plexin D1-SFN, as well as significantly improved pain. NLD-ENFD should be examined as well as LD-ENFD to see this effect. Further randomized controlled trials looking at NLD-ENFD as well as LD-ENFD improvement, along with pain and SFN-specific questionnaires, are needed to confirm these findings.

Neurology
Zhang Y, **Liu Z**, **Chopp M**, **Millman M**, **Li Y**, **Cepparulo P**, **Kemper A**, **Li C**, **Zhang L**, and **Zhang ZG**. Small extracellular vesicles derived from cerebral endothelial cells with elevated microRNA 27a promote ischemic stroke recovery. *Neural Regen Res* 2025; 20(1):224-233. PMID: 38767487. Full Text

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JOURNAL/nrgr/04.03/01300535-202501000-00030/figure1/v/2024-05-14T021156Z/r/image-tiff Axonal remodeling is a critical aspect of ischemic brain repair processes and contributes to spontaneous functional recovery. Our previous in vitro study demonstrated that exosomes/small extracellular vesicles (sEVs) isolated from cerebral endothelial cells (CEC-sEVs) of ischemic brain promote axonal growth of embryonic cortical neurons and that microRNA 27a (miR-27a) is an elevated miRNA in ischemic CEC-sEVs. In the present study, we investigated whether normal CEC-sEVs engineered to enrich their levels of miR-27a (27a-sEVs) further enhance axonal growth and improve neurological outcomes after ischemic

stroke when compared with treatment with non-engineered CEC-sEVs. 27a-sEVs were isolated from the conditioned medium of healthy mouse CECs transfected with a lentiviral miR-27a expression vector. Small EVs isolated from CECs transfected with a scramble vector (Scra-sEVs) were used as a control. Adult male mice were subjected to permanent middle cerebral artery occlusion and then were randomly treated with 27a-sEVs or Scra-sEVs. An array of behavior assays was used to measure neurological function. Compared with treatment of ischemic stroke with Scra-sEVs, treatment with 27a-sEVs significantly augmented axons and spines in the peri-infarct zone and in the corticospinal tract of the spinal grey matter of the denervated side, and significantly improved neurological outcomes. In vitro studies demonstrated that CEC-sEVs carrying reduced miR-27a abolished 27a-sEV-augmented axonal growth. Ultrastructural analysis revealed that 27a-sEVs systemically administered preferentially localized to the pre-synaptic active zone, while quantitative reverse transcription-polymerase chain reaction and Western Blot analysis showed elevated miR-27a, and reduced axonal inhibitory proteins Semaphorin 6A and Ras Homolog Family Member A in the peri-infarct zone. Blockage of the Clathrin-dependent endocytosis pathway substantially reduced neuronal internalization of 27a-sEVs. Our data provide evidence that 27a-sEVs have a therapeutic effect on stroke recovery by promoting axonal remodeling and improving neurological outcomes. Our findings also suggest that suppression of axonal inhibitory proteins such as Semaphorin 6A may contribute to the beneficial effect of 27a-sEVs on axonal remodeling.

Neurosurgery

Fadel HA, **Pawloski JA**, **Anzalone AJ**, **Haider S**, **Schultz LR**, **Kalkanis SN**, **Robin AM**, and **Lee IY**. Laser interstitial thermal therapy for first-line treatment of insular glioma. *J Neurosurg* 2024; 1-12. Epub ahead of print. PMID: 38788240. Full Text

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OBJECTIVE: Insular gliomas pose a significant surgical challenge due to the complex surrounding functional and vascular anatomy. The authors report their experience using a novel framework for the treatment of insular gliomas with laser interstitial thermal therapy (LITT) and provide representative case examples emphasizing indications, rationale, and technical pearls. METHODS: A prospectively gathered institutional database was used to identify patients with newly diagnosed insular gliomas who underwent LITT between 2015 and 2023. The proposed framework of insular glioma management is guided by tumor size and extent of extra-insular tumor involvement. Patients with tumors localized to the insula (insula-only) were treated with single-session or staged LITT. Patients with insular tumors with frontotemporal involvement (insular+) were treated with insular LITT and standard frontotemporal resection of extra-insular tumor. Clinical and volumetric lesional characteristics were analyzed, with particular emphasis on extent of cytoreductive treatment and safety. RESULTS: Of the 261 patients treated at the authors' institution with LITT between 2015 and 2023, 33 LITT procedures were identified involving 22 unique patients with treatment-naive insular gliomas. Of the 22 patients, 12 had insular-only tumors and were treated with LITT alone, while 10 patients had insular+ lesions and were treated with LITT and resection. The median tumor volume for insular-only tumors was 13.4 cm3 (IQR 10.6, 26.3 cm3), with a median extent of treatment of 100% (IQR 92.1%, 100%). Insular+ lesions were significantly larger, with a median volume of 81.2 cm3 (IQR 51.9, 97 cm3) and median extent of treatment of 96.6% (IQR 93.7%, 100%). All patients with insular-only tumors were discharged the day after ablation, while insular+ patients had significantly longer hospital stays, with 50% staying more than 3 days. Overall, 8% of insular-only patients had permanent neurological deficits compared with 33% of insular+ patients. Two patients' tumors progressed during follow-up: one patient with WHO grade 4 astrocytoma and the other with diffuse glioma not otherwise specified. Patients with grade 4 tumors had the highest rate of permanent neurological deficit (43%) and a larger decline in postoperative Karnofsky Performance Status score ($p = 0.046$). CONCLUSIONS: The authors present their experience using a novel insular glioma treatment paradigm that incorporates LITT into the broader framework of insular glioma surgery. Their findings suggest that insular LITT is feasible and may allow for high rates of cytoreduction while potentially ameliorating the risks of conventional insular glioma surgery.

Neurosurgery

Lita A, Sjöberg J, Păcioianu D, Siminea N, Celiku O, Dowdy T, Păun 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; Epub ahead of print. PMID: 38828478. Full Text

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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-CIMP-low 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.

Obstetrics, Gynecology and Women's Health Services

Hasbini YG, Sokol RJ, Green PM, Tarca AL, **Goyert G**, Ouweini HME, **Keerthy M**, Jones T, Thiel L, Youssef Y, Townsel C, Vengalil S, Paladino P, Wright A, **Ayyash M**, **Vadlamudi G**, Szymanska M, Sajja S, Crane G, Baracy M, Jr., Grace K, Houston K, Norman J, Girdler K, Gudicha DW, Bahado-Singh R, and Hassan SS. COVID-19 is associated with early emergence of preeclampsia: results from a large regional collaborative. *J Matern Fetal Neonatal Med* 2024; 37(1):2345852. PMID: 38797682. Full Text

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Objective: To investigate the relationship between preeclampsia and SARS-CoV-2 infection during pregnancy. Methods: This was a retrospective cohort study of pregnant women between March and October 2020. Pregnant patients admitted to 14 obstetrical centers in Michigan, USA formed the study population. Of the N = 1458 participants, 369 had SARS-CoV-2 infection (cases). Controls were uninfected pregnancies that were delivered in the same obstetric unit within 30 days of the index case. Robust Poisson regression was used to estimate relative risk (RR) of preterm and term preeclampsia and preeclampsia involving placental lesions. The analysis included adjustment for relevant clinical and demographic risk factors.Results: SARS-CoV-2 infection during pregnancy increased the risk of preeclampsia [adjusted aRR = 1.69 (1.26-2.26)], preeclampsia involving placental lesions [aRR = 1.97(1.14-3.4)] and preterm preeclampsia 2.48(1.48-4.17). Although the highest rate of preeclampsia was observed in patients infected with SARS-CoV-2 who were symptomatic (18.4%), there was increased risk even in asymptomatic SARS-CoV-2 infected patients (14.2%) relative to non-infected controls (8.7%) ($p < 0.05$). This association with symptomatology was also noted with preterm preeclampsia for which the rate doubled from 2.7% in controls to 5.2% in asymptomatic cases and reached 11.8% among symptomatic cases ($p < 0.05$). The rate of preterm preeclampsia among cases of pregnant people self-identified as Black reached 10.1% and was almost double the rate of the reminder of the group of infected pregnancies (5.3%), although the rate among uninfected was almost the same (2.7%) for both Black and non-Black groups (interaction $p = 0.05$).Conclusions: Infection with SARS-CoV-2 increases the risk of preeclampsia even in the absence of symptoms, although symptomatic persons are at even higher risk. Racial disparities in the development of preterm preeclampsia after SARS-CoV-2 infection may explain discrepancies in prematurity between different populations.

Obstetrics, Gynecology and Women's Health Services
Shu MK, **Moses E**, Korangy E, McGrath J, and Reyes HD. Durable response in platinum refractory small cell carcinoma of the ovary hypercalcemic type treated with combination pembrolizumab, oral cyclophosphamide, and bevacizumab. *Int J Gynecol Cancer* 2024; 34(5):777-782. PMID: 38719275. Full Text

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Ophthalmology and Eye Care Services
Corona ST, **Ali OI**, Yu HJ, and Schefler AC. Morphological Biomarkers Related to Visual Acuity in Patients With Radiation Retinopathy Treated With Intravitreal Ranibizumab. *Ophthalmic Surg Lasers Imaging Retina* 2024; 55(5):255-262. PMID: 38408221. Request Article

BACKGROUND AND OBJECTIVE: Our objective was to monitor variables via spectral-domain optical coherence tomography (SD-OCT) and identify the most relevant biomarkers related to best-corrected visual acuity (BCVA) in radiation retinopathy (RR). PATIENTS AND METHODS: A post-hoc analysis of the two-year Ranibizumab for Radiation Retinopathy (RRR) trial analyzed vision and OCT parameters including intraretinal fluid, ellipsoid zone (EZ) disruption, retinal pigment epithelium atrophy, hard exudates, retinal hemorrhage, retinal neovascularization, and subfoveal fluid. BCVA and SD-OCT parameters were evaluated by univariate analysis and a mixed-effects model. RESULTS: Forty eyes from the RRR trial were included. Intraretinal cyst vertical size (week 24: $P = 0.032$; week 48: $P = 0.021$),

neovascularization (week 48: P = 0.028; week 72: P = 0.025), and EZ disruption (week 72: P = 0.029; week 104: P = 0.019) were the clinical parameters most relevant to BCVA by univariate analysis in at least two time points. The mixed-effects model confirmed the relevance of intraretinal cyst vertical size (P = 0.001) and neovascularization (P = 0.001) but not EZ disruption (P = 0.119) over the course of the study. CONCLUSIONS: This study characterizes the course of visual loss in RR by identifying intraretinal cyst vertical size, neovascularization, and EZ disruption as biomarkers of poor BCVA over a span of two years. Larger multicenter studies are needed to confirm these findings.

Orthopedics/Bone and Joint Center

Bellamy JL, **Goodrich E**, Sabatini FM, Mounce SD, Ovadia SA, Kolin DA, Odum SM, Cohen-Rosenblum A, and Landy DC. Systematic Review of Gender and Sex Terminology Use in Arthroplasty Research: There is Room for Improvement. *J Arthroplasty* 2024; Epub ahead of print. PMID: 38734326. Full Text

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BACKGROUND: There is increasing appreciation of the distinction between gender and sex as well as the importance of accurately reporting these constructs. Given recent attention regarding transgender and gender nonconforming (TGNC) and intersex identities, it is more necessary than ever to understand how to describe these identities in research. This study sought to investigate the use of gender- and sex-based terminology in arthroplasty research. METHODS: The five leading orthopaedic journals publishing arthroplasty research were reviewed to identify the first twenty primary clinical research articles on an arthroplasty topic published after January 1, 2022. Use of gender- or sex-based terminology, whether use was discriminate, and whether stratification or adjustment based on gender or sex was performed, were recorded. RESULTS: There were 98 of 100 articles that measured a construct of gender or sex. Of these, 15 articles used gender-based terminology, 45 used sex-based terminology, and 38 used a combination of gender- and sex-based terminology. Of the 38 articles using a combination of terminology, none did so discriminately. All articles presented gender and sex as binary variables, and two attempted to explicitly define how gender or sex were defined. Of the 98 articles, 31 used these variables for statistical adjustments, though only six reported stratified results. CONCLUSIONS: Arthroplasty articles infrequently describe how gender or sex was measured, and frequently use this terminology interchangeably. Additionally, these articles rarely offer more than two options for capturing variation in sex and gender. Future research should be more precise in the treatment of these variables to improve the quality of results and ensure findings are patient-centered and inclusive.

Orthopedics/Bone and Joint Center

Castle JP, **Gaudiani MA**, **Kasto JK**, **Elagamy N**, **Gasparro MA**, **Corsi M**, **Jiang EX**, **Makhni EC**, **Mahylis JM**, and **Muh SJ**. Race, gender, and income negatively impact patient-reported outcomes following total shoulder arthroplasty. *Semin Arthroplasty* 2024. Epub ahead of print. PMID: Not assigned. Full Text

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Background: Social determinants of health (SDOH) refer to social and economic factors that influence a patient's health status. The purpose of this study was to investigate the impact of SDOH on preoperative and postoperative Patient-Reported Outcomes Measurement Information System (PROMIS) scores and postoperative resource utilization following primary shoulder arthroplasty (SA). Methods: This retrospective chart review evaluated data from all patients who underwent primary SA (including

anatomic, reverse, and hemiarthroplasty) at a single health system between May 2020 and May 2022. Patients without at least 6-month postoperative PROMIS questionnaires and those undergoing revision surgeries were excluded. The electronic medical record was used to identify SDOH for each patient, and PROMIS scores for Upper Extremity (PROMIS-UE), Pain Interference (PROMIS-PI), and Depression (PROMIS-D) were completed electronically at respective preoperative and postoperative visits. Univariate analysis using independent 2-group t-tests and Chi-squared tests were used to analyze the mean difference between patient groups based on SDOH. Multivariate linear regressions were performed with all predictors used in the univariate model using the least squares method. Results: The study included 248 patients who underwent SA, with a mean age of 67.9 years. Caucasian patients were over-represented in the highest quartile of median household income (MHI) compared to Black patients (35.1% vs. 17.2%) who were over-represented in the lowest MHI quartile (37.9% vs. 8.3%). At 6-month postoperative, black patients had significantly lower UE (33.8 ± 6.2 vs. 38.1 ± 9.0; P = .03) and greater PI scores (59.1 ± 6.1 vs. 55.6 ± 8.6; P = .145) compared to Caucasian patients. Similarly, at 6-month follow-up, the lowest MHI quartile had lower UE (33.8 ± 7.7 vs. 39.6 ± 8.8; P = .01) and higher PI scores (58.7 ± 6.5 vs. 54.3 ± 8.2; P < .01) compared to the highest MHI quartile, and females demonstrated lower UE (36.3 ± 7.9 vs. 38.6 ± 9.8; P = .04) and higher D scores (46.2 ± 9.1 vs. 42.0 ± 8.6; P = .046) compared to males. Government/public insurance demonstrated lower UE (36.8 ± 8.0 vs. 39.8 ± 10.4; P = .03) and higher D scores (45.9 ± 9.2 vs. 40.6 ± 7.6; P = .03) compared to private insurance. At 12-month follow-up, females demonstrated lower UE scores compared to males (36.0 ± 10.2 vs. 40.1 ± 11.3; P = .03). Black patients harbored lower UE, PI, and D scores compared to Caucasian patients, although not statistically significant. Conclusion: Several socioeconomic factors such as race, gender, and insurance status are associated with differential outcomes after SA. Patients who are Black, female, current smokers, and from the lowest income quartile are associated with inferior PROMIS function, pain, and depression outcomes following SA.

Orthopedics/Bone and Joint Center

Gaudiani MA, **Castle JP**, **Abbas MJ**, **Pratt BA**, Myles MD, **Moutzouros V**, and **Lynch TS**. ChatGPT-4 Generates More Accurate and Complete Responses to Common Patient Questions About Anterior Cruciate Ligament Reconstruction Than Google's Search Engine. *Arthrosc Sports Med Rehabil* 2024. Epub ahead of print. PMID: Not assigned. Full Text

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Purpose: To replicate a patient's internet search to evaluate ChatGPT's appropriateness in answering common patient questions about anterior cruciate ligament reconstruction compared with a Google web search. Methods: A Google web search was performed by searching the term “anterior cruciate ligament reconstruction.” The top 20 frequently asked questions and responses were recorded. The prompt “What are the 20 most popular patient questions related to ‘anterior cruciate ligament reconstruction?’” was input into ChatGPT and questions and responses were recorded. Questions were classified based on the Rothwell system and responses assessed via Flesch-Kincaid Grade Level, correctness, and completeness were for both Google web search and ChatGPT. Results: Three of 20 (15%) questions were similar between Google web search and ChatGPT. The most common question types among the Google web search were value (8/20, 40%), fact (7/20, 35%), and policy (5/20, 25%). The most common question types amongst the ChatGPT search were fact (12/20, 60%), policy (6/20, 30%), and value (2/20, 10%). Mean Flesch-Kincaid Grade Level for Google web search responses was significantly lower (11.8 ± 3.8 vs 14.3 ± 2.2; P = .003) than for ChatGPT responses. The mean correctness for Google web search question answers was 1.47 ± 0.5, and mean completeness was 1.36 ± 0.5. Mean correctness for ChatGPT answers was 1.8 ± 0.4 and mean completeness was 1.9 ± 0.3, which were both significantly greater than Google web search answers (P = .03 and P = .0003). Conclusions: ChatGPT-4 generated more accurate and complete responses to common patient questions about anterior cruciate ligament reconstruction than Google's search engine. Clinical Relevance: The use of artificial intelligence such as ChatGPT is expanding. It is important to understand the quality of information as well as how the results of ChatGPT queries compare with those from Google web searches

Orthopedics/Bone and Joint Center

Hadro A, Huyke-Hernandez FA, Kleinsmith RM, Doxey SA, Schweitzer A, Ristow J, Cunningham BP, and **Braman J**. Effect of post-operative NSAID use on rotator cuff repair outcomes. *J Orthop* 2024; 56:119-122. PMID: 38828472. Full Text

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BACKGROUND: The impact of non-steroidal anti-inflammatory drugs (NSAIDs) on rotator cuff repair is an ongoing area of study within orthopedics, with conflicting results in current literature. Despite concerns over the deleterious effects of NSAIDs on rotator cuff healing, they are becoming an integral part of a multimodal post-operative pain control regiment. The purpose of this study was to compare post-operative patient-reported outcomes (PROs), complications rates, and retear rates of arthroscopic rotator cuff repairs in patients using ibuprofen post-operatively to those who abstained from NSAIDs for six weeks after surgery. It was hypothesized that a short course of ibuprofen post-operatively would not lead to inferior PRO scores, increased retear rates, nor increased complication rates after arthroscopic rotator cuff repair. METHODS: Patients of the primary surgeon who underwent arthroscopic rotator cuff repair between 2012 and 2022 were evaluated by retrospective chart review. In May 2017 the primary surgeon changed his protocol from avoiding NSAIDs for six weeks after surgery to routinely prescribing two weeks of Ibuprofen 800 mg TID post-operatively. Patients who avoided NSAIDs for six weeks were compared to patients who were prescribed NSAIDs post-operatively. Patient demographic data, pre-operative MRI results, pre-operative and post-operative PROs were collected from the EMR. Additionally, post-operative complications and repair failures requiring reoperation within one year were evaluated. RESULTS: 125 patients met inclusion criteria for this study with 36 patients in the NSAID group and 89 in the no NSAID group. When comparing improvement in PROs, the NSAID group reached MCID at one year in 83.8 % of patients and the no NSAID group reached MCID at one year in 73.9 % of patients. There was no significant difference between the groups in reaching MCID improvement at one year ($p = 0.471$). Five post-operative complications were reported in the no NSAID group and two in the NSAID group (5.7 % vs 5.4 %, respectively, $p = 0.827$). Finally, there was no significant difference in the percentage of post-operative rotator cuff repair failures requiring revision in the first year between the groups (2.3 % vs 2.7 %, $p = 1.000$). CONCLUSION: There was no difference in percent of patients improving their PRO by the MCID between the groups that used ibuprofen and the group that did not. There was also no difference in post-operative complication rates and rates of symptomatic retear requiring reoperation between the groups. This supports that a short course of NSAIDs post-operatively, specifically ibuprofen, after rotator cuff repair does not increase reoperation rates nor lead to a clinically significant decrease in PROs at one year.

Orthopedics/Bone and Joint Center

James CL, **Haan J**, **Wager SG**, Hegde Y, **Wolterink TD**, and **Muh S**. Comparing the Clinical and Radiographic Outcomes of Humeral Shaft Fractures by Treatment Type. *Cureus* 2024; 16(4):e58658. PMID: 38770447. Full Text

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PURPOSE: Humeral shaft fractures are common orthopedic injuries, representing 1-5% of all fractures. There is conflicting literature regarding the superiority of operative versus nonoperative treatment of these fractures. The purpose of this study was to examine functional outcomes and time to radiographic union in humeral shaft fractures with the hypothesis that both would be improved in patients treated operatively relative to those treated nonoperatively. METHODS: This retrospective cohort study examined patients with humeral shaft fractures treated at a single large healthcare system between 2010 and 2020. A chart

and radiograph review were performed to collect information on demographics, fracture, treatment, and outcome information. These measures were compared between patients treated operatively and nonoperatively. RESULTS: Five hundred seventeen adult patients meeting inclusion criteria were identified; 233 were treated nonoperatively, and 284 were treated operatively. The mean patient age was 50.2 years in those who underwent surgery relative to 59.9 years in those treated without surgery (P<0.001). Operatively-treated patients had significantly faster time to radiographic union at a median of 113 days compared to a median of 161 days in nonoperatively-treated patients (P=0.001). The operative group was made weight-bearing as tolerated significantly faster than the nonoperative group (84 days versus 98 days, respectively, P=0.002). No statistically significant difference was seen between the two treatment groups in rates of complications or range of motion at the time of radiographic union. However, patients who underwent surgery were found to be up to two times more likely to achieve full shoulder forward elevation by the time of their final follow-up than those treated without surgery (P=0.011). CONCLUSION: Patients with humeral shaft fractures treated operatively have faster time to union, earlier weight bearing, and no change in the rate of complications compared to patients treated nonoperatively.

Orthopedics/Bone and Joint Center
Sanii RY, **Kasto JK**, **Wines WB**, **Mahylis JM**, and **Muh SJ**. Utility of Artificial Intelligence in Orthopedic Surgery Literature Review: A Comparative Pilot Study. *Orthopedics* 2024; 47(3):e125-e130. PMID: 38147494. Request Article

OBJECTIVE: Literature reviews are essential to the scientific process and allow clinician researchers to advance general knowledge. The purpose of this study was to evaluate if the artificial intelligence (AI) programs ChatGPT and Perplexity.AI can perform an orthopedic surgery literature review. MATERIALS AND METHODS: Five different search topics of varying specificity within orthopedic surgery were chosen for each search arm to investigate. A consolidated list of unique articles for each search topic was recorded for the experimental AI search arms and compared with the results of the control arm of two independent reviewers. Articles in the experimental arms were examined by the two independent reviewers for relevancy and validity. RESULTS: ChatGPT was able to identify a total of 61 unique articles. Four articles were not relevant to the search topic and 51 articles were deemed to be fraudulent, resulting in 6 valid articles. Perplexity.AI was able to identify a total of 43 unique articles. Nineteen were not relevant to the search topic but all articles were able to be verified, resulting in 24 valid articles. The control arm was able to identify 132 articles. Success rates for ChatGPT and Perplexity. AI were 4.6% (6 of 132) and 18.2% (24 of 132), respectively. CONCLUSION: The current iteration of ChatGPT cannot perform a reliable literature review, and Perplexity.AI is only able to perform a limited review of the medical literature. Any utilization of these open AI programs should be done with caution and human quality assurance to promote responsible use and avoid the risk of using fabricated search results.

Orthopedics/Bone and Joint Center
Wolterink TD, **Gaudiani MA**, Beydoun RS, **Kasto JK**, Sanii RY, **Moutzouros V**, and **Muh S**. Anterior Cruciate Ligament Reconstruction Surgery Outcomes: A Comparison Between Patients Who Underwent the Procedure During the COVID-19 Pandemic and a Cohort Treated Prior to the Pandemic. *Cureus* 2024; 16(4):e57840. PMID: 38721188. Full Text

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Background and objective During the coronavirus disease 2019 (COVID-19) pandemic, many elective orthopedic surgeries, including anterior cruciate ligament reconstruction (ACLR), were temporarily postponed. The purpose of this study was to compare the outcomes of ACLR in patients who underwent surgery during the COVID-19 pandemic with those in a cohort treated before the pandemic. Materials and methods This retrospective review compared patients who underwent primary ACLR during two periods: March to June 2020 (the pandemic group) and January to December 2018 (the pre-pandemic group). Matched cohorts (1:1) were created using propensity matching. Time from injury-to-first visit, injury-to-

surgery, and first visit-to-surgery were calculated. Subjective and objective outcomes, minimal clinically important difference (MCID) achievement, and complication rates were recorded for up to two years postoperatively. Statistical analysis included ?2 or Fisher's exact tests for categorical data, and t- or Wilcoxon signed-rank tests for continuous data with significance set at P < 0.05. Results The pandemic and pre-pandemic groups consisted of 33 and 217 patients, respectively. Matched cohorts consisted of 33 patients each. The time from injury-to-surgery and the first visit-to-surgery was prolonged in the pandemic group. When unmatched, visual analog scale (VAS) scores at three months postoperatively and Patient-Reported Outcomes Measurement Information System (PROMIS)-pain interference (PI) at six months postoperatively and at the final follow-up were higher in the pandemic group. When matched, PROMIS-PI at six months postoperatively was higher in the pandemic group, and VAS scores at one year postoperatively were higher in the pre-pandemic group. MCID achievement and complication rates did not significantly differ between the groups. Conclusions ACLR procedures were significantly delayed in the early months of the COVID-19 pandemic. While patients treated before and during the pandemic experienced varying pain levels during recovery, their functional outcomes, MCID achievement, and complication rates did not differ significantly.

Orthopedics/Bone and Joint Center

Zhong J, Lee NJ, Crutchfield C, Mueller J, Ahmad C, Trofa D, and **Lynch TS**. Characteristics of early complications in isolated primary anterior cruciate ligament reconstruction surgery. *Eur J Orthop Surg Traumatol* 2024; Epub ahead of print. PMID: 38748272. Full Text

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PURPOSE: The early complications of isolated anterior cruciate ligament reconstruction surgery (ACLR) have not been well characterized using large databases. This study aims to characterize incidence, impact, and risk factors for short-term operative complications following elective, isolated ACLR surgery. We hypothesize that demographic and perioperative factors may predict 30-day complications after isolated ACLR. METHODS: This case-control analysis of the American College of Surgeons National Surgical Quality Improvement Program Database (2005-2017) used Current Procedural Terminology codes to identify elective, isolated ACLR patients. Patients undergoing concomitant procedures were excluded. Complications were analyzed using bivariate analysis against demographic variables. Multiple stepwise logistic regression was used to identify independent risk factors for morbidity after ACLR. RESULTS: A total 12,790 patients (37.0% female, p = 0.674) were included with a mean age of 32.2 years old (SD 10.7 years, p < 0.001). Mean BMI was 27.8 kg/m(2) (6.5) where 28.9% of patients had a BMI > 30 (p = 0.064). The most common complications were wound-related (0.57%). In cases with complications, there were higher rates of (1.3% vs 0.8%, p = 0.004) prolonged operation (> 1.5 h), higher rate (2.9% vs 1.8%, p = 0.004) of extended length of stay (≥ 1 day), unplanned reoperation (15.8% vs 0.3%, p < 0.001), and unplanned readmission (17.5% vs 0.3%, p < 0.001). Multivariate analysis showed prolonged operative time (p = 0.001), dyspnea (p = 0.008), and non-ambulatory surgery (p = 0.034) to be predictive of any complication. Dependent functional status (p = 0.091), mFI-5 > 0.2 (= 0.173), female sex (p = 0.191), obesity (p = 0.101), and smoking (p = 0.113) were not risk factors for complications. CONCLUSION: ACLR is associated with low rates of morbidity and readmissions. The most common comorbidities, complications, and predictors of morbidities were identified to aid surgeons in further reducing adverse outcomes of ACLR. Operative time > 1.5 h, dyspnea, and non-ambulatory surgery are predictive of complications.

Otolaryngology – Head and Neck Surgery

Malinzak L, **Gartrelle K**, **Sragi Z**, **Segal A**, **Prashar R**, and **Jesse MT**. Access to robotic assisted kidney transplant for recipients: a systematic review and call for reporting standards. *J Robot Surg* 2024; 18(1):239. PMID: 38833043. Full Text

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Robot-assisted kidney transplantation (RAKT) is a relatively novel, minimally invasive option for kidney transplantation. However, clarity on recipient selection in the published literature is lacking thereby significantly limiting interpretation of safety and other outcomes. This systematic review aimed to identify and synthesize the data on selection of RAKT recipients, compare the synthesized data to kidney transplant recipients across the USA, and explore geographical clusters of availability of RAKT. Systematic literature review, in accordance with PRISMA, via OVID MEDLINE, Embase, and Web of science from inception to March 5, 2023. All data entry double blinded and quality via Newcastle Ottawa Scale. 44 full-text articles included, encompassing approximately 2402 kidney transplant recipients at baseline but with considerable suspicion for overlap across publications. There were significant omissions of information across studies on patient selection for RAKT and/or analysis. Overall, the quality of studies was very low. Given suspicion of overlap across studies, it is difficult to determine how many RAKT recipients received living (LD) versus deceased donor (DD) organs, but a rough estimate suggests 89% received LD. While the current RAKT literature provides preliminary evidence on safety, there are significant omissions in reporting on patient selection for RAKT which limits interpretation of findings. Two recommendations: (1) international consensus is needed for reporting guidelines when publishing RAKT data and (2) larger controlled trials consistently reporting recipient characteristics are needed to clearly determine selection, safety, and outcomes across both LD and DD recipients.

Pathology and Laboratory Medicine
Allo G, **Sitarik AR**, **Redding A**, **Coleman CM**, **Cassidy-Bushrow AE**, **Gaba A**, and **Straughen JK**. Maternal COVID-19 exposure and placental characteristics. *PLoS One* 2024; 19(5):e0302682. PMID: 38781150. Full Text

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INTRODUCTION: The impact of COVID-19 on the placenta is poorly described, particularly among minority women. MATERIALS AND METHODS: This is a retrospective case-control study. Micro- and macroscopic placental pathologic findings were compared for 15 COVID-19 positive and 36 negative mothers. Cases and controls were frequency matched on gestational age, race, maternal comorbidities, and delivery type. Data from the electronic medical record were supplemented with independent review of microscopic slides. RESULTS: Placentas from cases and controls were similar except the median distance from the site of the cord insertion to the nearest disk margin was statistically significantly shorter among placentas from COVID-19 positive cases (3.5 versus 6.0 cm, p = 0.006). Case status was not associated with an increased risk of placental pathologies. CONCLUSION: There are few pathologic differences between placentas of COVID-19 positive and negative mothers. Additional studies are needed to investigate the role of timing of infection.

Pathology and Laboratory Medicine
Hutchings H, **Theisen B**, Cox J, and **Okereke I**. Transdiaphragmatic sarcomatoid carcinoma of the lung: A case report. *Int J Surg Case Rep* 2024; 119:109675. PMID: 38718493. Full Text

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INTRODUCTION: Pulmonary sarcomatoid carcinoma is a very rare primary tumor of the lung. Although usually aggressive, these tumors have not been described previously to invade through the diaphragm into the liver. We present a patient with a pulmonary sarcomatoid carcinoma with transdiaphragmatic spread into the dome of the liver. PRESENTATION OF CASE: An 82-year-old female with a lifetime non-smoking history presented with generalized fatigue, fever, night sweats, cough, and pleuritic chest pain. She had recently traveled to the western United States. Additionally, she had recently undergone periodontal deep cleaning with no peri-procedural antibiotics. Laboratory testing was significant for a leukocytosis of 13.5 white blood cells per microliter and a negative viral panel. Computed tomography and magnetic resonance imaging revealed a large heterogeneous mass extending from the right pulmonary hilum through the diaphragm. Although initial radiology reports suggested hepatic abscess, percutaneous fine needle aspiration was performed. Biopsy revealed pulmonary sarcomatoid carcinoma. She was begun on systemic treatment. DISCUSSION: Pulmonary sarcomatoid carcinoma can exhibit transdiaphragmatic invasion into the liver. This clinical situation can easily be confused with a hepatic abscess, but suspicion should remain for abscess. Clinical suspicion for neoplasm should warrant biopsy when technically possible. CONCLUSION: Although hepatic abscesses can exhibit transdiaphragmatic spread into the chest, pulmonary sarcomatoid carcinoma can also invade the abdomen. Biopsy should be performed during the evaluation and workup of the patient.

Pathology and Laboratory Medicine

Logan SJ, Dehner CA, **Alruwaii FI**, Din NU, Olson DR, Fritchie KJ, Charville GW, Blessing MM, and Folpe AL. Myoepithelial tumors of soft tissue and bone in children and young adults: A clinicopathologic study of 40 cases occurring in patients ≤ 21 Years of age. *Hum Pathol* 2024; 149:10-20. PMID: 38782103. Full Text

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Myoepithelial tumors of the soft tissue and bone occurring in patients 21 years of age and younger are rare, and their clinicopathologic features remain incompletely understood. We studied a well-characterized series of 40 such tumors. Cases were retrieved from our archives for the period 2009-2022 and re-reviewed. Available immunohistochemical and molecular genetic data was collected. Clinical information including available follow-up was obtained. The tumors occurred in 18 males and 22 females, ranging from 3 months to 21 years of age (median 11.5 years), and involved a wide variety of soft tissue (n = 36) and bone (n = 4) locations. Histologically benign myoepithelial tumors tended to occur in adolescents (median age 14.5 years; range 5-21 years), whereas myoepithelial carcinomas occurred in younger patients (median age 8.5 years; range 3 months-20 years). Microscopically, the tumors showed a complex admixture of epithelioid, plasmacytoid and spindled cells in a variably hyalinized, myxoid, chondroid or chondromyxoid background. Small subsets of histologically malignant tumors had rhabdoid or "round cell" features. Immunohistochemistry showed 35/40 (88%) cases to be positive with at least one keratin antibody. The 5 keratin-negative tumors were uniformly positive for S100 protein and/or SOX10 and expressed EMA (4 cases) and/or p63 (3 cases). EMA, SMA and GFAP were positive in 21/25 (84%), 13/21 (62%), and 8/21 (38%) tumors, respectively. SMARCB1 and SMARCA4 expression was retained in 29/31 (94%) and 22/22 (100%) of cases, respectively. FISH for EWSR1 gene rearrangement was positive in 6/18 (33%) tested cases. Two EWSR1-negative tumors were also FUS-negative. NGS identified EWSR1::POU5F1, FUS::KLF17, and BRD4::CITED1 gene fusions in 3 tested cases. Clinical follow-up (22 patients; median 23 months; range 1-119 months) showed 3 patients with local recurrences and 5 with distant metastases (lymph nodes, lung, and brain). Three patients died of disease, 3 were alive with

recurrent or unresectable disease, and 16 were disease-free. Adverse clinical outcomes were seen only in patients with malignant tumors. We conclude that myoepithelial neoplasms of soft tissue and bone are over-repesented in patients ≤21 years of age, more often histologically malignant, and potentially lethal. Histologic evaluation appears to reliably predict the behavior of these rare tumors.

Pathology and Laboratory Medicine
Merritt JK, **Fang X**, Caylor RC, Skinner SA, Friez MJ, Percy AK, and Neul JL. Normalized Clinical Severity Scores Reveal a Correlation between X Chromosome Inactivation and Disease Severity in Rett Syndrome. *Genes (Basel)* 2024; 15(5). PMID: 38790223. Full Text

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Rett Syndrome (RTT) is a severe neurodevelopmental disorder predominately diagnosed in females and primarily caused by pathogenic variants in the X-linked gene Methyl-CpG Binding Protein 2 (MECP2). Most often, the disease causing the MECP2 allele resides on the paternal X chromosome while a healthy copy is maintained on the maternal X chromosome with inactivation (XCI), resulting in mosaic expression of one allele in each cell. Preferential inactivation of the paternal X chromosome is theorized to result in reduced disease severity; however, establishing such a correlation is complicated by known MECP2 genotype effects and an age-dependent increase in severity. To mitigate these confounding factors, we developed an age- and genotype-normalized measure of RTT severity by modeling longitudinal data collected in the US Rett Syndrome Natural History Study. This model accurately reflected individual increase in severity with age and preserved group-level genotype specific differences in severity, allowing for the creation of a normalized clinical severity score. Applying this normalized score to a RTT XCI dataset revealed that XCI influence on disease severity depends on MECP2 genotype with a correlation between XCI and severity observed only in individuals with MECP2 variants associated with increased clinical severity. This normalized measure of RTT severity provides the opportunity for future discovery of additional factors contributing to disease severity that may be masked by age and genotype effects.

Pathology and Laboratory Medicine
Monga J, **Ghosh R**, **Guddeti R**, **Chitale D**, **Khan G**, and **Ghosh J**. MK591 (Quiflapon), a 5-lipoxygenase inhibitor, kills pancreatic cancer cells via downregulation of protein kinase C-epsilon. *Front Oncol* 2024; 14:1387535. PMID: 38746674. Full Text

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INTRODUCTION: Pancreatic tumors and cell lines derived from them exhibit elevated expression of 5-lipoxygenase (5-Lox), whereas non-tumor glands or normal cells do not exhibit this overexpression. Arachidonic acid stimulates pancreatic cancer cell growth via metabolic conversion through the 5-Lox pathway, and inhibition of 5-Lox activity decreases the viability of pancreatic cancer cells. However, the downstream signaling mechanisms through which 5-Lox exerts its effects on the survival of pancreatic cancer cells remain to be elucidated. METHODS: The effects of 5-Lox inhibition on cell proliferation, apoptosis, and invasive potential were investigated in pancreatic cancer cells. The protein expression was analyzed by Western blot. Apoptosis was analyzed by Annexin-V binding assay and by detecting the degradation of chromatin-DNA to nucleosomal fragments. The protein kinase C-epsilon (PKCε) activity was measured by an immunoprecipitation-kinase assay. The in vivo effects of MK591 were evaluated in pancreatic tumor xenograft model. RESULTS: MK591, a specific inhibitor of 5-Lox activity, killed pancreatic cancer cells via induction of apoptosis, involving externalization of phosphatidylserine, cleavage of PARP (poly-ADP ribose polymerase) and degradation of chromatin DNA to nucleosomes. MK591 effectively blocked in vitro invasion and soft-agar colony formation by pancreatic cancer cells and decreased pancreatic tumor growth in nude mice xenografts. Furthermore, inhibition of 5-Lox

downregulated K-Ras and inhibited phosphorylation of c-Raf and ERKs. Interestingly, 5-Lox inhibition induced apoptosis in pancreatic cancer cells without the inhibition of Akt but the protein level of PKCε was dramatically downregulated. Furthermore, inhibition of 5-Lox decreased the phosphorylation of Stat3 at Serine-727. Pre-treatment of pancreatic cancer cells with peptide activators of PKCε prevented apoptosis induced by 5-Lox inhibition, suggesting that the mechanism by which 5-Lox inhibition causes cell death in pancreatic cancer involves downregulation of PKCε. The combination of low doses of MK591 and gemcitabine synergistically reduced the oncogenic phenotype and killed pancreatic cancer cells by inducing apoptosis. DISCUSSION: These findings indicate that inhibition of 5-Lox interrupts an Akt-independent, PKCε-dependent survival mechanism in pancreatic cancer cells and suggest that metabolism of arachidonic acid through the 5-Lox pathway plays an integral part in the survival of pancreatic cancer cells via signaling through PKCε, an oncogenic, pro-survival serine/threonine kinase.

Pathology and Laboratory Medicine

Zhang Y, **Liu Z**, **Chopp M**, **Millman M**, **Li Y**, **Cepparulo P**, **Kemper A**, **Li C**, **Zhang L**, and **Zhang ZG**. Small extracellular vesicles derived from cerebral endothelial cells with elevated microRNA 27a promote ischemic stroke recovery. *Neural Regen Res* 2025; 20(1):224-233. PMID: 38767487. Full Text

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JOURNAL/nrgr/04.03/01300535-202501000-00030/figure1/v/2024-05-14T021156Z/r/image-tiff Axonal remodeling is a critical aspect of ischemic brain repair processes and contributes to spontaneous functional recovery. Our previous in vitro study demonstrated that exosomes/small extracellular vesicles (sEVs) isolated from cerebral endothelial cells (CEC-sEVs) of ischemic brain promote axonal growth of embryonic cortical neurons and that microRNA 27a (miR-27a) is an elevated miRNA in ischemic CEC-sEVs. In the present study, we investigated whether normal CEC-sEVs engineered to enrich their levels of miR-27a (27a-sEVs) further enhance axonal growth and improve neurological outcomes after ischemic stroke when compared with treatment with non-engineered CEC-sEVs. 27a-sEVs were isolated from the conditioned medium of healthy mouse CECs transfected with a lentiviral miR-27a expression vector. Small EVs isolated from CECs transfected with a scramble vector (Scra-sEVs) were used as a control. Adult male mice were subjected to permanent middle cerebral artery occlusion and then were randomly treated with 27a-sEVs or Scra-sEVs. An array of behavior assays was used to measure neurological function. Compared with treatment of ischemic stroke with Scra-sEVs, treatment with 27a-sEVs significantly augmented axons and spines in the peri-infarct zone and in the corticospinal tract of the spinal grey matter of the denervated side, and significantly improved neurological outcomes. In vitro studies demonstrated that CEC-sEVs carrying reduced miR-27a abolished 27a-sEV-augmented axonal growth. Ultrastructural analysis revealed that 27a-sEVs systemically administered preferentially localized to the pre-synaptic active zone, while quantitative reverse transcription-polymerase chain reaction and Western Blot analysis showed elevated miR-27a, and reduced axonal inhibitory proteins Semaphorin 6A and Ras Homolog Family Member A in the peri-infarct zone. Blockage of the Clathrin-dependent endocytosis pathway substantially reduced neuronal internalization of 27a-sEVs. Our data provide evidence that 27a-sEVs have a therapeutic effect on stroke recovery by promoting axonal remodeling and improving neurological outcomes. Our findings also suggest that suppression of axonal inhibitory proteins such as Semaphorin 6A may contribute to the beneficial effect of 27a-sEVs on axonal remodeling.

Pediatrics

McGoron L, Towner EK, **Johnson-Hopper T**, Martel MM, Trentacosta CJ, and Ondersma SJ. Proof-of-Concept Trial of a Tablet-based Program in Pediatrics to Motivate Parental Use of an Online Behavioral Parent Training Program. *Child Health Care* 2024; 53(3):205-222. PMID: Not assigned. Request Article

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Internet-based parent training is a promising intervention approach for child disruptive behavior. However, engagement in these interventions is limited. The Parenting Young Children Check-up (PYCC) was designed to improve engagement in internet-based parent training programs via three components: 1) an initial "check-up", 2) text messages, and 3) a website. This proof-of-concept trial used feedback from parents and pediatric clinic staff to evaluate feasibility as well as the extent to which the initial "check-up" was associated with behavioral intentions to use the PYCC website. Pediatric staff and parents rated the PYCC highly, and parents reported interest in using the PYCC website.

Pharmacy
Arena CJ, **Kenney RM**, **Eriksson E**, **Brar I**, and **Veve MP**. Prescribing Practices of Recommended Treatment for Trichomonas vaginalis and Chlamydia trachomatis after 2021 STI Treatment Guideline Update. *Sex Transm Dis* 2024; Epub ahead of print. PMID: 38709026. Full Text

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We evaluated the proportion of patients with trichomoniasis and chlamydial infections who received recommended versus non-recommended antibiotic therapy after the updated 2021 Sexually Transmitted Infections Guideline. Of 712 patients, 473 (66%) received recommended therapy. Receipt of emergency department care was independently associated with recommended therapy (adjOR, 2.1; 95% CI 1.5-2.9).

Pharmacy
August BA, and Kale-Pradhan PB. Management of invasive candidiasis: A focus on rezafungin, ibrexafungerp, and fosmanogepix. *Pharmacotherapy* 2024; Epub ahead of print. PMID: 38721866. Full Text

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Management of invasive fungal infections is challenging with growing antifungal resistance. Broad antifungal use has resulted in greater intrinsic and acquired resistance among Candida spp. It is important for clinicians to recognize the relationship between host susceptibility, site of infection, Candida resistance profiles, specific drug pharmacokinetics and pharmacodynamics, and the role of novel antifungal agents. This narrative review covers the role of rezafungin, ibrexafungerp, and fosmanogepix in the management of invasive candidiasis (IC). The PubMed Database, Embase, and ClinicalTrials.gov were searched between January 2006 and January 2024 using the following terms: rezafungin, CD101, ibrexafungerp, SCY-078, fosmanogepix, APX001, candidemia, and invasive candidiasis. Review articles, prospective clinical trials, and observational studies published in the English language were reviewed. Studies evaluating pharmacology, pharmacokinetics, efficacy, and safety in animals and humans were also reviewed. Promising data continues to emerge in support of novel drug therapies for IC and candidemia. Rezafungin possesses a unique pharmacodynamic profile that might be advantageous compared to other echinocandins, with a practical, once-weekly dosing interval. Ibrexafungerp, currently approved for vulvovaginal candidiasis, has been studied off-label for use in IC and candidemia, and initial data is encouraging. Lastly, fosmanogepix, a mechanistically novel, investigational antifungal agent, may be a potential future option in the management of IC and candidemia. Future research is needed to evaluate the potential use of these agents among diverse patient populations.

Plastic Surgery

Gonte MR, **Brooks C**, **Klomparens K**, **Greenberg Y**, and **Janevski P**. Surgical Management of Tumoral Calcinosis of the Hand: A Case Report. *J Hand Microsurg* 2024; 16(2). PMID: Not assigned. Request Article

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Primary tumoral calcinosis is a rare and benign condition characterized by calcium salt deposition in periarticular soft tissues. It typically presents as a firm, rubbery mass that arises around large joints. While an estimated 250 cases have been described since its discovery, very few cases have been identified in the hand. We present a case of multiple calcified masses in the hand, one of which required meticulous dissection from a digital neurovascular bundle, and our technique for surgical excision. We present this case to lower the threshold for clinical suspicion of tumoral calcinosis for patients who present with a soft tissue mass in the hand. Furthermore, we recommend prompt surgical excision due to low success rates of alternative treatment options and to prevent potential neurovasculature or tendon injury.

Public Health Sciences

Allo G, **Sitarik AR**, **Redding A**, **Coleman CM**, **Cassidy-Bushrow AE**, **Gaba A**, and **Straughen JK**. Maternal COVID-19 exposure and placental characteristics. *PLoS One* 2024; 19(5):e0302682. PMID: 38781150. Full Text

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Department of Public Health Sciences, Henry Ford Health, Detroit, MI, United States of America.

INTRODUCTION: The impact of COVID-19 on the placenta is poorly described, particularly among minority women. MATERIALS AND METHODS: This is a retrospective case-control study. Micro- and macroscopic placental pathologic findings were compared for 15 COVID-19 positive and 36 negative mothers. Cases and controls were frequency matched on gestational age, race, maternal comorbidities, and delivery type. Data from the electronic medical record were supplemented with independent review of microscopic slides. RESULTS: Placentas from cases and controls were similar except the median distance from the site of the cord insertion to the nearest disk margin was statistically significantly shorter among placentas from COVID-19 positive cases (3.5 versus 6.0 cm, p = 0.006). Case status was not associated with an increased risk of placental pathologies. CONCLUSION: There are few pathologic differences between placentas of COVID-19 positive and negative mothers. Additional studies are needed to investigate the role of timing of infection.

Public Health Sciences

Dhar S, Jinadatha C, Kilgore PE, Henig O, **Divine GW**, **Todter EN**, Coppin JD, Carter MJ, Chopra T, Egbert S, Carling PC, and Kaye KS. Lowering the Acquisition of Multi-drug Resistant Organism (MDROs) with Pulsed-xenon (LAMP) Study: a cluster randomized controlled, double-blinded, interventional crossover trial. *Clin Infect Dis* 2024; Epub ahead of print. PMID: 38743564. Full Text

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BACKGROUND: Environmental disinfection is essential for reducing spread of healthcare associated infections (HAIs). Previous studies report conflicting results regarding the effects of ultraviolet light (UV) in reducing infections. This trial evaluated the impact of adding pulsed xenon UV (PX-UV) to standard terminal cleaning in reducing environmentally-implicated HAIs (eiHAIs). METHODS: The LAMP trial was conducted in 2 hospitals (15 inpatient wards) utilizing a cluster randomized controlled, double-blinded, interventional crossover trial comparing standard terminal cleaning followed by either pulsed xenon ultraviolet (PX-UV) disinfection (intervention arm) or sham disinfection (control arm). The primary outcome was incidence of eiHAIs from clinical microbiology tests on the 4th day of stay or later or within 3 days after discharge from the study unit. EiHAIs included clinical cultures positive for vancomycin-resistant enterococci (VRE), extended spectrum beta-lactamase-producing Escherichia coli or Klebsiella pneumonia, methicillin-resistant Staphylococcus aureus (MRSA), and Acinetobacter baumannii, and stool PCR positive for Clostridiodes difficile. FINDINGS: Between May 18, 2017 to Jan 7, 2020, 25,732 patients were included, with an incidence of 601 eiHAI and 180,954 patient days. There was no difference in the rate of eiHAIs in the intervention and sham arms (3.49 vs 3.17 infections/1000 patient days respectively, RR 1.10 CI (0.94, 1.29, p= 0.23)). Study results were similar when stratified by eiHAI type, hospital, and unit type. CONCLUSION: The LAMP study failed to demonstrate an effect of the addition of UV light disinfection following terminal cleaning on reductions in rates of eiHAIs. Further investigations targeting hospital environmental surfaces and the role of no touch technology to reduce HAIs are needed.

Public Health Sciences

Fadel HA, **Pawloski JA**, **Anzalone AJ**, **Haider S**, **Schultz LR**, **Kalkanis SN**, **Robin AM**, and **Lee IY**. Laser interstitial thermal therapy for first-line treatment of insular glioma. *J Neurosurg* 2024; 1-12. Epub ahead of print. PMID: 38788240. Full Text

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OBJECTIVE: Insular gliomas pose a significant surgical challenge due to the complex surrounding functional and vascular anatomy. The authors report their experience using a novel framework for the treatment of insular gliomas with laser interstitial thermal therapy (LITT) and provide representative case examples emphasizing indications, rationale, and technical pearls. METHODS: A prospectively gathered institutional database was used to identify patients with newly diagnosed insular gliomas who underwent LITT between 2015 and 2023. The proposed framework of insular glioma management is guided by tumor size and extent of extra-insular tumor involvement. Patients with tumors localized to the insula (insula-only) were treated with single-session or staged LITT. Patients with insular tumors with frontotemporal involvement (insular+) were treated with insular LITT and standard frontotemporal resection of extra-insular tumor. Clinical and volumetric lesional characteristics were analyzed, with particular emphasis on extent of cytoreductive treatment and safety. RESULTS: Of the 261 patients treated at the authors' institution with LITT between 2015 and 2023, 33 LITT procedures were identified involving 22 unique patients with treatment-naive insular gliomas. Of the 22 patients, 12 had insular-only tumors and were treated with LITT alone, while 10 patients had insular+ lesions and were treated with LITT and resection. The median tumor volume for insular-only tumors was 13.4 cm3 (IQR 10.6, 26.3 cm3), with a median extent of treatment of 100% (IQR 92.1%, 100%). Insular+ lesions were significantly larger, with a median volume of 81.2 cm3 (IQR 51.9, 97 cm3) and median extent of treatment of 96.6% (IQR 93.7%, 100%). All patients with insular-only tumors were discharged the day after ablation, while

insular+ patients had significantly longer hospital stays, with 50% staying more than 3 days. Overall, 8% of insular-only patients had permanent neurological deficits compared with 33% of insular+ patients. Two patients' tumors progressed during follow-up: one patient with WHO grade 4 astrocytoma and the other with diffuse glioma not otherwise specified. Patients with grade 4 tumors had the highest rate of permanent neurological deficit (43%) and a larger decline in postoperative Karnofsky Performance Status score ($p = 0.046$). CONCLUSIONS: The authors present their experience using a novel insular glioma treatment paradigm that incorporates LITT into the broader framework of insular glioma surgery. Their findings suggest that insular LITT is feasible and may allow for high rates of cytoreduction while potentially ameliorating the risks of conventional insular glioma surgery.

Public Health Sciences

Hauk M, **Todter E**, **Sitarik A**, **Lin CH**, **Joseph C**, **Kim H**, **Eapen A**, **Johnson C**, Ownby D, **Wegienka G**, and **Zoratti E**. Associations between FeNO and clinical characteristics of asthma and allergy among Black and White children. *J Allergy Clin Immunol Pract* 2024; Epub ahead of print. PMID: 38821439. Full Text

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Public Health Sciences

Jumah A, **Fu S**, **Albanna AJ**, **Agarwal U**, **Fana M**, **Choudhury O**, **Idris A**, **Elfaham A**, **Iqbal Z**, **Schultz L**, **Latack K**, **Brady M**, **Scozzari D**, and **Ramadan AR**. Early vs late anticoagulation in acute ischemic stroke with indications outside atrial fibrillation. *J Stroke Cerebrovasc Dis* 2024; 33(7):107757. PMID: 38705498. Full Text

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BACKGROUND: Current literature lacks guidance on the safety of administering anticoagulation in acute ischemic stroke with emergent indications that require anticoagulation other than atrial fibrillation. Therefore, we tend to rely on studies investigating acute ischemic stroke in atrial fibrillation for anticoagulation recommendations. METHODS: We retrospectively reviewed data for patients with acute ischemic stroke who had a non-atrial fibrillation emergent indication for anticoagulation (e.g., intra-arterial thrombus, intracardiac thrombus, acute coronary syndrome, acute limb ischemia, deep vein thrombosis

and pulmonary embolism) diagnosed within 3 days of acute ischemic stroke. Patients who received anticoagulation ≤ 3 days of stroke onset (Group A) were compared to those who either received it afterwards or did not receive it at all (Group B). RESULTS: Out of the 558 patients, only 88 patients met our inclusion criteria. Of the total cohort, 55.7 % patients were males, and basic demographics were similar in both groups except for milder strokes in Group A (national institute of health stroke scale 6 vs. 12.5, p = 0.03). Only 2 patients in Group A and 1 patient in Group B developed intracranial hemorrhage, which was not statistically significant. Group A patients had a lower incidence of both new diagnosis (2 % vs. 34.2 % %, p < 0.001) and propagation of an established venous thromboembolism. They also had a lower rate of any thromboembolic complication (2 % vs. 42 %, p < 0.001). CONCLUSION: Early anticoagulation (i.e., ≤ 3 days) in non-atrial fibrillation ischemic stroke patients with an emergent indication may be safe and carry a lower risk of thromboembolic complications than later anticoagulation.

Public Health Sciences

Mahmood S, **Sallowm Y**, Affan M, **Schultz L**, **Cerghet M**, and **Ali A**. Radiological features of patients with headache as a presenting symptom of neurosarcoidosis. *Headache* 2024; Epub ahead of print. PMID: 38780214. Full Text

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OBJECTIVE: To describe the radiological features of patients with headache as a presenting symptom of neurosarcoidosis. BACKGROUND: Neurologic complications occur in approximately 5%-10% of patients with sarcoidosis, and approximately 50% of these patients have neurologic deficits at the time sarcoidosis is first diagnosed. A wide spectrum of central and peripheral nervous system clinical manifestations may be observed, including cranial nerve palsies, sensory and/or motor deficits, and headache. Magnetic resonance imaging (MRI) results in patients with neurosarcoidosis may include abnormal contrast enhancement, structural masses, and demyelinating lesions. METHODS: This single-center retrospective cohort study assessed patients who were diagnosed with neurosarcoidosis in an urban tertiary care center between 1995 and 2016. We included patients who had MRI results at the time of diagnosis. Patients were divided into two groups based on the presence or absence of headache as a presenting symptom. The MRI result of meningeal contrast enhancement was reviewed. RESULTS: Of the 110 patients analyzed, 30 (27.3%) had an initial presenting symptom of headache while 80 (72.7%) did not. Patients with headache had a higher proportion of meningeal contrast enhancement on MRI (66.7% [20/30] vs. 25.0% [20/80]; p < 0.001) and leptomeningeal involvement (53.3% [16/30] vs. 7.5% [6/80], p < 0.001) compared to patients with no headache. However, those with headache had a lower proportion of spinal cord localization (13.8% [4/29] vs. 34.2% [26/76], p = 0.038) and intraparenchymal central nervous system involvement (16.7% [5/30] vs. 51.3% [41/80], p = 0.001) compared to patients with no headache. CONCLUSION: Patients with neurosarcoidosis who presented with headache as an initial symptom had a higher proportion of meningeal contrast enhancement seen by MRI than patients who presented with other neurological symptoms. This suggests a clinico-radiologic link between headache and meningeal disruption in patients with neurosarcoidosis.

Public Health Sciences

Rodriguez LA, Finertie H, Neugebauer RS, Gosiker B, Thomas TW, Karter AJ, Gilliam LK, Oshiro C, An J, Simonson G, **Cassidy-Bushrow AE**, Dombrowski S, Nolan M, O'Connor PJ, and Schmittdiel JA. Race and ethnicity and pharmacy dispensing of SGLT2 inhibitors and GLP-1 receptor agonists in type 2 diabetes. *Lancet Reg Health Am* 2024; 34:100759. PMID: 38745886. Full Text

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BACKGROUND: Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2i) and Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RA) improve cardiorenal outcomes in patients with type 2 diabetes. Equitable use of SGLT2i and GLP-1 RA has the potential to reduce racial and ethnic health disparities. We evaluated trends in pharmacy dispensing of SGLT2i and GLP-1 RA by race and ethnicity. METHODS: Retrospective cohort study of patients (≥18 years) with type 2 diabetes using 2014-2022 electronic health record data from six US care delivery systems. Entry was at earliest pharmacy dispensing of any type 2 diabetes medication. We used multivariable logistic regression to evaluate the association between pharmacy dispensing of SGLT2i and GLP1-RA and race and ethnicity. FINDINGS: Our cohort included 687,165 patients (median 6 years of dispensing data; median 60 years; 0.3% American Indian/Alaska Native (AI/AN), 16.6% Asian, 10.5% Black, 1.4% Hawaiian or Pacific Islander (HPI), 31.1% Hispanic, 3.8% Other, and 36.3% White). SGLT2i was lower for AI/AN (OR 0.80, 95% confidence interval 0.68-0.94), Black (0.89, 0.86-0.92) and Hispanic (0.87, 0.85-0.89) compared to White patients. GLP-1 RA was lower for AI/AN (0.78, 0.63-0.97), Asian (0.50, 0.48-0.53), Black (0.86, 0.83-0.90), HPI (0.52, 0.46-0.57), Hispanic (0.69, 0.66-0.71), and Other (0.78, 0.73-0.83) compared to White patients. INTERPRETATION: Dispensing of SGLT2is, and GLP-1 RAs was lower in minority group patients. There is a need to evaluate approaches to increase use of these cardiorenal protective drugs in patients from racial and ethnic minority groups with type 2 diabetes to reduce adverse cardiorenal outcomes and improve health equity. FUNDING: Patient-Centered Outcomes Research Institute and National Institutes of Health.

Public Health Sciences

Schildroth S, Geller RJ, Wesselink AK, Lovett SM, Bethea TN, Claus Henn B, Harmon QE, Taylor KM, Calafat AM, **Wegienka G**, Gaston SA, Baird DD, and Wise LA. Hair product use and urinary biomarker concentrations of non-persistent endocrine disrupting chemicals among reproductive-aged Black women. *Chemosphere* 2024; 361:142442. PMID: 38810806. Request Article

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BACKGROUND: Studies have shown an association between hair product use and adverse health outcomes. Scientists have hypothesized that exposure to endocrine-disrupting chemicals (EDCs) drives these associations, but few studies have directly evaluated associations between hair product use and biomarkers of EDCs. Even more limited are studies of Black women, who frequently use EDC-containing products (e.g., hair relaxers). OBJECTIVE: We estimated associations between hair product use and EDC biomarker concentrations. METHODS: We leveraged cross-sectional data from the Study of Environment, Lifestyle, and Fibroids, a cohort of females aged 23-34 years who self-identified as Black/African American from the Detroit-metropolitan area (USA; n = 425). On structured questionnaires, participants reported their past 24-h and past 12-month use of hair products, including

relaxers/straighteners/perms, styling products, moisturizers, oils, and hair food. We quantified urinary concentrations of 19 phthalate/phthalate alternative metabolites, 7 phenols, and 4 parabens using high performance liquid chromatography isotope dilution tandem mass spectrometry. EDC biomarker concentrations were creatinine-adjusted and natural log-transformed. We used multivariable linear regression to estimate mean percent differences in EDC biomarker concentrations and 95% confidence intervals (CIs) associated with hair product use, adjusting for sociodemographic confounders. RESULTS: Hair product use was associated with greater concentrations of multiple EDC biomarkers. Notably, use of hair products in the previous 24 h (compared with non-use) was associated with 16.2% (95% CI = 0.7%, 35.9%), 35.0% (95% CI = 2.6%, 77.6%), and 32.3% (95% CI = 8.8%, 92.0%) higher concentrations of mono-isobutyl phthalate, methyl paraben, and ethyl paraben, respectively. Use of hair relaxers/straighteners/perms, styling products, moisturizers, oils, and hair food in the past 12 months was also associated with higher concentrations of multiple phthalate, phenol, and paraben biomarkers. CONCLUSION: Hair product use was associated with higher biomarker concentrations of multiple phthalates, phenols, and parabens. These findings suggest that hair products are potentially important exposure sources for hormonally-active chemicals among Black women.

Public Health Sciences

Schildroth S, Wesselink AK, Bethea TN, Henn BC, Friedman A, Fruh V, Coleman CM, Lovett SM, Vines AI, Sjodin A, Botelho JC, Calafat AM, **Wegienka G**, Weuve J, Baird DD, and Wise LA. A Prospective Cohort Study of Persistent Endocrine Disrupting Chemicals and Perceived Stress. *Am J Epidemiol* 2024; Epub ahead of print. PMID: 38803157. Full Text

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Henry Ford Health System, Detroit, Michigan, United States.

Persistent endocrine disrupting chemicals (EDCs) can dysregulate the stress response. We evaluated associations between persistent EDCs and perceived stress among participants from the Study of Environment, Lifestyle and Fibroids (n=1,394), a prospective cohort study of Black women. Participants completed the Perceived Stress Scale (PSS-4) at baseline, and every 20 months through 60 months (range of scores: 0-16); higher scores indicated higher stress. EDCs, including per- and polyfluoroalkyl substances (PFAS), polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), and organochlorine pesticides, were quantified in plasma samples at baseline. We fit Bayesian Kernel Machine Regression (BKMR) and linear mixed effects models to estimate associations of EDCs (as a mixture and individually) with PSS-4 scores at baseline and at each follow-up visit, respectively. Increasing percentiles of the mixture were not strongly associated with PSS-4 scores at baseline, and no interactions were observed among EDCs. Several individual EDCs (e.g., PFDA, PCB 118, PBDE 99) were associated with higher PSS-4 scores at baseline or follow-up, while other EDCs (e.g., PCB 138/158) were associated with lower PSS-4 scores at baseline or follow-up. The directionality of associations for individual EDCs was inconsistent across follow-up visits. In conclusion, specific EDCs may be associated with perceived stress in Black women.

Public Health Sciences

Tinsley SA, **Finati M**, **Stephens A**, **Chiarelli G**, **Cirulli GO**, **Williams E**, **Morrison C**, **Richard C**, **Hares K**, Sood A, Buffi N, Lughezzani G, Bettocchi C, Salonia A, Briganti A, Montorsi F, Carrieri G, **Rogers C**, and **Abdollah F**. Race has no impact on prostate cancer-specific mortality, when comparing patients with similar risk of other-cause mortality: An analysis of a population-based cohort. *Cancer* 2024; Epub ahead of print. PMID: 38804713. Full Text

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BACKGROUND: Other-cause mortality (OCM) can serve as a surrogate for access-to-care. The authors sought to compare prostate cancer-specific mortality (PCSM) in Black versus White men matched based on their calculated OCM risk. METHODS: The Surveillance, Epidemiology, and End Results (SEER) database was queried for Black and White men diagnosed with prostate cancer between 2004 to 2009, to collect long-term follow-up. A Cox regression was used to calculate the OCM risk using all available covariates. This calculated OCM risk was used to construct a 1:1 propensity score matched (PSM) cohort. Then, a competing-risks multivariable tested the impact of race on PCSM. RESULTS: A total of 94,363 patients were identified, with 19,398 Black men and 74,965 White men. The median (IQR) follow-up was 11.3 years (9.8-12.8). In the unmatched-cohort at 10-years, PCSM and OCM were 5.5% versus 3.5% and 13.8% versus 8.4% in non-Hispanic Black (NHB) versus non-Hispanic White (NHW) patients (all $p < .0001$). The standardized mean difference was <0.15 for all covariates, indicating a good match. In the matched cohort at 10-years, OCM was 13.6% and 10.0% in NHB versus NHW ($p < .0001$), whereas the PCSM was 5.3% versus 4.7% ($p < .01$). On competing-risks multivariable analysis on PCSM, Black men had a hazard ratio of 1.08 (95% confidence interval, 0.98-1.20) compared to White men with a $p = .13$. CONCLUSIONS: The results of this study showed similar PCSM in Black and White patients, when matched with their calculated OCM risk. This report is the first to indicate at a population-based level that race has no impact on PCSM. PLAIN LANGUAGE SUMMARY: Prostate cancer is a very common cancer among men and it is associated with health disparities that disproportionately impact Black men compared to White men. There is an on-going discussion of whether disparities between these two groups stem from genetic or environmental factors. This study sought to examine if matching based on overall health status, a proxy for the impact of social determinants of health, mitigated significant differences in outcomes. When matched using risk of death from any cause other than prostate cancer, Black and White men had no significant differences in prostate cancer death.

Public Health Sciences

Valeriote FA, Brown SL, Media J, **Li P**, Maheshwari M, and Shaw J. Novel Small Molecule, UTS-1401, as a Radioprotector for Total-Body Irradiation. *Radiat Res* 2024; Epub ahead of print. PMID: 38802104. Request Article

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We report on a new radioprotector, UTS-1401, a small molecule that was synthesized (by one of us, JS) and evaluated here for its radioprotective effect against total-body irradiation (TBI). Female and male NIH Swiss mice were subjected to TBI at doses of 6.5, 7.5 and 8.5 Gy either with or without a 24 h pretreatment of UTS-1401 given ip and observed for 30 days. Survival rates were significantly increased when mice were treated with UTS-1401 compared to those not treated. The radioprotective effect of UTS-

1401 was drug-dose dependent for male mice exposed to 8.5 Gy TBI with 150 mg/kg of UTS-1401 as the optimal dose. The radioprotective effect of UTS-1401 on female mice exposed to 8.5 Gy TBI was observed at 50, 100, and 150 mg/kg, with no dose response relationship noted. Female mice were more radioresistant than male mice with LD50/30 values of 7.8 Gy vs. 6.8 Gy, respectively. Weight changes after UTS-1401 alone showed a significant body weight increase at 150 mg/kg. Both the ip and iv route for UTS-1401 were similarly effective for male mice exposed to 8 Gy TBI. Further analysis using an endogenous spleen colony assay demonstrated that pretreatment of UTS-1401 for up to 72h prior to TBI protected both spleen weight and hematopoietic stem cells with a treated/untreated ratio between 2.0 and 3.2 for the latter for times between 0.5 h and 72 h. A separate in vivo study showed that pretreatment of UTS-1401 protected bone marrow CFU-GM for mice exposed to TBI. In summary, UTS-1401 is a promising small-molecule radioprotective agent as demonstrated by whole animal, hematopoietic stem cell and bone marrow myeloid progenitor cell survival.

Pulmonary and Critical Care Medicine
Arora S, Vallabhajosyula S, **Aggarwal V**, **Basir MB**, **Kelly B**, and Atreya AR. Novel Risk Stratification and Hemodynamic Profiling in Acute Pulmonary Embolism: A Proposed Classification Inspired by Society for Cardiovascular Angiography and Intervention Shock Staging. *Interv Cardiol Clin* 2024. Epub ahead of print. PMID: Not assigned. Full Text

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Pulmonary and Critical Care Medicine
Gastesi A, and **Kapadia D**. Primary pleural lymphoma. *Respir Med Case Rep* 2024; 50. PMID: Not assigned. Full Text

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Primary pleural lymphoma is very rare and occurs in only seven percent (7%) of lymphoma cases [1]. There are very few reports of primary pleural lymphoma and even then, it has been described in association with Human Immunodeficiency Virus (HIV) infection or pyothorax [2]. However, we report a case of a patient with no history of HIV or pyothorax who presented with chronic cough and eventually progressively worsening dyspnea and found to have pleural thickening and a pleural-based mass. He was diagnosed with a rare case of primary pleural Hodgkin's lymphoma via thoracoscopy.

Radiation Oncology
Bhatnagar AR, **Siddiqui F**, **Khan G**, **Pompa R**, **Kwon D**, and **Nyati S**. Long-Term Follow-Up of Phase I Trial of Oncolytic Adenovirus-Mediated Cytotoxic and Interleukin-12 Gene Therapy for Treatment of Metastatic Pancreatic Cancer. *Biomedicines* 2024; 12(5). PMID: 38791027. Full Text

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The long-term follow-up findings of the phase I trial evaluating the efficacy of oncolytic adenovirus-mediated cytotoxic and interleukin-12 gene therapy in metastatic pancreatic cancer (mPC) seem very promising. The study employed a replication-competent Adenovector in combination with chemotherapy in a dose-escalation format. The trial demonstrated a clinically meaningful median overall survival (OS) benefit, with patients in the highest dose cohort exhibiting an impressive median OS of 18.4 months. This contrasts starkly with patients receiving lower doses who experienced a median OS of 4.8 and 3.5 months, respectively. Remarkably, subject number 10, who received the highest dose, demonstrated an extraordinary survival of 59.1 months, presenting a compelling case for further exploration. Additionally, this patient displayed complete responses in lung and liver metastases, a rare occurrence in mPC treatment. Statistical analyses supported the observed survival benefit. The unprecedented OS results emphasize the potential of this treatment strategy and pave the way for future investigations into this promising gene therapy approach.

Radiation Oncology

Fang B, McGeachy P, Husain S, Meyer T, **Thind K**, and Martell K. Acute toxicity outcomes from salvage high-dose-rate brachytherapy for locally recurrent prostate cancer after prior radiotherapy. *J Contemp Brachytherapy* 2024; 16(2):111-120. PMID: 38808210. Full Text

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PURPOSE: Isolated intra-prostatic recurrence of prostate adenocarcinoma after definitive radiotherapy presents a challenging clinical scenario. Salvage options require specialized expertise and pose risks of harm. This study aimed to present the acute toxicity results from using salvage high-dose-rate brachytherapy (sHDR-BT) as treatment in locally recurrent prostate cancer cases. MATERIAL AND METHODS: Seventeen consecutive patients treated with sHDR-BT between 2019 and 2022 were evaluated retrospectively. Eligible patients had to have received curative intent prostate radiotherapy previously, and showed evidence of new biochemical failure. Evaluation with American Urological Association (AUA) and Common Terminology Criteria for Adverse Events (CTCAE) symptom assessments were performed for each case. RESULTS: The median (inter-quartile range) age prior to salvage treatment was 68 (66-74) years. The median post-sHDR-BT follow-up time was 20 (13-24) months. At baseline prior to sHDR-BT, 8 (47%) patients had significant lower urinary tract symptoms. The median AUA score prior to sHDR-BT was 7 (3-18). Three (18%) patients reported irregular bowel function and 2 (12%) reported hematochezia prior to sHDR-BT. One-month post-treatment, the median AUA score was 13 (8-21, p = 0.21). Using CTCAE scoring, there were no cases of grade 2+ bowel or rectal toxicity, and no cases of grade 3+ urinary toxicity. Reported grade 2 urinary toxicities included 10 (59%) cases of bladder spasms, 2 (12%) cases of incontinence, 1 (6%) urinary obstruction, and 4 (24%) reports of urinary urgency. All these adverse events were temporary. CONCLUSIONS: This study adds to the existing literature by demonstrating that the acute toxicity profile of sHDR-BT is acceptable even without intra-operative magnetic resonance (MR) guidance or image registration. Further study is ongoing to determine long-term efficacy and toxicity of treatment.

Radiation Oncology

Herr DJ, Yin H, Bergsma D, Dragovic AF, Matuszak M, Grubb M, Dominello M, **Movsas B**, Kestin LL, Boike T, Bhatt A, Hayman JA, Jolly S, Schipper M, and Paximadis P. Factors associated with acute esophagitis during radiation therapy for lung cancer. *Radiother Oncol* 2024; 197:110349. PMID: 38815695. Full Text

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INTRODUCTION: Limiting acute esophagitis remains a clinical challenge during the treatment of locally advanced non-small cell lung cancer (NSCLC). METHODS: Demographic, dosimetric, and acute toxicity data were prospectively collected for patients undergoing definitive radiation therapy +/- chemotherapy for

stage II-III NSCLC from 2012 to 2022 across a statewide consortium. Logistic regression models were used to characterize the risk of grade 2 + and 3 + esophagitis as a function of dosimetric and clinical covariates. Multivariate regression models were fitted to predict the 50 % risk of grade 2 esophagitis and 3 % risk of grade 3 esophagitis. RESULTS: Of 1760 patients, 84.2 % had stage III disease and 85.3 % received concurrent chemotherapy. 79.2 % of patients had an ECOG performance status ≤ 1. Overall rates of acute grade 2 + and 3 + esophagitis were 48.4 % and 2.2 %, respectively. On multivariate analyses, performance status, mean esophageal dose (MED) and minimum dose to the 2 cc of esophagus receiving the highest dose (D2cc) were significantly associated with grade 2 + and 3 + esophagitis. Concurrent chemotherapy was associated with grade 2 + but not grade 3 + esophagitis. For all patients, MED of 29 Gy and D2cc of 61 Gy corresponded to a 3 % risk of acute grade 3 + esophagitis. For patients receiving chemotherapy, MED of 22 Gy and D2cc of 50 Gy corresponded to a 50 % risk of acute grade 2 + esophagitis. CONCLUSIONS: Performance status, concurrent chemotherapy, MED and D2cc are associated with acute esophagitis during definitive treatment of NSCLC. Models that quantitatively account for these factors can be useful in individualizing radiation plans.

Radiation Oncology

Summerfield N, Morris E, Banerjee S, He Q, **Ghanem AI**, Zhu S, Zhao J, Dong M, and Glide-Hurst C. Enhancing Precision in Cardiac Segmentation for MR-Guided Radiation Therapy through Deep Learning. *Int J Radiat Oncol Biol Phys* 2024; Epub ahead of print. PMID: 38797498. Full Text

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INTRODUCTION: Cardiac substructure dose metrics are more strongly linked to late cardiac morbidities than whole-heart metrics. MR-guided radiation therapy (MRgRT) enables substructure visualization during daily localization, allowing potential for enhanced cardiac sparing. We extend a publicly available state-of-the-art deep learning (DL) framework, nnU-Net, to incorporate self-distillation (nnU-Net.wSD) for substructure segmentation for MRgRT. METHODS: Eighteen (Institute A) patients who underwent thoracic or abdominal radiation therapy on a 0.35 T MR-guided linac were retrospectively evaluated. On each image, one of two radiation oncologists delineated reference contours of 12 cardiac substructures (chambers, great vessels, and coronary arteries) used to train (n=10), validate (n=3), and test (n=5) nnU-Net.wSD leveraging a teacher-student network and comparing to standard 3D U-Net. The impact of using simulation data or including 3-4 daily images for augmentation during training was evaluated for nnU-Net.wSD. Geometric metrics (Dice similarity coefficient (DSC), mean distance to agreement (MDA), and 95% Hausdorff distance (HD95)), visual inspection, and clinical dose volume histograms (DVHs) were evaluated. To determine generalizability, Institute A's model was tested on an unlabeled dataset from Institute B (n=22) and evaluated via consensus scoring and volume comparisons. RESULTS: nnU-Net.wSD yielded a DSC (reported mean ± standard deviation) of 0.65±0.25 across the 12 substructures (Chambers: 0.85±0.05, Great Vessels: 0.67±0.19, and Coronary Arteries 0.33±0.16, mean MDA <3 mm, and mean HD95 <9 mm) while outperforming the 3D U-Net (0.583±0.28, $p<0.01$). Leveraging fractionated data for augmentation improved over a single MR-SIM timepoint (0.579±0.29, $p<0.01$). Predicted contours yielded DVHs that closely matched the clinical treatment plans where mean and D(0.03cc) doses deviated by 0.32±0.5 Gy and 1.42±2.6 Gy respectively. No statistically significant differences between Institute A and B volumes ($p>0.05$) for 11 of 12 substructures with larger volumes requiring minor changes and coronary arteries exhibiting more variability. CONCLUSIONS: This work is a critical

step to rapid and reliable cardiac substructure segmentation to improve cardiac sparing in low-field MRgRT.

Rheumatology

Robinson C, Minhas JS, **Kisule A**, and **Zebda H**. Eosinophilic Granulomatosis With Polyangiitis: A Case Report. *Cureus* 2024; 16(4):e58211. PMID: 38741799. Full Text

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Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare form of necrotizing small-to-medium vessel vasculitis that can be associated with antineutrophil cytoplasmic antibody (ANCA) positivity, asthma, and eosinophilia. We present the case of a 65-year-old male with a past medical history of asthma who presented to the emergency department with bilateral upper and lower extremity paresthesias, as well as right foot drop, persisting for a two-week duration. His lab work revealed leukocytosis of 20.6 K/uL with 12.36 K/uL of absolute eosinophils as well as elevated inflammatory markers with an erythrocyte sedimentation rate of 32 mm/hr and CRP of 7.3 mg/dL. Both c-ANCA and p-ANCA titers were also elevated at 1:320. An eventual MRI of the entire spine did not reveal any neurologic or anatomic lesions to explain the patient's symptoms. CT imaging was also remarkable for airspace opacities involving the anterior right and bilateral lower posterior lung regions, as well as pansinusitis. A nerve biopsy showed axonopathy as well as evidence of healed vasculitis. Pulse dose steroids were started, which conferred benefits to the patient after other forms of treatment were unsuccessful. Given the rarity of EGPA, we think it is important to add new cases to the literature with a thorough discussion of the steps leading up to how the diagnosis was made.

Sleep Medicine

Roth T. Letter to the Editor regarding: "Implications of Oxybate Dosing Regimen for Sleep, Sleep Architecture, and Disrupted Nighttime Sleep in Patients with Narcolepsy: A Commentary" by R. Rosenberg et al. *Neurol Ther* 2024; Epub ahead of print. PMID: 38795308. Full Text

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Surgery

Ahmed O, Doyle MBM, **Abouljoud MS**, Alonso D, Batra R, Brayman KL, Brockmeier D, Cannon RM, Chavin K, Delman AM, DuBay DA, Finn J, Fridell JA, Friedman BS, Fritze DM, Ginos D, Goldberg DS, Halff GA, Karp SJ, Kohli VK, Kumer SC, Langnas A, Locke JE, Maluf D, Meier RPH, Mejia A, Merani S, Mulligan DC, Nibuhanupudy B, Patel MS, Pelletier SJ, Shah SA, Vagefi PA, Vianna R, Zibari GB, Shafer TJ, and Orloff SL. Liver Transplant Costs and Activity After United Network for Organ Sharing Allocation Policy Changes. *JAMA Surg* 2024; Epub ahead of print. PMID: 38809546. Full Text

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IMPORTANCE: A new liver allocation policy was implemented by United Network for Organ Sharing (UNOS) in February 2020 with the stated intent of improving access to liver transplant (LT). There are growing concerns nationally regarding the implications this new system may have on LT costs, as well as access to a chance for LT, which have not been captured at a multicenter level. OBJECTIVE: To characterize LT volume and cost changes across the US and within specific center groups and demographics after the policy implementation. DESIGN, SETTING, AND PARTICIPANTS: This cross-sectional study collected and reviewed LT volume from multiple centers across the US and cost data with attention to 8 specific center demographics. Two separate 12-month eras were compared, before and after the new UNOS allocation policy: March 4, 2019, to March 4, 2020, and March 5, 2020, to March 5, 2021. Data analysis was performed from May to December 2022. MAIN OUTCOMES AND MEASURES: Center volume, changes in cost. RESULTS: A total of 22 of 68 centers responded comparing 1948 LTs before the policy change and 1837 LTs postpolicy, resulting in a 6% volume decrease. Transplants using local donations after brain death decreased 54% (P < .001) while imported donations after brain death increased 133% (P = .003). Imported fly-outs and dry runs increased 163% (median, 19; range, 1-75, vs 50, range, 2-91; P = .009) and 33% (median, 3; range, 0-16, vs 7, range, 0-24; P = .02). Overall hospital costs increased 10.9% to a total of $46 360 176 (P = .94) for participating centers. There was a 77% fly-out cost increase postpolicy ($10 600 234; P = .03). On subanalysis, centers with decreased LT volume postpolicy observed higher overall hospital costs ($41 720 365; P = .048), and specifically, a 122% cost increase for liver imports ($6 508 480; P = .002). Transplant centers from low-income states showed a significant increase in hospital (12%) and import (94%) costs. Centers serving populations with larger proportions of racial and ethnic minority candidates and specifically Black candidates significantly increased costs by more than 90% for imported livers, fly-outs, and dry runs despite lower LT volume. Similarly, costs increased significantly (>100%) for fly-outs and dry runs in centers from worse-performing health systems. CONCLUSIONS AND RELEVANCE: Based on this large multicenter effort and contrary to current assumptions, the new liver distribution system appears to place a disproportionate burden on populations of the current LT community who already experience disparities in health care. The continuous allocation policies being promoted by UNOS could make the situation even worse.

Surgery

Behinaein P, and **Okereke IC**. Comprehensive inclusion: demographics of clinical trials. *Lancet* 2024; 403(10440):1986-1987. PMID: 38762320. Full Text

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Surgery

Bhatnagar AR, **Siddiqui F**, **Khan G**, **Pompa R**, **Kwon D**, and **Nyati S**. Long-Term Follow-Up of Phase I Trial of Oncolytic Adenovirus-Mediated Cytotoxic and Interleukin-12 Gene Therapy for Treatment of Metastatic Pancreatic Cancer. *Biomedicines* 2024; 12(5). PMID: 38791027. Full Text

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The long-term follow-up findings of the phase I trial evaluating the efficacy of oncolytic adenovirus-mediated cytotoxic and interleukin-12 gene therapy in metastatic pancreatic cancer (mPC) seem very promising. The study employed a replication-competent Adenovector in combination with chemotherapy in a dose-escalation format. The trial demonstrated a clinically meaningful median overall survival (OS) benefit, with patients in the highest dose cohort exhibiting an impressive median OS of 18.4 months. This contrasts starkly with patients receiving lower doses who experienced a median OS of 4.8 and 3.5 months, respectively. Remarkably, subject number 10, who received the highest dose, demonstrated an extraordinary survival of 59.1 months, presenting a compelling case for further exploration. Additionally, this patient displayed complete responses in lung and liver metastases, a rare occurrence in mPC treatment. Statistical analyses supported the observed survival benefit. The unprecedented OS results emphasize the potential of this treatment strategy and pave the way for future investigations into this promising gene therapy approach.

Surgery

Chamseddine H, Chahrour M, Aboul Hosn M, and **Kabbani L**. In patients with heart failure undergoing carotid endarterectomy, locoregional anesthesia is not associated with decreased mortality, stroke or myocardial infarction compared to general anesthesia. *Ann Vasc Surg* 2024; Epub ahead of print. PMID: 38821474. Full Text

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OBJECTIVE: While existing literature reports no benefit of locoregional anesthesia (LRA) over general anesthesia (GA) in patients undergoing carotid endarterectomy (CEA), the effect of LRA on patients with congestive heart failure (CHF) has not been explored. This study aims to assess whether the choice of anesthesia plays a role in influencing outcomes within this population. METHODS: Using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) files between 2005-2022 and the procedural targeted ACS-NSQIP database for CEA between 2011-2022, all patients receiving CEA were identified, and the subset of patients with CHF was included. Patient characteristics and 30-day outcomes were compared using $\chi(2)$ or Fischer's exact test as appropriate for categorical variables and the independent t-test or Mann-Whitney U test as appropriate for continuous variables. Mortality, stroke, myocardial infarction (MI), and major adverse cardiac events (MACE) were compared between patients receiving general anesthesia (GA) and locoregional anesthesia (LRA) using univariate analysis. RESULTS: A total of 3,040 patients (2,733 undergoing GA, 307 undergoing LRA) with a diagnosis of CHF undergoing CEA were identified. No difference in mortality (GA 3.1% vs LRA 4.6%, $p=0.162$), MI (GA 3.0% vs LRA 2.3%, $p=0.478$), stroke (2.4% vs 2.6%, $p=0.805$) or MACE (GA 7.4% vs LRA 8.1%, $p=0.654$) was observed. LRA patients had a significantly lower hospital stay compared to GA patients (1 day [IQR 1-3] vs 2 days [IQR 1-4], $p<0.001$). Shunt was more commonly used in patients receiving GA (32.9% vs 12.5%, $p<0.001$) compared to LRA. CONCLUSION: While utilizing LRA compared to GA during carotid endarterectomy in patients with CHF is associated with a shorter hospital stay and less intraoperative shunting, the choice of anesthesia did not impact the outcomes of mortality, MI or stroke. Further research is needed to determine the effect of LRA on the outcomes of CEA among patients with different stages of heart failure.

Surgery

Fedson S, Lavee J, **Bryce K**, Egan T, Olland A, Kanwar M, Courtwright A, and Holm AM. Ethical considerations in xenotransplantation of thoracic organs - a call for a debate on value based decisions. *J Heart Lung Transplant* 2024; 43(7):1033-1038. PMID: 38775760. Full Text

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Xenotransplant covers a broad ethical territory and there are several ethical questions that have arisen in parallel with the technological advances that have allowed the first porcine transplants to occur. This brief communication highlights ethical considerations regarding heart and lung xenotransplantation, with an emphasis on unresolved value-based concerns in the field. The aim of this text is therefore to encourage the readers to consider the vast potential of this emerging technique to do good, but also the risk of doing harm, and to participate in a discussion. The list of questions presented here is not exhaustive but hopefully represents some of the questions that appear to be most pressing as the field advances. The focus is on the value-based, or ethical questions, not the questions related to the practical medical procedures.

Surgery

Finotti M, Wall A, D'Alessandro A, Schwartz G, Sonnenday C, Goldberg D, Shah AS, Friend P, Orlowski JP, McKenna G, Newton S, Adams B, Chapman WC, Mathur A, **Abouljoud M**, Pruett T, Hessheimer A, Trotter JF, Asrani SK, and Testa G. The Dallas Donation after Circulatory Death Transplantation Summit: expanding donation after circulatory death procedures through process improvement, broader utilization, and innovation. *Hepatobiliary Surgery and Nutrition* 2024:14. PMID: Not assigned. Full Text

[Finotti, Michele; Wall, Anji; Mckenna, Greg; Newton, Steve; Adams, Brad; Chapman, William C.; Mathur, Amit; Abouljoud, Marwan; Pruett, Tim; Hessheimer, Amelia; Trotter, James F.; Asrani, Sumeet K.; Testa, Giuliano] Baylor Univ, Med Ctr, Simmons Transplant Inst, Dallas, TX USA. [Finotti, Michele; Chapman, William C.] Univ Padua, Reg Hosp Treviso, DISCOG, Hepatobiliary & Gen Surg Unit, Padua, Italy. [D'Alessandro, Anthony; Mathur, Amit] Univ Wisconsin, Sch Med & Publ Hlth, Dept Surg, Div Transplantat, Madison, WI USA. [Schwartz, Gary; Abouljoud, Marwan] Baylor Univ, Med Ctr, Ctr Adv Heart & Lung Dis, Dept Thorac Surg & Lung Transplantat, Dallas, TX USA. [Sonnenday, Chris; Pruett, Tim] Univ Michigan, Dept Surg, Ann Arbor, MI USA. [Goldberg, David; Hessheimer, Amelia] Univ Miami, Dept Med, Miller Sch Med, Div Digest Hlth & Liver Dis, Miami, FL USA. [Shah, Ashish] Vanderbilt Univ, Med Ctr, Dept Cardiothorac Surg, Nashville, TN USA. [Friend, Peter] Univ Oxford, Nuffield Dept Surg Sci, Oxford, England. [Orlowski, Jeff P.] LifeShare Transplant Donor Serv Oklahoma, Oklahoma City, OK USA. [Newton, Steve] Baylor Univ, Med Ctr, Adm, Dallas, TX USA. [Adams, Brad] Southwest Transplant Alliance, Dallas, TX USA. [Chapman, William C.] Washington Univ, Dept Surg Transplantat, St Louis, MO USA. [Mathur, Amit] Alix Sch Med, Mayo Clin Arizona, Dept Surg, Div Transplant Surg, Phoenix, AZ USA. [Abouljoud, Marwan] Henry Ford Hosp, Div Transplant & Hepatobiliary Surg, Detroit, MI USA. [Pruett, Tim] Univ Minnesota, Dept Surg, Minneapolis, MN USA. [Hessheimer, Amelia] Hosp Univ La Paz, Gen & Digest Surg, IdiPAZ, Madrid, Spain. [Finotti, Michele] Baylor Univ, Med Ctr, Simmons Transplant Inst,

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Despite a significant increase in utilization over the past decade, the number of donation after circulatory death (DCD) organs that are procured and transplanted in the United States (US) remains well below its potential. There is still room for expansion, as utilizing DCD organs to the fullest extent is currently the most viable solution to the persistent mismatch between supply and demand in transplantation. We convened a multidisciplinary transplantation summit to examine various aspects of DCD, with faculty members from around the world with clinical and academic interest in DCD donation and transplantation, including abdominal and cardiothoracic surgeons, organ procurement organization directors, hepatologists, and gastroenterologists. The conference focused on identifying barriers to DCD organ utilization and strategies to overcome these barriers. We divide the barriers to DCD utilization into three mains categories: (I) policy and process variation; (II) logistical and transportation challenges; and (III) higher risk perceptions related to DCD outcomes. For each barrier, we proposed a variety of solutions, providing an overview of the status of DCD donation in the US and suggestions on how to increase the use of DCD. There is a specific focus on ex situ machine perfusion, normothermic regional perfusion, and other opportunities to expand DCD utilization without negatively impacting recipient outcomes.

Surgery
Hider AM, Bonham A, **Carlin A**, Finks J, Ghaferi A, **Varban O**, and Ehlers AP. Association of Sex Differences on Weight Loss and Complications Following Bariatric Surgery. *J Surg Res* 2024; 299:359-365. PMID: 38795559. Full Text

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INTRODUCTION: Sex as a biologic variable remains largely understudied, even for the most commonly performed operations. The most effective treatment for obesity and obesity-associated comorbidities is bariatric surgery. There are limited data to describe potential differences in outcomes between male and female patients, particularly with regards to weight loss. Within this context, we examined weight loss and complications up to 1 y following sleeve gastrectomy or gastric bypass within a statewide bariatric quality improvement collaborative. METHODS: We performed a retrospective cohort study among patients who had bariatric surgery. Using a state-wide bariatric-specific data registry, all patients who underwent gastric bypass or sleeve gastrectomy between June 2006 and June 2022 were identified. The primary outcome was percent excess body weight loss and change in body mass index (BMI) at 1 y. The secondary outcome was 30-d risk-adjusted complications. RESULTS: Among 107,504 patients, the majority (n = 85,135; 79.2%) were female and most patients (n = 49,731; 58%) underwent sleeve gastrectomy. Compared to female patients, male patients were older (47.6 y versus 44.8 y; P < 0.0001), had higher baseline weight (346.6 lbs versus 279.9 lbs; P < 0.0001), had higher preoperative BMI (49.9 kg/m(2)versus 47.2 kg/m(2); P < 0.0001), and higher prevalence of most comorbid conditions including hypertension, hyperlipidemia, diabetes, and sleep apnea (P < 0.0001). Compared to female patients, male patients experienced greater total body weight loss (105.1 lbs versus 84.9 lbs; P < 0.0001) and higher excess body weight loss (60.0% versus 58.8%; P < 0.0001) but had higher BMI overall

(34.0 kg/m(2)versus 32.8 kg/m(2); P < 0.0001) at 1-y follow-up. Males had higher rates of serious complications (2.5% versus 1.9%; P < 0.0001), leak and perforation (0.5% versus 0.4%; P < 0.0001), venous thromboembolism (0.7% versus 0.4%; P < 0.0001), and medical complications (1.5% versus 1%; P < 0.0001). CONCLUSIONS: In this study we found that both males and females experienced excellent weight loss with a low risk of complications following bariatric surgery. Male sex was associated with slightly greater weight loss and slightly higher incidence of complications. However, although statistically significant, clinically, the differences in weight loss was not. Due to males having higher prevalence of comorbidities, providers should consider referring males earlier for bariatric surgery which may improve outcomes for this population.

Surgery
Hutchings H, **Theisen B**, Cox J, and **Okereke I**. Transdiaphragmatic sarcomatoid carcinoma of the lung: A case report. *Int J Surg Case Rep* 2024; 119:109675. PMID: 38718493. Full Text

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INTRODUCTION: Pulmonary sarcomatoid carcinoma is a very rare primary tumor of the lung. Although usually aggressive, these tumors have not been described previously to invade through the diaphragm into the liver. We present a patient with a pulmonary sarcomatoid carcinoma with transdiaphragmatic spread into the dome of the liver. PRESENTATION OF CASE: An 82-year-old female with a lifetime non-smoking history presented with generalized fatigue, fever, night sweats, cough, and pleuritic chest pain. She had recently traveled to the western United States. Additionally, she had recently undergone periodontal deep cleaning with no peri-procedural antibiotics. Laboratory testing was significant for a leukocytosis of 13.5 white blood cells per microliter and a negative viral panel. Computed tomography and magnetic resonance imaging revealed a large heterogeneous mass extending from the right pulmonary hilum through the diaphragm. Although initial radiology reports suggested hepatic abscess, percutaneous fine needle aspiration was performed. Biopsy revealed pulmonary sarcomatoid carcinoma. She was begun on systemic treatment. DISCUSSION: Pulmonary sarcomatoid carcinoma can exhibit transdiaphragmatic invasion into the liver. This clinical situation can easily be confused with a hepatic abscess, but suspicion should remain for abscess. Clinical suspicion for neoplasm should warrant biopsy when technically possible. CONCLUSION: Although hepatic abscesses can exhibit transdiaphragmatic spread into the chest, pulmonary sarcomatoid carcinoma can also invade the abdomen. Biopsy should be performed during the evaluation and workup of the patient.

Surgery
Jesse MT. Education Is Necessary but not Sufficient for Navigating Evaluations for Transplantation. *Prog Transplant* 2024; 34(1-2):7-8. PMID: 38713549. Full Text

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Surgery
Malinzak L, **Gartrelle K**, **Sragi Z**, **Segal A**, **Prashar R**, and **Jesse MT**. Access to robotic assisted kidney transplant for recipients: a systematic review and call for reporting standards. *J Robot Surg* 2024; 18(1):239. PMID: 38833043. Full Text

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Robot-assisted kidney transplantation (RAKT) is a relatively novel, minimally invasive option for kidney transplantation. However, clarity on recipient selection in the published literature is lacking thereby

significantly limiting interpretation of safety and other outcomes. This systematic review aimed to identify and synthesize the data on selection of RAKT recipients, compare the synthesized data to kidney transplant recipients across the USA, and explore geographical clusters of availability of RAKT. Systematic literature review, in accordance with PRISMA, via OVID MEDLINE, Embase, and Web of science from inception to March 5, 2023. All data entry double blinded and quality via Newcastle Ottawa Scale. 44 full-text articles included, encompassing approximately 2402 kidney transplant recipients at baseline but with considerable suspicion for overlap across publications. There were significant omissions of information across studies on patient selection for RAKT and/or analysis. Overall, the quality of studies was very low. Given suspicion of overlap across studies, it is difficult to determine how many RAKT recipients received living (LD) versus deceased donor (DD) organs, but a rough estimate suggests 89% received LD. While the current RAKT literature provides preliminary evidence on safety, there are significant omissions in reporting on patient selection for RAKT which limits interpretation of findings. Two recommendations: (1) international consensus is needed for reporting guidelines when publishing RAKT data and (2) larger controlled trials consistently reporting recipient characteristics are needed to clearly determine selection, safety, and outcomes across both LD and DD recipients.

Surgery
Musgrove H, **Morales P**, **Ruby A**, **Thompson Y**, **Chami E**, and **Gupta A**. Improving Early Detection of Clostridioides difficile Infections Through Electronic Reports. *J Nurs Care Qual* 2024; Epub ahead of print. PMID: 38768430. Full Text

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Surgery
Park JH, **Siddiqui N**, Hrebec WK, **Szymanski TJ**, **Uribe-Marquez S**, **Miletic KG**, and Krishnan S. Management of Anticoagulation and Antifibrinolytics in Catastrophic Antiphospholipid Syndrome. *Semin Cardiothorac Vasc Anesth* 2024; Epub ahead of print. PMID: 38705843. Full Text

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Antiphospholipid syndrome (APS) is an autoimmune disorder that presents with hypercoagulability and results in a lab artifact of prolonged PTT. The most severe form is catastrophic antiphospholipid antibody syndrome (CAPS), which manifests as rapidly progressing thromboses in multiple organ systems leading to multi-organ ischemia. The mainstay management CAPS is anticoagulation and systemic corticosteroids. Antifibrinolytic agents have previously been thought to be relatively contraindicated in CAPS due to the pro-thrombotic nature of the disease; the complex coagulation profile of CAPS can make it difficult to assess the risks and benefits of antifibrinolytic therapy. Also, should a patient with CAPS require cardiopulmonary bypass (CPB) for surgery, it poses a unique challenge in providing appropriate anticoagulation in the setting of prolonged ACT. We present a case of a 32-year-old postpartum female with CAPS requiring heart transplant who safely received intraoperative antifibrinolytic therapy and was successfully anticoagulated during CPB after perioperative plasmapheresis.

Urology
Ditonno F, Franco A, Veccia A, Bertolo R, Wu Z, Wang L, **Abdollah F**, **Finati M**, Simone G, Tuderti G, Helstrom E, Correa A, De Cobelli O, Ferro M, Porpiglia F, Amparore D, Tufano A, Perdonà S, Bhanvadia R, Margulis V, Brönimann S, Singla N, Puri D, Derweesh IH, Mendiola DF, Gonzalgo ML, Ben-David R, Mehrazin R, Moon SC, Rais-Bahrami S, Yong C, Sundaram CP, Moghaddam FS, Ghoreifi A, Djaladat H, Autorino R, and Antonelli A. Decisional and prognostic impact of diagnostic ureteroscopy in high-risk upper tract urothelial carcinoma: A multi-institutional collaborative analysis (ROBUUST collaborative group). *Urol Oncol* 2024; Epub ahead of print. PMID: 38760274. Full Text

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Icahn School of Medicine at Mount Sinai Hospital, Department of Urology, New York, NY.
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BACKGROUND: Diagnostic ureteroscopy (URS) with or without biopsy remains a subject of contention in the management of upper tract urothelial carcinoma (UTUC), with varying recommendations across different guidelines. The study aims to analyse the decision-making and prognostic role of diagnostic ureteroscopy (URS) in high-risk UTUC patients undergoing curative surgery. MATERIALS AND METHODS: In this retrospective multi-institutional analysis of high-risk UTUC patients from the ROBUUST dataset, a comparison between patients who received or not preoperative URS and biopsy before curative surgery was carried out. Logistic regression analysis evaluated differences between patients receiving URS and its impact on treatment strategy. Survival analysis included 5-year recurrence-free survival (RFS), metastasis-free survival (MFS), cancer-specific survival (CSS) and overall survival (OS). After adjusting for high-risk prognostic group features, Cox proportional hazard model estimated significant predictors of time-to-event outcomes. RESULTS: Overall, 1,912 patients were included, 1,035 with preoperative URS and biopsy and 877 without. Median follow-up: 24 months. Robot-assisted radical nephroureterectomy was the most common procedure (55.1%), in both subgroups. The 5-year OS ($P = 0.04$) and CSS ($P < 0.001$) were significantly higher for patients undergoing URS. The 5-year RFS ($P = 0.6$), and MFS ($P = 0.3$) were comparable between the 2 groups. Preoperative URS and biopsy were neither a significant predictor of worse oncological outcomes nor of a specific treatment modality. CONCLUSIONS: The advantage in terms of OS and CSS in patients undergoing preoperative URS could derive from a better selection of candidates for curative treatment. The treatment strategy is likely more influenced by tumor features than by URS findings.

Urology
Japari A, Moorthy D, and **Rambhatla A**. Andrology laboratory technique for analysis of semen in men with azoospermia. *Asian J Androl* 2024; Epub ahead of print. PMID: 38759095. Full Text

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Discovery of spermatozoa during the 17th century led to developing technologies for semen analysis in the early 1900s, and then, standard techniques were implemented during the 20th century. Semen

analysis has a pivotal role in the male infertility evaluation, and azoospermia is an important finding. Azoospermia is identified in 15% of infertile men. However, the accurate laboratory assessment of azoospermia poses certain technical challenges. Laboratories currently perform semen assessment with great variability; thus, a standard method should be used. Planning suitable management and determining the cause of infertility require a precise evaluation of azoospermia. This review aims to address the definition of azoospermia and highlight laboratory methods in the assessments of azoospermia. Basic methods such as centrifugation, repeat pellet analysis, and staining and advanced methods such as genetic testing and biomarkers have been discussed. These methods have helped in standardizing the protocol for accurate azoospermia assessments with less variability.

Urology

Monga J, **Ghosh R**, **Guddeti R**, **Chitale D**, **Khan G**, and **Ghosh J**. MK591 (Quiflapon), a 5-lipoxygenase inhibitor, kills pancreatic cancer cells via downregulation of protein kinase C-epsilon. *Front Oncol* 2024; 14:1387535. PMID: 38746674. Full Text

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INTRODUCTION: Pancreatic tumors and cell lines derived from them exhibit elevated expression of 5-lipoxygenase (5-Lox), whereas non-tumor glands or normal cells do not exhibit this overexpression. Arachidonic acid stimulates pancreatic cancer cell growth via metabolic conversion through the 5-Lox pathway, and inhibition of 5-Lox activity decreases the viability of pancreatic cancer cells. However, the downstream signaling mechanisms through which 5-Lox exerts its effects on the survival of pancreatic cancer cells remain to be elucidated. METHODS: The effects of 5-Lox inhibition on cell proliferation, apoptosis, and invasive potential were investigated in pancreatic cancer cells. The protein expression was analyzed by Western blot. Apoptosis was analyzed by Annexin-V binding assay and by detecting the degradation of chromatin-DNA to nucleosomal fragments. The protein kinase C-epsilon (PKCε) activity was measured by an immunoprecipitation-kinase assay. The in vivo effects of MK591 were evaluated in pancreatic tumor xenograft model. RESULTS: MK591, a specific inhibitor of 5-Lox activity, killed pancreatic cancer cells via induction of apoptosis, involving externalization of phosphatidylserine, cleavage of PARP (poly-ADP ribose polymerase) and degradation of chromatin DNA to nucleosomes. MK591 effectively blocked in vitro invasion and soft-agar colony formation by pancreatic cancer cells and decreased pancreatic tumor growth in nude mice xenografts. Furthermore, inhibition of 5-Lox downregulated K-Ras and inhibited phosphorylation of c-Raf and ERKs. Interestingly, 5-Lox inhibition induced apoptosis in pancreatic cancer cells without the inhibition of Akt but the protein level of PKCε was dramatically downregulated. Furthermore, inhibition of 5-Lox decreased the phosphorylation of Stat3 at Serine-727. Pre-treatment of pancreatic cancer cells with peptide activators of PKCε prevented apoptosis induced by 5-Lox inhibition, suggesting that the mechanism by which 5-Lox inhibition causes cell death in pancreatic cancer involves downregulation of PKCε. The combination of low doses of MK591 and gemcitabine synergistically reduced the oncogenic phenotype and killed pancreatic cancer cells by inducing apoptosis. DISCUSSION: These findings indicate that inhibition of 5-Lox interrupts an Akt-independent, PKCε-dependent survival mechanism in pancreatic cancer cells and suggest that metabolism of arachidonic acid through the 5-Lox pathway plays an integral part in the survival of pancreatic cancer cells via signaling through PKCε, an oncogenic, pro-survival serine/threonine kinase.

Urology

Tinsley SA, **Finati M**, **Stephens A**, **Chiarelli G**, **Cirulli GO**, **Williams E**, **Morrison C**, **Richard C**, **Hares K**, Sood A, Buffi N, Lughezzani G, Bettocchi C, Salonia A, Briganti A, Montorsi F, Carrieri G, **Rogers C**, and **Abdollah F**. Race has no impact on prostate cancer-specific mortality, when comparing patients with similar risk of other-cause mortality: An analysis of a population-based cohort. *Cancer* 2024; Epub ahead of print. PMID: 38804713. Full Text

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BACKGROUND: Other-cause mortality (OCM) can serve as a surrogate for access-to-care. The authors sought to compare prostate cancer-specific mortality (PCSM) in Black versus White men matched based on their calculated OCM risk. METHODS: The Surveillance, Epidemiology, and End Results (SEER) database was queried for Black and White men diagnosed with prostate cancer between 2004 to 2009, to collect long-term follow-up. A Cox regression was used to calculate the OCM risk using all available covariates. This calculated OCM risk was used to construct a 1:1 propensity score matched (PSM) cohort. Then, a competing-risks multivariable tested the impact of race on PCSM. RESULTS: A total of 94,363 patients were identified, with 19,398 Black men and 74,965 White men. The median (IQR) follow-up was 11.3 years (9.8-12.8). In the unmatched-cohort at 10-years, PCSM and OCM were 5.5% versus 3.5% and 13.8% versus 8.4% in non-Hispanic Black (NHB) versus non-Hispanic White (NHW) patients (all $p < .0001$). The standardized mean difference was <0.15 for all covariates, indicating a good match. In the matched cohort at 10-years, OCM was 13.6% and 10.0% in NHB versus NHW ($p < .0001$), whereas the PCSM was 5.3% versus 4.7% ($p < .01$). On competing-risks multivariable analysis on PCSM, Black men had a hazard ratio of 1.08 (95% confidence interval, 0.98-1.20) compared to White men with a $p = .13$. CONCLUSIONS: The results of this study showed similar PCSM in Black and White patients, when matched with their calculated OCM risk. This report is the first to indicate at a population-based level that race has no impact on PCSM. PLAIN LANGUAGE SUMMARY: Prostate cancer is a very common cancer among men and it is associated with health disparities that disproportionately impact Black men compared to White men. There is an on-going discussion of whether disparities between these two groups stem from genetic or environmental factors. This study sought to examine if matching based on overall health status, a proxy for the impact of social determinants of health, mitigated significant differences in outcomes. When matched using risk of death from any cause other than prostate cancer, Black and White men had no significant differences in prostate cancer death.

Behavioral Health Services/Psychiatry/Neuropsychology
Drake C, **Mahr G**, **Reffi A**, **Son K**, Seymour G, **Sagong C**, **Jankowiak L**, Pawirosetiko J, **Hehr A**, **Cheng P**, **Kalmbach D**, **Roth T**, and **Moore D**. DEVELOPMENT OF THE AFFECTIVE NEUROSCIENCE DREAM RATING SCALE. *Sleep* 2024; 47:A402. Full Text

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Introduction: Methods for quantifying emotional dream content have been developed. These approaches have yielded significant insights into dream content, their relation to waking cognition, and mental health. The current dream rating scale was developed to improve upon previous approaches by conceptualizing the scale based on the known fundamental affective neuronal circuits within the brain. Methods: Seventy-seven items were developed representing fundamental emotions (SEEKING, RAGE, FEAR, LUST, CARE, GRIEF and PLAY). One-hundred dreams were randomly selected from a dream database (www.dream-bank.net). To determine interrater agreement, two raters scored all 77-items for each of the 100 dreams based on if the emotional content was present or not. Items with an interrater agreement (kappa) below .5 were excluded. Nightmares (i.e., extremely unpleasant or disturbing dreams) were independently identified by a sleeptrauma expert and compared to non-nightmares for the 7 scales. Results: Thirty-three items (kappa > 0.5; range .5-.82) were retained for the final scale. Of the items retained, 29 (85%) were endorsed in 10% or more of dreams. The most frequently identified items in the final scale were danger (44%) and fear (45%). Seven emotional dream scales were apriori identified with 3-9 items each being retained in the final scales. Scales were significantly correlated between raters (r = .54 to .88, p< .001). Across the 100 dreams FEAR was the highest endorsed emotion scale while GRIEF was lowest. As expected, nightmares had significantly elevated scores compared to non-nightmares on the FEAR, RAGE, SEEKING and GRIEF scales (p< .001) but not CARE, LUST, or PLAY. Conclusion: This dream rating scale based on mammalian emotional circuits previously identified through affective neuroscience shows promise for quantifying and understanding the emotional content of dreams. Future studies will need to further validate this preliminary affective dream content scale using different populations including individuals exposed to trauma and those with mental health and sleep disorders to determine its clinical utility.

Cardiology/Cardiovascular Research
Shah Y, Shah T, Schwartz A, Poddar K, **O'Neill W**, Anderson M, Wohns D, Meraj P, Palacios I, Kapur N, Almedhychy A, and Lansky A. Safety And Efficacy Of Impella RP Support For Acute Right Ventricular Failure Complicated By Cardiogenic Shock: Post Market Approval SubAnalysis Of The CVAD Registry. *J Card Fail* 2024; 30(1):269-269. Full Text

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INTRODUCTION: Takotsubo cardiomyopathy (TTC) is characterized by reversible apical ballooning without severe coronary artery disease. TTC with left ventricular outflow tract obstruction (LVOTO) is classically managed with phenylephrine, beta-blockers, and fluid resuscitation, avoiding inotropic agents due to concern for worsening obstruction. Management is further complicated in the setting of hemodynamically significant mitral regurgitation (MR), where fluid resuscitation may worsen cardiopulmonary status. In such cases, depending on the patient's clinical status and hemodynamics, they may either benefit from short-term mechanical circulatory support (MCS), such as an intra-aortic balloon pump, or may have LVOTO exacerbated. We describe a case of TTC with LVOTO and severe

MR successfully managed with pharmacologic therapy avoiding mechanical and inotropic support. CASE: A 70-year-old female presented with acute onset of dyspnea and presyncope during strenuous exercise. On presentation, she was hypotensive (76/52 mmHg), tachypneic (29 breaths/min), and hypoxic requiring a high-flow nasal cannula at 40L/min at 100% FiO2. Initial laboratory tests included high-sensitivity troponin T 334 ng/L, proBNP 566 pg/mL, and lactic acid 2.5 mmol/L. Electrocardiogram showed normal sinus rhythm, right bundle branch block, and non-specific ST abnormalities in lateral leads. Initial bedside echocardiogram demonstrated left ventricular (LV) apical akinesis with a hyperdynamic base with an ejection fraction (EF) of <30% concerning TTC. Color doppler showed severe posteriorly directed MR, and pulse-wave doppler at the LV outflow tract showed a late peaking jet with a peak gradient of 46.4 mmHg. Left-heart catheterization showed minimal coronary artery obstruction. Right-heart catheterization showed elevated RAP 13 mmHg, PAP 57/24 mmHg (mean 39 mmHg), and PCWP 29 mmHg with Fick calculated CO 4.48 L/min and CI 2.5L/min/m 2 . Phenylephrine, esmolol, and IV furosemide were initiated. Short-term MCS was deferred, and she was successfully weaned from vasopressor within three days. Follow-up echocardiogram seven days following admission showed recovered EF of 70% and resolution of LVOTO. CONCLUSION: Our case represents a challenging scenario of TTC with LVOTO in a patient with severe MR. In cases with mitral insufficiency, up to 36% of patients may require an IABP; however, its use is controversial in LVOTO due to its counter-pulsation effect which reduces afterload consequently increasing the pressure gradient between the LV and aorta. Our patient was successfully managed by a pharmacological approach, including Esmolol as a superior beta-blocker as it is a beta-one cardio-selective drug with a short half-life. It allows accurate titration to help optimize heart rate and cardiac filling times. Despite the current recommendations for IV fluids in patients with TTC with LVOTO, in the setting of severe MR, an RHC to assess hemodynamics may be critical in guiding therapy. This approach can decrease the need for short-term MCS and provide an alternative to patients who defer invasive therapies.

Center for Individualized and Genomic Medicine Research

Littleton S, Luzum J, Dorsch M, **Lanfear D**, and **Liu B**. ADDRESSING THE RACIAL DISPARITY OF ANGIOTENSIN INHIBITOR ASSOCIATED REDUCTION IN HFREF HOSPITALIZATIONS: DISTINGUISHING BETWEEN RACE AND ANCESTRY. *Clin Pharmacol Ther* 2024; 115:S11-S11. Full Text

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BACKGROUND: Angiotensin inhibitors are vital for heart failure (HF) treatment and reducing HF-related hospitalizations. Despite this, HF hospitalization rates in the US remain high, with unexplained racial disparities between Black and White HF patients. This work aimed to investigate the influence of genomic ancestry and self-identified race on the racial disparities in angiotensin inhibitor-associated reductions in HF hospitalizations. METHODS: The work included 977 patients from a registry at Henry Ford Health System (HFPGR) and 810 patients from the GUIDE-IT clinical trial, all with heart failure reduced ejection fraction (HFrEF). At Henry Ford, 492 self-identified Black and 485 self-identified White patients were followed for an average of 3.0 years. Additionally, 381 patients had >80% African genomic ancestry, while 471 had <5%. In GUIDE-IT, 322 self-identified Black patients and 488 self-identified White patients were followed for an average of 1.2 years. Angiotensin inhibitor exposure was calculated from pharmacy claims, and African genomic ancestry was determined by a genome-wide array in Henry Ford patients. Fine and Gray time-dependent Cox proportional hazards models were used to assess the association of drug exposure with the first recorded HF hospitalization by self-identified race in both Henry Ford and GUIDE-IT patients or by the proportion of African ancestry in Henry Ford patients. A P-value of <0.05 was considered statistically significant for main effects, and <0.1 for interactions. Both models were evaluated unadjusted and adjusted for baseline risk factors (eg. age, sex, ejection fraction) and angiotensin inhibitor propensity score. RESULTS: Results are presented in the Figure. CONCLUSION: In summary, these results demonstrated no significant difference in angiotensin inhibitor-associated reduction in HFrEF hospitalizations by self-identified race or genomic ancestry. Black patients and those with >80% African ancestry did not show increased risk, while White patients and those with <5% African ancestry had a slightly elevated risk. Overall, no racial disparities in angiotensin inhibitor-associated reductions in HFrEF

hospitalizations were observed in these patient cohorts. This suggests the need for future research to explore the social context of self-identified race, including social determinants of health.

Dermatology
Bissonnette R, **Gold L**, Kircik L, Eichenfield L, Hong H, Papp K, Tallman A, Piscitelli S, Rubenstein D, Brown P, and Silverberg J. Tapinarof cream 1% once daily: Interim analysis of ADORING 3 phase 3 long-term extension trial in adults and children down to age 2 years with atopic dermatitis. *J Manag Care Spec Pharm* 2024; 30(4-a):S89. Full Text

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BACKGROUND: Tapinarof cream 1% once daily (QD) demonstrated significant efficacy vs vehicle and was well tolerated in adults and children aged 2 years or older with atopic dermatitis (AD) in 2 pivotal phase 3 trials (ADORING 1 and 2). OBJECTIVE: To present baseline characteristics and outcomes from the prespecified interim analysis of ADORING 3, the long-term extension trial assessing safety and efficacy of up to 48-weeks' open-label tapinarof cream 1% QD for adults and children with AD. METHODS: Patients completing the 8-week ADORING 1 and 2 trials, 4-week maximal usage pharmacokinetics trial, and direct-enrollers were eligible for 48-weeks' open-label treatment with tapinarof cream 1% QD. RESULTS: A total of 728 patients enrolled in ADORING 3, representing a large, diverse AD population comprising a high proportion (91%) of eligible patients from the pivotal ADORING trials, 28 patients from a 4-week maximal usage pharmacokinetics trial, and an additional 76 tapinarofnaive patients aged 2-17 years with various disease severities (mild; or moderate or worse with body surface area ≥40%), who were ineligible for preceding trials. The majority of patients in ADORING 3 were pediatric; 26.6% were aged 2-6 years, 27.1% 7-11 years, 29.3% 12-17 years, and 17.0% were adults. Overall, 46.6% were male, 52.6% White, 11.1% Asian, 30.1% Black/African American, and 4.4% other race categories. CONCLUSIONS: Patients with AD present with different phenotypes and treatment responses. A high proportion of primarily pediatric patients elected to rollover from previous trials, and the diverse population enrolled in ADORING 3 is representative across the broad spectrum of disease severity, body surface area affected (up to 95%), and demographics. No new safety signals were reported with long-term treatment in this interim analysis. The full analysis in 2024 will report further safety and efficacy data with tapinarof cream 1% QD.

Dermatology
Silverberg J, Eichenfield L, Hebert A, Simpson E, **Gold L**, Bissonnette R, Papp K, Browning J, Kwong P, Korman N, Brown P, Rubenstein D, Piscitelli S, Somerville M, Tallman A, and Kircik L. Tapinarof cream 1% once daily: Significant efficacy in atopic dermatitis in two phase 3 trials in adults and children down to age 2 years. *J Manag Care Spec Pharm* 2024; 30(4-a):S88. Full Text

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BACKGROUND: ADORING 1 and 2 were 2 identical phase 3, randomized, double-blind, vehicle-controlled trials of tapinarof cream 1% (VTAMA, Dermavant Sciences, Inc.) once daily (QD) in adults and children aged 2 years or older with atopic dermatitis (AD). OBJECTIVE: To report pivotal phase 3 efficacy and safety from ADORING 1 and 2. METHODS: Patients with a Validated Investigator Global Assessment for Atopic DermatitisTM (vIGA-ADTM) score of at least 3, Eczema Area and Severity Index (EASI) score of at least 6, and body surface area involvement of 5%-35% were randomized to tapinarof cream or vehicle QD for 8 weeks. The primary efficacy endpoint was vIGA-ADTM response (score of clear [0] or almost clear [1] and ≥2-grade improvement from baseline at week 8). Secondary efficacy endpoints included at least 75% improvement in EASI score (EASI75) and proportion of patients (aged ≥12 years) with baseline Peak Pruritus Numerical Rating Scale score of at least 4 achieving at least 4-point reduction at week 8. Safety assessments included the incidence of adverse events (AEs). RESULTS: A total of 407 and 406 patients were randomized in ADORING 1 and 2, respectively. At baseline, 84.%-89.9% of patients had a vIGA-ADTM score of 3 (moderate), mean EASI score of 12.5-13.3, and mean body surface area affected of 16.7%-16.9% across trials. At week 8, primary and secondary efficacy endpoints were met with statistical significance with tapinarof vs vehicle: vIGA-ADTM

response (45.4% vs 13.9% and 46.4% vs 18.0% [both P < 0.0001]), EASI75 response (55.8% vs 22.9% and 59.1% vs 21.2% [both P < 0.0001]), and at least 4-point reduction in Peak Pruritus Numerical Rating Scale (55.8% vs 34.2% [P = 0.0366] and 52.8% vs 24.1% [P = 0.0015]), in ADORING 1 and 2, respectively. AEs were mostly mild or moderate; the most frequent (≥5% any group) were folliculitis, headache, and nasopharyngitis. Trial discontinuation rates because of AEs were lower with tapinarof vs vehicle (ADORING 1: 1.9% vs 3.6%; ADORING 2: 1.5% vs 3.0%, respectively). CONCLUSIONS: Tapinarof cream 1% QD demonstrated statistically significant efficacy vs vehicle for both primary and secondary endpoints in adults and children aged 2 years or older with AD. Tapinarof was well tolerated, with no new safety signals. AEs were mostly mild to moderate and led to low rates of trial discontinuation, demonstrating the predictable safety profile of tapinarof cream 1% QD.

Dermatology

Simpson E, Silverberg J, Bissonnette R, **Gold L**, Armstrong A, Hebert A, Serrao R, Jakus J, Brown P, Rubenstein D, Piscitelli S, Tallman A, and Eichenfield L. Rapid and early onset of itch relief with tapinarof cream 1% once daily in two pivotal phase 3 trials in adults and children down to age 2 years with atopic dermatitis. *J Manag Care Spec Pharm* 2024; 30(4-a):S85. Full Text

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BACKGROUND: Itch is the most bothersome symptom for patients with atopic dermatitis (AD) and has a significant negative impact on health-related quality of life. Rapid onset of pruritus relief with sustained efficacy is a key outcome for AD therapies. In ADORING 1 and 2, 2 identical phase 3, double-blind, vehicle-controlled trials, tapinarof cream 1% (VTAMA, Dermavant Sciences, Inc.) once daily (QD) demonstrated efficacy and was well tolerated in adults and children aged 2 years or older with AD. OBJECTIVE: To evaluate time to onset of itch relief in the pivotal phase 3 trials. METHODS: In ADORING 1 and 2, patients with a Validated Investigator Global Assessment for Atopic DermatitisTM score of 3 or more, an Eczema Area and Severity Index score of 6 or more, and body surface area involvement of 5%-35% were randomized 2:1 to tapinarof cream or vehicle QD for 8 weeks. Itch relief was assessed by changes in Peak Pruritus Numerical Rating Scale (PP-NRS) score, daily and by visit, from baseline through week 8. PP-NRS considers itch over the past 24 hours; lower scores indicate less pruritus. RESULTS: A total of 407 and 406 patients were randomized in ADORING 1 and 2, respectively. At baseline, mean PP-NRS scores were 6.7 and 6.8 in both trials, respectively. For daily evaluations of itch from baseline, greater reductions in mean PP-NRS scores for tapinarof vs vehicle were observed as early as day 1, 24 hours after initial application in ADORING 1 (-1.2 vs -0.9), and day 2 in ADORING 2 (-1.6 vs -1.4). Daily itch improvements continued through week 8 in both trials. Statistically significant reductions in mean weekly PP-NRS scores occurred as early as week 1 (earliest assessment) with tapinarof vs vehicle (-2.0 vs -1.2 [P < 0.0001]) and (-2.0 vs -1.3 [P = 0.0010]) in ADORING 1 and 2, respectively. Significantly greater reductions in mean PP-NRS scores with tapinarof vs vehicle were seen for all visits through week 8 (-4.1 vs -2.6 and -4.1 vs -2.4 [both P < 0.0001]). CONCLUSIONS: Tapinarof cream 1% QD demonstrated rapid, significant, and clinically meaningful pruritus relief from 24 hours after initial application, with improvements increasing through week 8 in both trials in adults and children aged 2 years or older with AD.

Gastroenterology

Pohl H, Rex DK, Barber J, Moyer M, Elmunzer J, Rastogi A, Gordon S, Zolotarevsky E, Levenick JM, Aslanian H, **El Atrache M**, Von Renteln D, Bhaumik B, Keswani R, Kumta N, Pleskow DK, Smith Z, **Abu Ghanimeh MK**, Sanaei O, Jensen LL, Mackenzie T, and **Piraka C**. Cold snare endoscopic resection for large colon polyps – a randomized trial. *Endoscopy* 2024; 56:S7-S7. Full Text.

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Aims: Despite improvements in technique, severe adverse events (SAE), including post-procedure bleeding, remain a major concern following endoscopic resection of large colorectal polyps. We examined whether cold resection without the use of electrocautery reduces the risk of SAE and affords completeness of resection. Methods: We performed a multicenter, randomized trial of patients with a large nonpedunculated colon polyp (≥20 mm) at 10 medical centers in North America from October 2019 through January 2023. Patients were randomly assigned to endoscopic mucosal resection (EMR) without electrocautery (cold EMR group) or with electrocautery (hot EMR group) and were followed until their first surveillance colonoscopy. Hot EMR included margin treatment and defect closure as indicated. The primary outcome were SAEs in intention to treat analysis, defined as an event that required hospitalization, a blood transfusion, colonoscopy, surgery, or another invasive intervention within 30 days after completion of the colonoscopy. The secondary outcome was the rate of polyp recurrence at surveillance colonoscopy. Because crossover from cold to hot EMR was expected (assumed 10%), we also performed a per protocol analysis. Additional subgroup analysis considered polyp characteristics and use of periprocedural antithrombotic medications. Results: 660 patients were randomized, and 518 (78.5%) completed their first surveillance colonoscopy. Crossover occurred in 14.6% in the cold EMR group and in 13.4% in the hot EMR group. An SAE was observed in 2.1% of patients in the cold EMR group and in 4.3% in the hot EMR group (p=0.62) with postprocedure bleeding in 0.9% and 2.8%, respectively (p=0.52). When the analysis was restricted to patients who received the intervention as randomized (per protocol analysis), significantly fewer SAEs occurred in the cold EMR group as compared to the hot EMR group (1.4% vs 4.9%, p=0.017), with postprocedure bleeding in 1.1% and 2.5%, respectively (p=0.34). Polyp recurrence was detected in 28.0% in the cold EMR group and 14.2% in the hot EMR group (p<0.001). In the per protocol analysis recurrence rates were 28.7% and 15.4% (p<0.001), respectively. In subgroup analysis SAE risk differences between groups remained unchanged. However, risk of recurrence was similar for the subgroup of 20-29 mm polyps (18.5% vs 15.7%) and for sessile serrated polyps (15.0% vs 14.5%). The greatest recurrence risk was noted for adenomas with high grade dysplasia (46.5% vs 18.4%, respectively, p=0.004). Conclusions This large multicenter trial showed no significant safety benefit of universal cold EMR for large colorectal polyps. However, after accounting for a high crossover rate, cold EMR had a significantly lower SAE rate compared to hot EMR. This safety benefit of cold EMR is offset by a greater recurrence rate, particularly for advanced pathology. Our findings do not support the universal application of cold EMR for large non-pedunculated colorectal polyps.

Global Health Initiative

Blasko EG, González MJ, Bardossy AC, Sosa EJ, **Prentiss T**, Suleyman G, Jagjeet K, Maki G, Ruiz SE, Fernández Do Porto D, Bocco JL, Saka HA, Amé V, **Zervos M**, and Sola C. CONTRIBUTION OF FRESH RIVER WATER TO THE DISSEMINATION OF HOSPITAL-ASSOCIATED ENTEROCOCCUS FAECIUM CC17 STRAINS IN CÓRDOBA. *Biocell* 2024; 48:78-79. Full Text

E.G. Blasko, Centro de Investigaciones en Bioquímica Clínica e Inmunología (CIBICI) CONICET, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina

E. faecium is a bacterium capable of causing serious infections mostly acquired in hospitals. This bacterium is commonly found in the intestine of healthy humans and animals, allowing it to enter the

environment through feces. The rise of vancomycin-resistant Enterococcus (VRE) has led to treatment challenges in hospital settings worldwide. Our study aimed to investigate whether fresh river water contributes to the transmission of hospital-associated VRE clonal lineages. We conducted a comprehensive analysis of the antibiotic resistome, virulome, and phylogenomic lineages of vancomycin-resistant E. faecium (VREfm) isolates using whole-genome sequencing (WGS) and bioinformatics tools. The isolates were obtained from various sources, including hospital-acquired infections (n: 3), hospital-associated colonization samples [from rectal swabs (n: 9) and chronic ulcers (n: 1)], and isolates collected from freshwater sources (Suquia River, n: 5) in an area downstream of the Córdoba city and the wastewater treatment plant (WWTP). The antibiotic susceptibility was determined by diffusion/Vitek2, CLSI2019 and the presence of vanA/B genes by PCR. All the VREfm isolates were resistant to vancomycin (vanA+), teicoplanin, ampicillin and ciprofloxacin, with 77.8% presenting resistance to minocycline. VREfm belonged to clonal complex (CC) 17, ST17 (n= 6), ST736 (n= 6), and ST792 (n = 6). Ampicillin resistance was associated with predicted amino acid changes in the PBP5 protein. Most isolates harbored the following resistance genes: macrolides/lincosamides [msr(C), erm(B)], minocycline [tet(M), and tet(L)], aminoglycoside [aac(6)-aph(2), ant(6)-Ia, aph(3)-III, aac(6)-Iid] and trimethoprim (dfrG). Fluoroquinolone resistance was associated with amino acid substitutions in GyrA (Ser84Tyr: 66.7%; n =12) or Ser84Ile: 33.3%; n=6 and ParC (Ser82Arg: 100%; n=18). A total of 23 different virulence genes were identified including those encoding for adhesion (acm, scm, esp, sgrA, fms6 and fms22), capsule (cpsA/uppS, cpsB/cdsA) and biofilm formation (bopD). Phylogenetic analysis revealed two clearly defined groups: one consisted of isolates with the ST17 profile (which grouped the 3 infection isolates and 3 environmental isolates), while the other showed ST736 and ST792 profiles (which grouped the 10 colonization isolates and 2 environmental isolates). Consequently, in both groups, genomes of environmental origin were identified. Moreover, no significant differences were observed in terms of genes related to resistance or virulence between them. These results support the hypothesis that the environment may act as a reservoir and/or means of dissemination for these hospital associated high-risk clones. Therefore, it is essential to prioritize the monitoring of resistance in environmental sources from urban areas and implement wastewater treatment strategies aimed at preventing the release of VRE into the environment.

Hospital Medicine

Bugazia S, Boshnaf M, and **Sreenivasan A**. SUBARACHNOID HEMORRHAGE MORTALITY TRENDS IN U.S. PATIENTS WITH CIRCULATORY DISEASE (1999-2020). *Crit Care Med* 2024; 52(1):S114. Full Text

S. Bugazia, Henry Ford Macomb Hospitals, Sterling Heights, MI, United States

INTRODUCTION: Subarachnoid hemorrhage is a neurological emergency that occurs as a result of bleeding into the subarachnoid space, with a mortality rate of approximately 44% and a worldwide annual occurrence estimated to be around 6.1 events per 100,000 individuals. Improved understanding of the determinants of ethnic variances and underlying comorbidities can assist primary prevention, which may lead to a reduced burden of subarachnoid hemorrhage within society, improve outcomes and lower healthcare costs. METHODS: Using the CDC multiple causes of death database (ICD-10 revision codes), we identified all patients who have circulatory system disease who died of subarachnoid hemorrhage (I60.x registered as the underlying cause of death) in two races (Caucasians and African Americans), between 1999 and 2020 in the United States. Age-adjusted mortality rates were calculated per 1,000,000 persons (PMP), standardized to the US census data from 1999, and stratified by race. RESULTS: Between 1999 and 2020, a total of 118,881 deaths were due to subarachnoid hemorrhage in patients with circulatory system disease identified in two races, with an overall age-adjusted mortality of 17.4 PMP. We identified a total of 17,770 deaths among African Americans, while 101,111 deaths in Caucasian populations. The overall age-adjusted mortality was 22.4 PMP in African Americans and, 16.7 PMP in Caucasians. Over the 21 years, the ageadjusted mortality decreased by 46 % in African Americans (from 33 PMP in 1999 to 17.7 PMP in 2020) and decreased by 34 % in Caucasians (from 22.2 PMP in 1999 to 14.6 PMP in 2020). CONCLUSIONS: This study finds that between 1999 and 2020, African Americans have the highest rates of subarachnoid hemorrhage age-adjusted mortality among patients with circulatory system disease, whereas Caucasians have the lowest proportion despite having a 584%

higher incidence rate in this ethnic subgroup. Interestingly, over the twenty-one years, mortality has decreased in both races.

Internal Medicine
Badhwar A, **Shakaroun D**, **Bugazia S**, **Carlin A**, **Roehrs T**, and **Skiba V**. PREDICTORS OF PAP COMPLIANCE ONE MONTH AFTER BARIATRIC SURGERY. *Sleep* 2024; 47:A248. Full Text

A. Badhwar, Henry Ford Hospital, United States

Introduction: Obesity is a major risk factor for Obstructive sleep apnea (OSA). Bariatric surgery is a popular treatment modality for sustainable weight loss in obese patients with OSA. Metaanalysis of several randomized controlled trials and observational studies showed that bariatric surgery led to improvement in OSA severity but not cure. These patients will likely need continued treatment for OSA to minimize its complications. It is unclear what factors influence positive airway pressure (PAP) therapy adherence and compliance postoperatively. Our study aims to identify predictors of PAP compliance 1 month after bariatric surgery. Methods: Patients who underwent bariatric surgery at our institution between April and October 2023 and had diagnosed obstructive sleep apnea were identified. The 140 patients were followed prospectively through surgery and 30-day post-surgery. Medical health records, polysomnography or home sleep study results, and on-line databases of PAP use were reviewed for each patient. We used Pearson correlation coefficient testing and t-test to examine potential predictors of PAP use in the 30-day post-operative period. Results: There are statistically significant correlations ($p < 0.05$) between post-surgical PAP use and use during 7 days of initial set up ($r = 0.642$), time spent below 90% SpO2 during sleep testing ($r = 0.425$), time spent below 88% SpO2 ($r = 0.246$), preoperative STOP-BANG ($r = 0.200$), and time from sleep testing to surgery ($r = 0.242$). Pre-surgical AHI and having been evaluated by a sleep physician pre-operatively did not show statistically significant association with post-operative PAP use. Conclusion: PAP use during 7 days of initial set up is highly predictive of 1-month post-operative PAP use and may serve as a valuable marker to intervene on those patients with low use to improve long-term PAP use. Patients who were diagnosed with OSA close to their surgery had lower PAP use, suggesting patients may benefit from more time to get used to the treatment before having surgery.

Internal Medicine
Bugazia S, **Badhwar A**, **Shakaroun D**, **Carlin A**, **Roehrs T**, and **Skiba V**. PAP THERAPY IMPACT ON BARIATRIC SURGERY COMPLICATIONS: A 30-DAY PRE-OPERATIVE EVALUATION. *Sleep* 2024; 47:A249-A250. Full Text

S. Bugazia, Henry Ford Macomb Hospital, United States

Introduction: The coexistence of obstructive sleep apnea (OSA) and obesity creates an intricate clinical scenario, particularly for individuals pursuing bariatric surgery. OSA increases perioperative risks, including prolonged stay, re-intubation, and cardiovascular events. It is generally recommended that patients with OSA start using Positive Airway Pressure (PAP) therapy before surgery, however studies are mixed on whether use of PAP reduces postoperative or long-term complications, and many include only subjective compliance data. We examined objective pre-operative PAP use among OSA patients undergoing bariatric surgery and its impact in reducing post-operative complications. Methods: Our study included data from 140 individuals who underwent bariatric surgery gathered over a 6-month period, with 79 having verified PAP use in the 30-days before surgery. A correlation analysis was conducted comparing 30-day preoperative PAP use to total operative time, time in the Post- Anesthesia Care Unit (PACU), length of inpatient stay, collective PACU and inpatient time, ED visits within the 30 days post-op. There were no deaths, ICU transfers, respiratory or surgical complications in this sample. Furthermore, PAP use was categorized into tertiles, and an analysis of variances was completed for the following secondary variables: Apnea-Hypopnea Index (AHI), time with oxygen saturation < 88% and < 90%, age, and weight. Mean PAP use in minutes was 376±59 for the highestuse group, 183±61 for intermediate-use group, and 10±16 for lowest-use group. Results: Our correlation analysis revealed no significant associations between 30-day pre-operative PAP use and abovementioned outcomes. Upon PAP use stratification into tertiles, a statistically significant effect became apparent in relation to PACU time (p =

0.008), with oxygen saturation < 88% as a significant covariate. The PACU time in minutes varied across tertiles, with the highest-use group having a PACU time of 169±106, the intermediate-use group with 217± 156s, and the lowest-use group with 202±129. Conclusion: Overall, complications rates after bariatric surgery were low. Increased PAP use was significantly associated with shorter stays in the PACU, perhaps related to faster time to recovery from anesthesia due to lower number of desaturations, hence mitigating need for continued nursing monitoring which could potentially lower healthcare associated cost.

Internal Medicine
Bugazia S, Boshnaf M, and **Sreenivasan A**. SUBARACHNOID HEMORRHAGE MORTALITY TRENDS IN U.S. PATIENTS WITH CIRCULATORY DISEASE (1999-2020). *Crit Care Med* 2024; 52(1):S114. Full Text

S. Bugazia, Henry Ford Macomb Hospitals, Sterling Heights, MI, United States

INTRODUCTION: Subarachnoid hemorrhage is a neurological emergency that occurs as a result of bleeding into the subarachnoid space, with a mortality rate of approximately 44% and a worldwide annual occurrence estimated to be around 6.1 events per 100,000 individuals. Improved understanding of the determinants of ethnic variances and underlying comorbidities can assist primary prevention, which may lead to a reduced burden of subarachnoid hemorrhage within society, improve outcomes and lower healthcare costs. METHODS: Using the CDC multiple causes of death database (ICD-10 revision codes), we identified all patients who have circulatory system disease who died of subarachnoid hemorrhage (I60.x registered as the underlying cause of death) in two races (Caucasians and African Americans), between 1999 and 2020 in the United States. Age-adjusted mortality rates were calculated per 1,000,000 persons (PMP), standardized to the US census data from 1999, and stratified by race. RESULTS: Between 1999 and 2020, a total of 118,881 deaths were due to subarachnoid hemorrhage in patients with circulatory system disease identified in two races, with an overall age-adjusted mortality of 17.4 PMP. We identified a total of 17,770 deaths among African Americans, while 101,111 deaths in Caucasian populations. The overall age-adjusted mortality was 22.4 PMP in African Americans and, 16.7 PMP in Caucasians. Over the 21 years, the ageadjusted mortality decreased by 46 % in African Americans (from 33 PMP in 1999 to 17.7 PMP in 2020) and decreased by 34 % in Caucasians (from 22.2 PMP in 1999 to 14.6 PMP in 2020). CONCLUSIONS: This study finds that between 1999 and 2020, African Americans have the highest rates of subarachnoid hemorrhage age-adjusted mortality among patients with circulatory system disease, whereas Caucasians have the lowest proportion despite having a 584% higher incidence rate in this ethnic subgroup. Interestingly, over the twenty-one years, mortality has decreased in both races.

Internal Medicine
Zaheer A, **Venkatesh H**, and **Azar M**. MEDULLARY THYROID CARCINOMA PRESENTING WITH SEVERE HYPOKALEMIA. *Am J Kidney Dis* 2024; 83(4):S64. Full Text

Medullary thyroid carcinoma (MTC) accounts for about 5-7% of all thyroid malignancies. Most MTC are sporadic in nature. The age at initial presentation ranges between 41 and 55 years. Aside from signs and symptoms of Cushing's disease, other clinical features included weakness, exertional dyspnea, galactorrhea, back or hip pain and pathological fractures. 38 year old male presented to the hospital due to left upper extremity swelling and redness. On arrival, labs were significant for hypokalemia, 2.6 mmol/L and hyperglycemia at 166 mg/dL. He was diagnosed with acute cellulitis and started on antibiotics. Replacement of potassium resulted in minimal improvement and recurrence of severe hypokalemia prompting further work up. Urine electrolyte panel results were suggestive of renal potassium wasting defect. Aldosterone level was 5 ng/dL and direct renin level was 9.4 pg/ml. Random cortsiol level was high. Dexamethasone suppression test showed elevated cortisol levels confirming ectopic ACTH. Brain MRI revealed no pituitary lesions. Due to lack of improvement in the left arm swelling, patient underwent CT scan for possible obstruction. It showed mass in the thyroid region with abdominal lymph nodes, and multiple hepatic lesion. Liver biopsy was done which was consistent with medullary thyroid carcinoma. Patient was started on metyrapone with improvement of cortisol levels. Patient was then started on Selpercatinib, with follow up with heme/onc, nephrology, and endocrinology. Currently, patient's

potassium is well controlled. The diagnosis of ectopic ACTH production secondary to MTC is based on the presence of hypercortisolism not suppressed by high cortisol, absence of pituitary adenoma, and Cushing syndrome symptom. Treatment for ACTH production include adrenolytic. In extreme cases bilateral adrenolectomy may be needed. Tyrosine kinase inhibitors including selpercatinib, and vandetanib are used for chemotherapy for MTC. Immunotherapy was found to significantly decrease cortisol and ACTH levels. Other substances associated with MTC include production of corticotrophin-releasing factor and serotonin, occurring typically in distant metastases. Ectopic ACTH must be considered in the differential diagnosis in the setting of thyroid neoplasm, while investigating for severe refractory hypokalemia.

Nephrology

Kaur S, **Mahfouz R**, **Osorio L**, and **Atchison D**. A MEDICAL EMERGENCY: HYPERCALCEMIC CRISIS DUE TO VITAMIN D MISUSE REQUIRING HEMODIALYSIS. *Am J Kidney Dis* 2024; 83(4):S28. Full Text

Hypercalcemic crisis results from severe hypercalcemia leading to renal failure and altered mental status. Primary hyperparathyroidism and hypercalcemia of malignancy are the most frequent causes of hypercalcemic crisis. Rarely, vitamin D intoxication can cause it as well. A 58-year-old female presented with altered mental status and somnolence to the emergency room. On physical examination, the patient was obtunded. Vital signs included blood pressure 118/74 mm Hg, heart rate 106 beats per minute, temperature 36.4 degrees Centigrade, breathing 12 respirations/minute. Laboratory workup revealed severe hypercalcemia 15.1 mg/dl, ionized calcium of 1.71 mmol/l, lactic acid 9.2 mmol/l, potassium 8.1 mEq/l, BUN 106 mg/dl, creatinine 13.17 mg/dl, elevated 25-hydroxyvitamin D above 120 ng/ml, elevated 1,25-dihydroxyvitamin D of 168 pg/ml, normal intact PTH 45 pg/ml, low PTH related protein 10 pg/ml, urine albumin/creatinine ratio 3,893 mg/g, urine protein/creatinine ratio 10.70 g/g. Kidney biopsy showed acute tubular injury and nodular diabetic glomerulosclerosis. The patient initiated emergent hemodialysis. There was gradual improvement in the patient's mental status and calcium level after serial treatments with continuous and intermittent hemodialysis. As she became more alert, she endorsed taking over the counter cholecalciferol >10,000 I.U. a day over several months. Her calcium levels and renal function improved, and hemodialysis was stopped prior to discharge. Her hypercalcemia and 1,25-dihydroxyvitamin D is slowly improving and her 25-hydroxyvitamin D remains elevated above 120 ng/mL one month later. Due to the increasing use of vitamin D supplementation, patients should be educated and made aware of severe, potentially life-threatening adverse effects. Hemodialysis is rare, but efficient mode of therapy in hypercalcemic crisis.

Neurosurgery

Asmaro K, Lee C, Mohyeldin A, Ljubimov V, Vigo V, and Fernandez-Miranda J. Repeat Expanded Endoscopic Surgery for Residual Growth Hormone Producing Tumors and Persistent Acromegaly. *J Neurol Surg B Skull Base* 2024; 85. Full Text

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

Background: Surgical excision for growth-hormone producing tumors remains the preferred first line treatment for acromegaly. Surgical outcomes and biochemical remission rates depend on tumor location and approach taken-as nearly half of the tumors exhibit cavernoinvasive behavior. Nearly half of patients require adjuvant therapy, medical or radiotherapy, after surgery to achieve remission. The utilization of transcavernous surgery has enhanced surgical remission rates from approximately 50% to nearly 90%. However, transcavernous surgery for previously operated tumors with residual disease remains controversial and unstudied. Objective: We aim to study the surgical outcomes after endoscopic transcavernous surgery for previously operated pituitary tumors with residual tumor and active disease. Methods: A prospectively collected and retrospective cohort analysis of previously operated pituitary tumors with residual disease from two centers, between 2018 and 2023. We tabulated clinical outcomes and results of repeat surgery in patients with acromegaly undergoing reoperation for residual. Results: A total of 28 consecutive patients with acromegaly undergoing repeat endonasal surgery at two centers were analyzed. 25 patients had undergone one prior surgery, 2 had two prior surgeries, and 1 patient had undergone three prior surgeries. There were 18 Knosp grade 0-2 tumors on preoperative imaging, 6 grade 3, and 4 grade 4. A transcavernous approach was done in 27 patients of which 25 (93%) had

positive cavernous sinus disease. Three-month follow up data was available in 20 patients, of which, 16 (80%) had achieved biochemical remission with surgery alone and 19 (90%) with surgery and adjuvant therapy. There were no post-operative CSF leaks or unplanned return to the operating room. Five patients had postoperative diplopia, all of which recovered. Conclusions: Surgery for acromegaly remains the mainstay modality of treatment. Results can vary depending on surgeon experience and approach taken. Transcavernous surgery offers enhanced gross total resection and remission rates. Repeat surgery with a transcavernous approach for patients with active disease and had undergone traditional transsphenoidal surgery is safe and efficacious in achieving biochemical remission.

Neurosurgery
Eide J, **Mason W**, **Mackie H**, **Cook B**, **Ray A**, **Asmaro K**, **Robin A**, **Rock J**, and **Craig J**. Diagnostic Accuracy of Beta-2 Transferrin GEL Electrophoresis for Detecting Cerebrospinal Fluid Rhinorrhea. *J Neurol Surg B Skull Base* 2024; 85. Full Text

J. Eide, Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, Detroit, MI, United States

Background: Unilateral thin clear rhinorrhea (UTCR) is a common presenting rhinologic complaint and may represent a variety of pathologies, the most concerning being cerebrospinal fluid (CSF) rhinorrhea. Assessing for beta-2 transferrin (B2Tf) on gel electrophoresis (GE) has become the preferred initial noninvasive testing modality for confirming CSF rhinorrhea due to reportedly high sensitivity (87-100%) and specificity (71-100%). However, despite widespread use, there have been relatively few studies assessing its diagnostic accuracy. The purpose of this single-institution study was to determine the accuracy of B2Tf GE in detecting CSF rhinorrhea. Methods: A single-center retrospective review was conducted from 2015 and 2021 for all patients who presented with UTCR and underwent B2Tf GE. Institutional review board approval was obtained for this study. The gold standard for diagnostic confirmation of true and false positives (TP, FP) as well as false negatives (FN) was endoscopic exploration. The gold standard for true negative (TN) was response to medical therapy. A true positive was defined as a positive B2Tf GE result with positive endoscopic exploration and repair. Indeterminate B2Tf GE results were recorded but not included in analyses. Results: A total of 72 patients underwent 100 B2Tf GE tests. Of these, 35 patients (48.6%) were diagnosed with CSF rhinorrhea. Of the 100 B2Tf GE tests, there were 42 TPs, 40 TNs, 12 FPs, and 6 FNs yielding 87.5% sensitivity, 76.9% specificity, 77.8% positive predictive value, and 87% negative predictive value. Conclusion: While this single-institutional data demonstrates sensitivities, specificities, and predictive values within ranges previously reported in the literature, it also demonstrates potential diagnostic limitations. Clinicians should be aware that FP and FN results can occur. On a case-by-case basis, especially if B2Tf GE results deviate from clinical suspicion, one must consider the utility of repeat B2Tf GE versus other forms of confirmatory diagnostic testing. Future studies should explore reasons for erroneous B2Tf GE results and how these may change clinical decision-making.

Neurosurgery
Fadel H, **Hamilton T**, **Pawloski J**, **Ray A**, **Eide J**, **Abdulhak M**, **Craig J**, and **Asmaro K**. Endoscopic Endonasal Far Medial Approach for Resection of Craniocervical Chordoma. *J Neurol Surg B Skull Base* 2024; 85. Full Text

H. Fadel, Henry Ford Health, Detroit, MI, United States

A 24-year-old gentleman with history of chronic cervicogenic and occipital headaches who presented with right tongue deviation and atrophy. MRI showed a mass at the craniocervical junction, consistent with a chordoma. A transpterygoid transeustachian far medial approach was undertaken for resection of tumor. The patient was kept in a Halo overnight and underwent an occipitocervical fixation the following day. MRI showed gross total resection. He did well without new deficits or complaints and preoperative headaches resolved.

Neurosurgery

Fadel HA, **Pawloski J**, **Shaftel K**, **Ray A**, **Eide J**, **Craig J**, and **Asmaro KP**. Endoscopic Endonasal Transcavernous Approach to Pituitary Adenomas with Cavernous Sinus Invasion: A Single-Center Experience. *J Neurol Surg B Skull Base* 2024; 85. Full Text

H.A. Fadel, Henry Ford Hospital, Detroit, MI, United States

Introduction: Sellar tumors with extension into the cavernous sinus (CS) are associated with higher rates of subtotal resection, failed biochemical remission, recurrence, and potentially devastating vascular injury. Recent advancements in expanded endoscopic transcavernous techniques have provided safe access to the cavernous sinus. However, the improved exposure of paraseller tumors comes with an increased risk of arterial or venous injury and cranial nerve deficits. In particular, the expected low-flow venous cavernous bleeding is managed with light hemostatic matrix packing, presenting an added theoretical threat of iatrogenic venous sinus thrombosis that has not previously been studied. Objective: To report the clinical, radiographic, and vascular outcomes of patients who underwent endoscopic endonasal transcavernous surgery for pituitary adenomas with extension into the cavernous sinus, with a particular focus on potential vascular operative morbidity. Methods: A single-institution database was queried to identify all patients who underwent endoscopic endonasal transcavernous surgery for pituitary adenomas with extension into the cavernous sinus. All included patients had postoperative contrast-enhanced MRIs to evaluate for extent of tumor resection and patency of cavernous arterial and venous vasculature. Clinical, demographic, procedural and survival characteristics were also determined. Results: Between 2022 and 2023, ten patients with pituitary adenomas with cavernous sinus invasion underwent endoscopic endonasal transcavernous surgery. Of the ten patients, 70% were previously inadequately treated and 70% had biochemically functional tumors. Bilateral cavernous sinus invasion was noted in 40% of patients. Gross total resection was achieved in 90% of patients and all functional tumors achieved biochemical remission. No patients were found to have intraoperative vascular injury. On postoperative contrast-enhanced imaging, no patients were found to have venous thrombosis although hemostatic matrix was used freely in all cases. Only one patient was found to have a new cranial nerve deficit postoperatively that improved on long-term follow-up. One patient was found to have transient weakness secondary to a new ischemic stroke thought to be related to resection of a tumor with parenchymal invasion. Median length of stay was 4 days (2-20) and 90% of patients were discharged home postoperatively. Conclusion: Endoscopic endonasal transcavernous surgery for pituitary adenomas that invade the cavernous sinus is safe, effective, and allows for complete resection of previously incompletely treated tumors. We also report that, despite the theoretical risk of venous thrombosis given the increased use of hemostatic matrix packing, no patients were found to have cavernous sinus thrombosis postoperatively.

Neurosurgery

Lee CK, **Asmaro KP**, Ljubimov V, Rodrigues AJ, Lamano J, Mohyeldin A, Vigo V, Chang J, Katznelson LJ, and Fernandez-Miranda JC. Outcomes of Endoscopic Endonasal Transcavernous Surgery for Pituitary Adenomas: A ByCompartment Analysis. *J Neurol Surg B Skull Base* 2024; 85. Full Text

C.K. Lee, Stanford University, Stanford, CA, United States

Objective: Endoscopic endonasal transcavernous surgery can be employed effectively and safely to resect pituitary tumors which extend into the cavernous sinus. The cavernous sinus is divided into multiple compartments by the cavernous internal carotid artery. The anatomical configuration and neurovascular contents of each compartment dictates the accessibility and surgical nuance for resecting tumor in that compartment. The purpose of this study was to analyze the cavernous sinus invasion patterns of pituitary adenomas and examine the outcomes of transcavernous surgery on a bycompartment basis. Methods: Prospectively collected data from patients undergoing endoscopic endonasal surgery for functioning and nonfunctioning pituitary adenomas in 2018 to 2023 were analyzed as a retrospective cohort analysis. Cavernous sinus compartment invasion patterns were identified based on intra-operative observations. Patients undergoing first-time surgery and those undergoing repeat surgery for recurrent or residual disease were both included. Results: A total of 320 consecutive endoscopic endonasal surgeries were analyzed, of which 168 (53%) employed transcavernous surgery

(TCS). Rates of TCS were higher for repeat surgery patients (85%) compared to first-time surgery patients (45%; $p < 0.0001$). Rates of TCS were higher for functioning adenomas (67%) than nonfunctioning adenomas (37%; $p < 0.0001$). There was a higher likelihood of bilateral cavernous sinus involvement in repeat surgery patients (22%) compared to first-time surgery patients (7%; $p = 0.008$). For first-time surgery patients, there was no difference in surgical outcomes between those with unilateral and bilateral cavernous sinus invasion, in terms of gross total resection rates (82% vs. 88%; $p = 0.23$) and biochemical remission rates for functioning tumors (82% vs. 83%; $p = 0.85$). For repeat surgery patients, although there was a higher rate of gross total resection for unilateral cavernous sinus invasion (83%) compared to bilateral cavernous sinus invasion cases (55%; $p < 0.0001$), there was no difference in biochemical remission rate for patients with functioning tumors after surgery alone (76% vs. 67%; $p = 0.16$) or after adjuvant-assisted treatment (83% vs 83%; $p = 1.0$). Analysis of all 336 cavernous sinuses of the 168 TCS patients demonstrated that the probability of medial wall invasion was 53% in our series. Compartment invasion was most frequent for posterior (21%) and superior (20%) compartments, followed by inferior (17%), clinoidal (9%) and lateral (4%) compartments. The likelihood of gross total resection if a given compartment was involved was highest for medial wall (81%) and clinoidal compartment (81%), followed by inferior (79%), superior (68%), posterior (62%) and lateral (50%) compartments. Conclusions: Pituitary adenomas involving the cavernous sinus can be resected via the transcavernous approach to achieve high rates of complete tumor resection and biochemical remission for functioning pituitary adenomas. Differences in clinical outcomes between tumors invading different compartments of the cavernous sinus should be considered when planning transcavernous surgery for these tumors.

Neurosurgery
Pawloski J, **Eide J**, **Ray A**, **Rock J**, **Craig J**, and **Asmaro K**. Transpterygoid Transcavernous Approach for Resection of Previously Radiated Recurrent Chordoma with Temporoparietal Fascia Flap Reconstruction. *J Neurol Surg B Skull Base* 2024; 85. Full Text

J. Pawloski, Henry Ford Health, Detroit, MI, United States

65-year-old gentleman with a history of recurrent clival chordoma involving the sella and bilateral cavernous sinuses was referred for a second opinion. The tumor had progressed significantly despite endonasal subtotal resection 1 year prior and subsequent proton beam radiotherapy. The video demonstrates expanded endoscopic transpterygoid transcavernous approach for resection of disease. Skull base reconstruction was done utilizing a regional rotational temporoparietal fascia flap as there were no viable nasoseptal flaps given the previous surgery.

Neurosurgery
Pawloski JA, **Shaftel K**, **Fadel HA**, **Craig J**, **Eide J**, **Ray A**, **Asmaro K**, and **Rock J**. Symptomatic Keratoconjunctivitis Sicca Is Rare after Vidian Neurectomy during Expanded Endonasal Skull Base Approaches. *J Neurol Surg B Skull Base* 2024; 85. Full Text

J.A. Pawloski, Department of Otolaryngology, Henry Ford Health, Detroit, MI, United States

Introduction: Keratoconjunctivitis Sicca (KCS) or dry, irritated eyes due to lack of tear production, can be very uncomfortable to patients and require ongoing medical treatments to avoid ocular complications. Autoimmune or other disorders that affect the lacrimal gland are associated with KCS. The secretory function of the lacrimal gland is innervated by sympathetic and parasympathetic fibers by way of the nerve of the pterygoid canal, or Vidian nerve. Vidian neurectomy has been used as a treatment for refractory allergic rhinitis and other sinonasal conditions, taking advantage of the augmentation of autonomic innervation. Previous studies have shown that vidian neurectomy can reduce tear production for at least two months after the procedure. Due to this important role in lacrimation, the vidian nerve is often preserved during transcranial skull base approaches. However, in the era of expanded endoscopic endonasal approaches (EEAs), vidian neurectomy is often necessary to safely expose the anterior cavernous sinus dura, cavernous carotid artery, foramen lacerum and adjacent structures. Objective: The objective of this report is to determine the safety of vidian neurectomy during endoscopic endonasal skull base surgery, specifically with regard to the incidence of symptomatic dry eyes (KCS) in patients who have undergone vidian neurectomy during expanded EEA. Methods: Cases of a single neurosurgeon

between October 2022 and July 2023 were retrospectively reviewed to identify patients who underwent vidian neurectomy as part of an endonasal skull base approach. These patient records were reviewed in detail with attention to reports of KCS symptoms at postoperative follow up as well as postoperative ophthalmology encounters. Results: 13 patients (Female = 7) underwent vidian neurectomy as part of expanded EEA during the study period (left = 3; right = 9; bilateral = 1). The pathologies for which the surgery was performed were pituitary adenoma (N = 8), as well as chordoma (N = 2), meningioma (N = 1), squamous cell carcinoma (N = 1), and fibrous dysplasia (N = 1). No patients reported symptomatic dry eyes at initial neurosurgery follow up at 2 weeks or any subsequent visits. Three patients did see ophthalmology postoperatively for routine follow up of baseline visual deficits or cranial neuropathies but were not found to have any new symptoms related to KCS. Conclusions: Vidian neurectomy is necessary to adequately expose parasellar structures during expanded endonasal approaches to the cavernous sinus or adjacent structures. The procedure is well-tolerated, and clinical symptoms of KCS following vidian neurectomy were not observed in any of our patients.

Neurosurgery

Rychen J, **Asmaro K**, Ljubimov V, Lee MH, Rinaldi M, Xiao L, Constanzo F, Gambatesa E, Vigo V, and Fernandez-Miranda JC. Endoscopic Endonasal Pituitary Sacrifice for Selected Complex Tumors with Retrochiasmatic and Retroclival Extension: Surgical Anatomy, Step-by-Step Operative Technique and Case Series. *J Neurol Surg B Skull Base* 2024; 85. Full Text

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Background: Tumors located in the retrochiasmatic region with extension to the third ventricle might be difficult to access when the pituitary-chiasmatic corridor is narrow. Similarly, tumor extension into the retroclival space poses a surgical challenge. Pituitary transposition techniques have been developed to gain additional access to the retroclival space. However, when preoperative pituitary function is already impaired or the risk for postoperative panhypopituitarism (PH) is considered particularly high, removal of the pituitary gland might be the preferred option. Objective: Aim of this study is to describe the relevant surgical anatomy, the operative steps and our clinical experience with the endoscopic endonasal pituitary sacrifice (EE-PS) technique. Methods: Anatomical dissections of five postmortem specimens were performed. In addition, a retrospective analysis of clinical data was performed to report clinical characteristics, indications, and outcomes. Results: After a standard endoscopic endonasal approach, a wide exposure of the sella turcica and anterior walls of the cavernous sinus (CS) is performed. The boundaries of the bony exposure are as follows: the lateral opticocarotid recesses laterally, the limbus sphenoidale superiorly, and the sellar floor inferiorly. After opening of the dura, the gland is mobilized off the medial walls of the CS ([Figs. 1A] and [2A]). The descending branches of the superior hypophyseal artery are coagulated and the stalk transected ([Fig. 1B] and [2B]). After removal of the gland, bilateral posterior clinoidectomy followed by drilling of the dorsum sellae is performed ([Figs. 1C] and [2C]). The dura is opened again to access the hypothalamic region, interpeduncular and prepontine cisterns ([Figs. 1D] and [2D]). A total of 13 patients underwent EE-PS. The cohort comprised 10 (77%) craniopharyngiomas, 2 (15%) teratomas, and 1 (8%) hemangioblastoma. Nine (69%) patients had partial or complete anterior gland dysfunction preoperatively while 6 (46%) had preoperative diabetes insipidus. Due to the specific tumor configuration, the chance of preserving endocrine function was estimated to be very low in patients with intact function. The main reasons for PS were impaired surgical accessibility to the retrochiasmatic and retroclival space. Ten patients (77%) had gross total tumor resection (GTR) and 3 (23%) had a near total resection. Two (15%) patients experienced a postoperative cerebrospinal fluid leak, requiring surgical revision. Illustrative case 1: A 15-year-old male with a craniopharyngioma and partial pituitary dysfunction. The lesion extended extensively to the retrochiasmatic and retroclival space ([Fig. 3A, B]), which justified EE-PS. GTR could be achieved without hypothalamic injury ([Fig. 3C, D]). Illustrative case 2: A 16-year-old male with a nongerminomatous germ cell tumor ([Fig. 4A]) and PH. Despite chemotherapy, a vital tumor portion remained in the hypothalamic region ([Fig. 4B]). Due to the very limited pituitarychiasmatic corridor and the narrow space between the chiasm and the dorsum sella, PS was deemed necessary to access the retrochiasmatic space. GTR was achieved with no complications ([Fig. 4C, D]). Conclusion:: When preoperative pituitary function is already impaired or the risk for postoperative PH is considered particularly high, PS is a feasible surgical option to improve

visibility and accessibility to the retroclival and retrochiasmatic space, thus increasing tumor resectability. (Figure Presented).

Neurosurgery
Shaftel K, **Craig J**, **Ray A**, **Eide J**, and **Asmaro K**. Endoscopic Endonasal Transtuberculum Approach for Excision of Heavily Calcified Tuberoinfundibular Craniopharyngioma. *J Neurol Surg B Skull Base* 2024; 85. Full Text

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A 17-year-old boy with a history of frontal headaches who presented with decreased vision and bitemporal hemianopsia. He was found to have a large, heavily calcified sellar, suprasellar, and third ventricular mass, consistent with craniopharyngioma. He underwent endoscopic endonasal transtuberculum approach for resection of tumor with anatomical preservation of the pituitary gland and infundibulum. Postoperative MRI showed gross total resection. He was neurologically intact at the last follow-up.

Neurosurgery
Shaftel K, **Hamilton T**, **Brainard L**, **Angster K**, and **Rock J**. Twenty Years of Success with an Otomimix Technique for Repairing CSF Leak after Middle Cranial Fossa Craniotomy. *J Neurol Surg B Skull Base* 2024; 85. Full Text

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Introduction: Spontaneous CSF leaks from the floor of the middle cranial fossa and not uncommon and are associated with a complaint of ear fullness and hearing loss which is generally conductive. We have successfully surgically managed over 30 patients over the last 20 years by middle fossa craniotomy and CSF leak repair. Methods: A middle fossa craniotomy followed with extradural exposure of the leak site and associated encephalocoele. After removal of the encephalocoele, placement of Gelfoam in the defect followed by placement of Otomimix closes the leak primarily. Then Duragen is placed over the dural defect and tenting sutures are placed in the dura and the craniotomy closed. Results: All patients had preoperative high resolution temporal bone CT for identification of leak location. Eighteen patients with follow-up data have had identical surgical technique for leak closure and all leaks were successfully closed with no recurrence of the leak on 3- to 6-month follow-up. Discussion: Various surgical techniques have been used for management of postoperative middle cranial fossa CSF leaks due to tegmen defects. It is not uncommon for the mastoidectomy cavity to be filled with an abdominal fat graft followed by glue. More complex options include autologous temporalis fascia, split calvarial bone grafts, cellulose grafts, or auricular cartilage are also often used. There is a paucity in the literature comparing the statistical outcomes of these various techniques. Our technique using Otomimix, however, has 100% efficacy in treating CSF leaks. Otomimix is a hydroxyapatite bone cement initially designed for repair of the ossicles within the middle ear. It has the benefits of easy preparation, rapidly hardening in a wet environment, as well as osseointegration into bone for a permanent effect, making it ideal for the application of tegmen defects. While it has been documented to have roughly 5% risk of infection, none of our patients experienced an infection after the use of Otomimix. Our technique using Otomimix is to first place a Gelfoam plug into the middle fossa defect to prevent extrusion of the Otomimix onto the ossicular heads, which would lead to a conductive hearing loss. We then apply the Otomimix over the entire exposed surface of the middle fossa to prevent persistent microdefects from leaking postoperatively. Duragen is then applied over the dural defect as well as tenting sutures in the dura prior to closure of the craniotomy with a plating system. Conclusions: The described surgical technique for CSF leak closure is simple and effective.

Neurosurgery
Shaftel K, **Pawloski J**, **Fadel H**, **Lim S**, **Ray A**, **Eide J**, **Rock J**, **Craig J**, and **Asmaro K**. Bedside Pneumoencephalography in the Era of Modern Endoscopic Endonasal Surgery: Bringing a Century-Old Technique to Today's Practice. *J Neurol Surg B Skull Base* 2024; 85. Full Text

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Introduction and Objective: The use of expanded endoscopic endonasal approaches (EEA) is an increasingly popular and effective technique for the treatment of skull base tumors. There is an expected risk of temporary postoperative pneumocephalus due to the nature of intradural and subarachnoid dissection. The degree of pneumocephalus can be exacerbated by lumbar drainage, a known modality to aid in skull base reconstruction. This is due to the increased pressure gradient from the CSF flow diversion, leading to increased air accumulation from the skull base defect. Meanwhile, oxygen therapy has been previously described as a therapy to expedite the improvement in pneumocephalus, often monitored with serial CT scans. To date, no published research explores the efficacy of skull X-rays for monitoring pneumocephalus resolution in the postoperative period. The purpose of this proof-of-concept study is (1) to show the efficacy of bedside skull X-rays to monitor for worsening of pneumocephalus in patients requiring postoperative lumbar drainage, (2) show the reliability of high fraction inspired oxygen (FIO) as an effective method of relieving pneumocephalus, and (3) compare the reduction in hospital costs and radiation exposure by using this method instead of repeat CT scans. Methods: Patients from a single surgeon and institution between September 2022 and June 2023 who underwent expanded EEA for skull base pathologies. Inclusion criteria included patients who underwent intradural dissection, required lumbar drain placement postoperatively, experienced moderate to severe postoperative pneumocephalus shown on post-op CT head which was treated with high FIO (delivered via a non-rebreather facemask) and monitored with serial skull X-rays. Hospital costs of inpatient X-ray and CT scans were also examined. Radiation dose delivery of a skull X-ray and head CT were explored. Results: Nine patients who underwent expanded EEA requiring lumbar drain postoperatively had moderate to severe postoperative pneumocephalus, four men and four women between ages 37 and 68. Of these tumors, three were pituitary adenomas, four meningiomas, one tuberoinfundibular pilocytic astrocytoma, and one esthesioneuroblastoma. One patient developed significant agitation and was found to have worsening postoperative pneumocephalus after starting lumbar drainage of CSF as confirmed on bedside skull X-rays. The other patients were treated with post-operative oxygen via nonrebreather mask, and improvement of pneumocephalus was seen in all patients with bedside skull X-rays while undergoing lumbar drainage. An inpatient skull X-ray at this institution cost roughly $203 compared to a CT head costing roughly $1,071, a five-fold increase in cost. Radiation of skull X-ray is 0.1 mSv, which is 20 times less than the 2.0 mSv dose of a head CT. Conclusion: Bedside skull X-rays can aid in monitoring postoperative pneumocephalus status when there is a concern for over drainage and subsequent air being drawn through the surgical defect. Meanwhile, high FIO can aid in accelerating the resorption of trapped gaseous content within the intracranial cavity. The use of bedside X-rays supplants the need for patient transfer to the CT scanner while significantly reducing cost and radiation exposure ([Figs. 1], [2]).

Obstetrics, Gynecology and Women's Health Services

Dunietz L, Olson A, Tittle L, **Kalmbach D**, **Pitts D**, Yang CL, Jansen E, Kerver J, Hirko K, Burgess H, Swanson L, and O'Brien L. SLEEP TIMING AND DEPRESSION RISK IN PREGNANCY. *Sleep* 2024; 47:A311. Full Text

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Introduction: There is growing evidence that sleep timing is linked to health outcomes. Poorly timed sleep has been associated with metabolic risk factors and mood problems although there is a lack of data in the pregnant population. Emerging data suggest that late sleep timing during pregnancy may be associated with gestational diabetes, gestational hypertension, and preterm birth. However, data on sleep timing and mood during pregnancy are lacking. Methods: Pregnant women were recruited from prenatal clinics at a large Midwestern tertiary referral center. Women were eligible if they were at least 18 years old and pregnant in their second or third trimester with a single fetus. There were no other exclusion criteria. Participants were queried about their sleep including questions about the time they went to bed, the time they woke up and their typical nocturnal sleep duration. Sleep mid-point was calculated as the time midway between bedtime and wake time and a delayed midpoint was defined as being after 4:00am. Demographic information was abstracted from medical records. Women were considered to have depression with a score of 13 or more on the Edinburgh Postnatal Depression Scale (EPDS) or a clinical diagnosis of depression. Results: A total of 1349 women were included in the analysis, of which 15%

were classified as having depression. Mean age was 30.7 years (SD 5.6 years) and mean gestational age was 33.8 weeks (SD 4.3 weeks). Overall, 26% of women had a sleep midpoint after 4:00am. In a regression model, women with a delayed sleep midpoint had a significantly increased odds ratio for depression (OR 1.4, 95%CI 1.1-1.8), which did not appreciably change after controlling for age, race, presence of hypertension or diabetes, first pregnancy, marital status, and sleep duration (aOR 1.5, 95%CI 1.1-2.2). Conclusion: We provide initial evidence suggesting a link between self-reported late sleep midpoint and depressive symptoms in pregnancy. Assessment of sleep timing during pregnancy may have potential for identification of women at risk of depression.

Obstetrics, Gynecology and Women's Health Services

Kalmbach D, **Hirata M**, **Iqal J**, **Bayoneto A**, **Cheng P**, **Reffi A**, **Pitts D**, Swanson L, Ong J, Fresco D, O'Brien L, and **Drake C**. CONSTRUCT VALIDATION OF THE PERINATAL RUMINATION SCALE AT NIGHT IN PREGNANT PATIENTS SEEKING INSOMNIA TREATMENT. *Sleep* 2024; 47:A164. Full Text

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Introduction: Perseverating on perinatal concerns at night (nocturnal perinatal rumination) increases insomnia, depression, and suicidal ideation (SI) during pregnancy. Poorly sleeping pregnant women identify reducing nocturnal perinatal rumination as critical for alleviating insomnia during pregnancy. However, no validated measures of nocturnal perinatal rumination exist, thereby limiting research in this area. We sought to develop and validate a brief survey to assess nocturnal perinatal rumination. Methods: This study was a cross-sectional analysis of 223 pregnant women seeking insomnia treatment. Our team developed 11 questions to create the Perinatal Rumination Scale-Night (PRS-Night). Participants rated how intensely they experienced intrusive thoughts related to pregnancy while trying to sleep at night. Responses ranged from 0=not at all to 5=extremely (item examples: worry about your pregnancy or baby; have thoughts or concerns about childbirth). We conducted an exploratory factor analysis (EFA) with varimax rotation to identify the number of latent variables in our measure. Finally, we evaluated the measure's internal consistency, convergent validity, and discriminant validity. Results: 159 patients (71.3%) screened positive for clinical insomnia (insomnia severity index [ISI]≥11), 88 patients (39.5%) screened positive for PND (Edinburgh postnatal depression scale [EPDS]≥10), and 161 patients (72.2%) screened positive for high cognitive arousal (pre-sleep arousal scale's cognitive factor [PSASC]≥18). Bartlett's test of sphericity was significant ($p<.001$) and KMO was >.90, supporting EFA. The scree plot revealed one factor (Eigenvalue=6.10) consisting of all 11 items. Internal consistency was excellent (Cronbach's $\alpha=.92$). The PRS-Night yielded good convergent validity with the PSASC ($r=.56$, $p<.001$), ISI ($r=.53$, $p<.001$), EPDS ($r=.58$, $p<.001$), and perinatal anxiety questionnaire-revised ($r=.54$, $p<.001$). SI rates were elevated for pregnant patients with high rumination (PRSNight median-split high vs low: 19.6% vs 9.5%). The PRS-Night yielded good discriminant validity with the Epworth sleepiness scale ($r=.13$, ns) and patient-rated chronotype ($r=.10$, ns). Conclusion: This study supports the psychometric validity of the PRS-Night for assessing nocturnal perinatal rumination. Given patient stakeholder interest in perinatal rumination at night, the PRS-Night has immense potential to help researchers better understand disease processes related to perinatal rumination and evaluate this construct as an important target mechanism in prenatal insomnia care.

Orthopedics/Bone and Joint Center

Friedli J, and **Moeller J**. Pediatric Problem in an Adult Ankle. *Clin J Sport Med* 2024; 34(2):e36-e37. Full Text

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History: A 52-year-old male presented to the Sports Medicine clinic for evaluation of 6 months of left ankle pain. He denied any history of injury or trauma. He first noticed the pain while running a half-marathon, and it became severe enough that he could not finish the race. His pain was reported as a dull ache with an insidious onset. Pain did not improve with conservative measures such as rest, ice, compression, elevation, and over-the-counter pain-relieving medications. The patient reported increased pain with activities such as running and skiing. He denied ankle instability, swelling, or radiation of symptoms to his foot or knee. He denied constitutional symptoms such as fevers, chills, night sweats, and unintentional

weight loss. Physical Exam: Fifty-two-year-old male in no acute distress and with normal gait. No skin changes or swelling. Patient reported a deep-seated pain in his left fibula, proximal to the lateral malleolus, with no bony tenderness upon palpation. Full range of motion with dorsiflexion and plantarflexion. Negative anterior drawer test. 5/5 strength with inversion, eversion, dorsiflexion, and plantarflexion. Neurological exam revealed 21 deep tendon reflex at Achilles, and sensation of the lower extremities was intact to light touch. Normal distal pulses. Differential Diagnosis: 311. Peroneal tendinitis 312. Stress fracture 313. Ankle sprain 314. Sinus tarsi syndrome 315. Primary bone tumor Test Results: X-rays of the left ankle revealed no fracture, arthritis, or soft tissue calcifications. There was a subtle cortical irregularity of the medial fibula. MRI without contrast of the left ankle revealed erosion of the cortex of the medial distal fibular diaphysis with extension into an associated 3 × 2 cm soft tissue mass. Biopsy of the mass in the distal fibula was positive for sarcoma. PET scan was positive for malignancy with no evidence of metastasis. Final Diagnosis: Ewing's Sarcoma. Discussion: Ewing's Sarcoma is a rare bone malignancy that occurs in the diaphysis of long bones such as the femur, tibia, and humerus. Incidence is reported to be 3 per 1,000,000. It is primarily found in young adults under the age of 25 and is the second most common primary malignant bone tumor in children. It may be caused by a de novo genetic translocation of t(11;22). Biopsy is required for diagnosis, and metastasis frequently occurs to lungs, bone, and bone marrow. Ewing's Sarcoma in a patient in their 50's is extremely rare, but this case did fit the typical presentation with a prolonged course of symptoms before diagnosis. Outcome: The patient was referred to orthopedic oncology for further management. He subsequently underwent resection of the distal fibular diaphysis and chemotherapy. Follow-Up: Following surgery and chemotherapy, the patient developed a foot drop and deficits in sensation of his left foot. Weight-bearing activities, recreational sports, and ambulation were limited due to pain. He used an ankle brace for support. He was referred to physical therapy for functional rehabilitation.

Orthopedics/Bone and Joint Center

Khalaff T, Kokorelias K, Singh H, and **Ali SA**. EXERCISE PRACTICES IN SOUTH ASIAN COMMUNITIES WITH OSTEOARTHRITIS: A SCOPING REVIEW. *Osteoarthritis Cartilage* 2024; 32(6):824-825. Full Text

Purpose (the aim of the study): Osteoarthritis (OA) is a common chronic disease with a significant impact on South Asian (SA) populations, where reports of OA prevalence range widely and reach up to 83%. Given the demonstrated benefits of exercise on OA outcomes, we aimed to conduct a scoping review to explore the current state of the literature on exercise practices among SA individuals living with OA; these communities' unique cultural norms may impact health-related behaviors associated with exercise interventions. Methods: We conducted a scoping review and used a mixed methods approach for data analysis. Our literature search spanned the databases Medline, Embase, PsycINFO, PubMed, and the Sports Medicine & Education Index, focusing on peer-reviewed studies published between 2007 and 2022. We selected studies that expressly reported on ‘exercise’ in the context of OA management. ‘South Asian populations’ refer to individuals from Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, and Sri Lanka. We applied Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-SCr) criteria. We used Covidence software for deduplication, screening (by two independent reviewers), and data extraction. Disputes over study selection were handled through consensus or by consulting a third reviewer. Our analysis included quantitative assessments (capturing countries, exercise types, study types, and measurement tools) as well as qualitative methods, with an emphasis on inductive coding to allow themes to emerge directly from the data. We also compared our findings to the exercise recommendations outlined in the 2019 guideline for the management of OA. Results: Our literature search returned 678 records, with 434 titles and abstracts screened after removing duplicates. From this, 54 full-text articles were screened, and 33 articles were determined to meet our selection criteria. The majority of included articles were from India (22 of 33), with studies focused primarily on resistance-based exercises (21 of 33), and predominantly using randomized controlled trials with the Western Ontario and McMaster Universities Arthritis Index (WOMAC) as the most common outcome measure. Notably, the language in which the WOMAC was administered was not explicitly stated. Our content analysis identified four overarching themes. First, 'Perception of Illness and Exercise' reflects how SA communities’ cultural beliefs on OA (particularly with respect to pain) influence their exercise habits and attitudes. Second, 'Yoga as a Prevalent Exercise Practice' emphasizes the common use of yoga for managing OA in these cultural groups. Third, 'Cultural

Nuances in Research Design' captures the role of cultural factors in defining research methodology and exercises selected for OA management. Fourth, 'Accessibility & Personalized OA Management' identifies the need for tailored exercise regimens that are readily integrated into daily routines of SA communities (e.g., simple stretching or strength-building exercises that can be done while performing activities of daily living, not requiring specialized equipment or settings). Finally, we found that the exercises reported in the included articles were generally consistent with those recommended in established OA management guidelines, with a focus on preferred exercises such as yoga. Conclusions: This scoping review revealed four key findings that highlight important effects of cultural norms on exercise interventions for OA management in SA populations: 'Perception of Illness and Exercise', 'Yoga as a Prevalent Exercise Practice', 'Cultural Nuances in Research Design', and 'Accessibility & Personalized OA Management'. Taken together, these findings emphasize the need to tailor exercise interventions to the specific health perspectives and preferences held by a cultural group. Our findings are most relevant to Indian populations since the majority of included studies were conducted in India. Our findings also highlight the need for more researc into the cultural adaptation of outcome measures such as WOMAC, specifically its linguistic suitability for SA communities, to improve studies on OA management in diverse cultural contexts. Ultimately, a better understanding of the cultural norms surrounding exercise practices is expected to inform more appropriate interventions to improve OA management in SA populations.

Otolaryngology – Head and Neck Surgery

Creighton E, DeKloe J, Tekumalla S, **Plawecki A**, Kaffenberger T, Alapati R, Doghramji K, Boon M, and Huntley C. CPAP TOLERANCE SCORES ARE EFFECTIVE IN PREDICTING CPAP USAGE IN THE SHORT-TERM. *Sleep* 2024; 47:A240. Full Text

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Introduction: Our group previously presented work demonstrating the value of a 10-question CPAP tolerance survey in predicting therapy compliance at 30-90 days after CPAP prescription. We conducted a follow-up survey in the same cohort 6 months after CPAP prescription to examine the utility of the survey in predicting CPAP compliance. Methods: This was a prospective study at a single tertiary care hospital. Patients diagnosed with clinically significant OSA (moderate disease, mild disease with symptoms, or mild disease with a comorbidity) between January-March 2023 that had initiated PAP therapy and attended a follow-up visit were provided a 10-question survey regarding symptoms and attitudes related to CPAP at their first follow up visit and again 6-9 months later. Data collected used for statistical analysis included: tolerance survey scores, CPAP usage, attendance of 6-month follow-up visit, demographics, OSA severity, and Epworth Sleepiness Scale (ESS) scores. Univariate and multivariate regression were used to analyze relationships between survey responses and CPAP usage data. Adherence was defined as using PAP therapy for ≥ 4hrs for ≥ 70% of nights in a 30-day period. Results: Of the 105 respondents to the initial survey, 56 (53.3%) responded to the 6-month survey. Tolerance scores at 6-months correlated with % adherence at 6-months ($p = 0.02$) and minutes of CPAP usage at 6-months ($p = 0.04$). Each point of increase in 6-month survey scores was associated with an additional 2.7 minutes of use, on average. Initial tolerance survey scores did not significantly correlate with compliance 6-months later ($p = 0.17$). Initial tolerance survey scores did, however, correlate with tolerance survey scores 6 -months later (ß = 0.77, $p < 0.001$) and there was no significant difference between initial tolerance survey scores and scores at 6-months (mean difference -2.81, $p = 0.11$). Stepwise regression models showed minimized error when age, ESS at first follow-up, OSA severity and 6-month tolerance scores were used as covariates for an outcome of minutes of CPAP usage at 6-months. Conclusion: CPAP tolerance surveys have utility in estimating CPAP compliance in the short-term but may not capture important changes in patient attitudes that allow for the prediction of long-term CPAP compliance.

Otolaryngology – Head and Neck Surgery

Eide J, **Mason W**, **Mackie H**, **Cook B**, **Ray A**, **Asmaro K**, **Robin A**, **Rock J**, and **Craig J**. Diagnostic Accuracy of Beta-2 Transferrin GEL Electrophoresis for Detecting Cerebrospinal Fluid Rhinorrhea. *J Neurol Surg B Skull Base* 2024; 85. Full Text

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Background: Unilateral thin clear rhinorrhea (UTCR) is a common presenting rhinologic complaint and may represent a variety of pathologies, the most concerning being cerebrospinal fluid (CSF) rhinorrhea. Assessing for beta-2 transferrin (B2Tf) on gel electrophoresis (GE) has become the preferred initial noninvasive testing modality for confirming CSF rhinorrhea due to reportedly high sensitivity (87-100%) and specificity (71-100%). However, despite widespread use, there have been relatively few studies assessing its diagnostic accuracy. The purpose of this single-institution study was to determine the accuracy of B2Tf GE in detecting CSF rhinorrhea. Methods: A single-center retrospective review was conducted from 2015 and 2021 for all patients who presented with UTCR and underwent B2Tf GE. Institutional review board approval was obtained for this study. The gold standard for diagnostic confirmation of true and false positives (TP, FP) as well as false negatives (FN) was endoscopic exploration. The gold standard for true negative (TN) was response to medical therapy. A true positive was defined as a positive B2Tf GE result with positive endoscopic exploration and repair. Indeterminate B2Tf GE results were recorded but not included in analyses. Results: A total of 72 patients underwent 100 B2Tf GE tests. Of these, 35 patients (48.6%) were diagnosed with CSF rhinorrhea. Of the 100 B2Tf GE tests, there were 42 TPs, 40 TNs, 12 FPs, and 6 FNs yielding 87.5% sensitivity, 76.9% specificity, 77.8% positive predictive value, and 87% negative predictive value. Conclusion: While this single-institutional data demonstrates sensitivities, specificities, and predictive values within ranges previously reported in the literature, it also demonstrates potential diagnostic limitations. Clinicians should be aware that FP and FN results can occur. On a case-by-case basis, especially if B2Tf GE results deviate from clinical suspicion, one must consider the utility of repeat B2Tf GE versus other forms of confirmatory diagnostic testing. Future studies should explore reasons for erroneous B2Tf GE results and how these may change clinical decision-making.

Otolaryngology – Head and Neck Surgery
Fadel H, **Hamilton T**, **Pawloski J**, **Ray A**, **Eide J**, **Abdulhak M**, **Craig J**, and **Asmaro K**. Endoscopic Endonasal Far Medial Approach for Resection of Craniocervical Chordoma. *J Neurol Surg B Skull Base* 2024; 85. Full Text

H. Fadel, Henry Ford Health, Detroit, MI, United States

A 24-year-old gentleman with history of chronic cervicogenic and occipital headaches who presented with right tongue deviation and atrophy. MRI showed a mass at the craniocervical junction, consistent with a chordoma. A transpterygoid transeustachian far medial approach was undertaken for resection of tumor. The patient was kept in a Halo overnight and underwent an occipitocervical fixation the following day. MRI showed gross total resection. He did well without new deficits or complaints and preoperative headaches resolved.

Otolaryngology – Head and Neck Surgery
Fadel HA, **Pawloski J**, **Shaftel K**, **Ray A**, **Eide J**, **Craig J**, and **Asmaro KP**. Endoscopic Endonasal Transcavernous Approach to Pituitary Adenomas with Cavernous Sinus Invasion: A Single-Center Experience. *J Neurol Surg B Skull Base* 2024; 85. Full Text

H.A. Fadel, Henry Ford Hospital, Detroit, MI, United States

Introduction: Sellar tumors with extension into the cavernous sinus (CS) are associated with higher rates of subtotal resection, failed biochemical remission, recurrence, and potentially devastating vascular injury. Recent advancements in expanded endoscopic transcavernous techniques have provided safe access to the cavernous sinus. However, the improved exposure of paraseller tumors comes with an increased risk of arterial or venous injury and cranial nerve deficits. In particular, the expected low-flow venous cavernous bleeding is managed with light hemostatic matrix packing, presenting an added theoretical threat of iatrogenic venous sinus thrombosis that has not previously been studied. Objective: To report the clinical, radiographic, and vascular outcomes of patients who underwent endoscopic endonasal transcavernous surgery for pituitary adenomas with extension into the cavernous sinus, with a particular focus on potential vascular operative morbidity. Methods: A single-institution database was queried to identify all patients who underwent endoscopic endonasal transcavernous surgery for pituitary adenomas

with extension into the cavernous sinus. All included patients had postoperative contrast-enhanced MRIs to evaluate for extent of tumor resection and patency of cavernous arterial and venous vasculature. Clinical, demographic, procedural and survival characteristics were also determined. Results: Between 2022 and 2023, ten patients with pituitary adenomas with cavernous sinus invasion underwent endoscopic endonasal transcavernous surgery. Of the ten patients, 70% were previously inadequately treated and 70% had biochemically functional tumors. Bilateral cavernous sinus invasion was noted in 40% of patients. Gross total resection was achieved in 90% of patients and all functional tumors achieved biochemical remission. No patients were found to have intraoperative vascular injury. On postoperative contrast-enhanced imaging, no patients were found to have venous thrombosis although hemostatic matrix was used freely in all cases. Only one patient was found to have a new cranial nerve deficit postoperatively that improved on long-term follow-up. One patient was found to have transient weakness secondary to a new ischemic stroke thought to be related to resection of a tumor with parenchymal invasion. Median length of stay was 4 days (2-20) and 90% of patients were discharged home postoperatively. Conclusion: Endoscopic endonasal transcavernous surgery for pituitary adenomas that invade the cavernous sinus is safe, effective, and allows for complete resection of previously incompletely treated tumors. We also report that, despite the theoretical risk of venous thrombosis given the increased use of hemostatic matrix packing, no patients were found to have cavernous sinus thrombosis postoperatively.

Otolaryngology – Head and Neck Surgery
Pawloski J, **Eide J**, **Ray A**, **Rock J**, **Craig J**, and **Asmaro K**. Transpterygoid Transcavernous Approach for Resection of Previously Radiated Recurrent Chordoma with Temporoparietal Fascia Flap Reconstruction. *J Neurol Surg B Skull Base* 2024; 85. Full Text

J. Pawloski, Henry Ford Health, Detroit, MI, United States

65-year-old gentleman with a history of recurrent clival chordoma involving the sella and bilateral cavernous sinuses was referred for a second opinion. The tumor had progressed significantly despite endonasal subtotal resection 1 year prior and subsequent proton beam radiotherapy. The video demonstrates expanded endoscopic transpterygoid transcavernous approach for resection of disease. Skull base reconstruction was done utilizing a regional rotational temporoparietal fascia flap as there were no viable nasoseptal flaps given the previous surgery.

Otolaryngology – Head and Neck Surgery
Pawloski JA, **Shaftel K**, **Fadel HA**, **Craig J**, **Eide J**, **Ray A**, **Asmaro K**, and **Rock J**. Symptomatic Keratoconjunctivitis Sicca Is Rare after Vidian Neurectomy during Expanded Endonasal Skull Base Approaches. *J Neurol Surg B Skull Base* 2024; 85. Full Text

J.A. Pawloski, Department of Otolaryngology, Henry Ford Health, Detroit, MI, United States

Introduction: Keratoconjunctivitis Sicca (KCS) or dry, irritated eyes due to lack of tear production, can be very uncomfortable to patients and require ongoing medical treatments to avoid ocular complications. Autoimmune or other disorders that affect the lacrimal gland are associated with KCS. The secretory function of the lacrimal gland is innervated by sympathetic and parasympathetic fibers by way of the nerve of the pterygoid canal, or Vidian nerve. Vidian neurectomy has been used as a treatment for refractory allergic rhinitis and other sinonasal conditions, taking advantage of the augmentation of autonomic innervation. Previous studies have shown that vidian neurectomy can reduce tear production for at least two months after the procedure. Due to this important role in lacrimation, the vidian nerve is often preserved during transcranial skull base approaches. However, in the era of expanded endoscopic endonasal approaches (EEAs), vidian neurectomy is often necessary to safely expose the anterior cavernous sinus dura, cavernous carotid artery, foramen lacerum and adjacent structures. Objective: The objective of this report is to determine the safety of vidian neurectomy during endoscopic endonasal skull base surgery, specifically with regard to the incidence of symptomatic dry eyes (KCS) in patients who have undergone vidian neurectomy during expanded EEA. Methods: Cases of a single neurosurgeon between October 2022 and July 2023 were retrospectively reviewed to identify patients who underwent vidian neurectomy as part of an endonasal skull base approach. These patient records were reviewed in

detail with attention to reports of KCS symptoms at postoperative follow up as well as postoperative ophthalmology encounters. Results: 13 patients (Female = 7) underwent vidian neurectomy as part of expanded EEA during the study period (left = 3; right = 9; bilateral = 1). The pathologies for which the surgery was performed were pituitary adenoma (N = 8), as well as chordoma (N = 2), meningioma (N = 1), squamous cell carcinoma (N = 1), and fibrous dysplasia (N = 1). No patients reported symptomatic dry eyes at initial neurosurgery follow up at 2 weeks or any subsequent visits. Three patients did see ophthalmology postoperatively for routine follow up of baseline visual deficits or cranial neuropathies but were not found to have any new symptoms related to KCS. Conclusions: Vidian neurectomy is necessary to adequately expose parasellar structures during expanded endonasal approaches to the cavernous sinus or adjacent structures. The procedure is well-tolerated, and clinical symptoms of KCS following vidian neurectomy were not observed in any of our patients.

Otolaryngology – Head and Neck Surgery
Shaftel K, **Craig J**, **Ray A**, **Eide J**, and **Asmaro K**. Endoscopic Endonasal Transtuberculum Approach for Excision of Heavily Calcified Tuberoinfundibular Craniopharyngioma. *J Neurol Surg B Skull Base* 2024; 85. Full Text

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

A 17-year-old boy with a history of frontal headaches who presented with decreased vision and bitemporal hemianopsia. He was found to have a large, heavily calcified sellar, suprasellar, and third ventricular mass, consistent with craniopharyngioma. He underwent endoscopic endonasal transtuberculum approach for resection of tumor with anatomical preservation of the pituitary gland and infundibulum. Postoperative MRI showed gross total resection. He was neurologically intact at the last follow-up.

Otolaryngology – Head and Neck Surgery
Shaftel K, **Hamilton T**, **Brainard L**, **Angster K**, and **Rock J**. Twenty Years of Success with an Otomimix Technique for Repairing CSF Leak after Middle Cranial Fossa Craniotomy. *J Neurol Surg B Skull Base* 2024; 85. Full Text

K. Shaftel, Department of Neurological Surgery, Henry Ford Health, Detroit, MI, United States

Introduction: Spontaneous CSF leaks from the floor of the middle cranial fossa and not uncommon and are associated with a complaint of ear fullness and hearing loss which is generally conductive. We have successfully surgically managed over 30 patients over the last 20 years by middle fossa craniotomy and CSF leak repair. Methods: A middle fossa craniotomy followed with extradural exposure of the leak site and associated encephalocoele. After removal of the encephalocoele, placement of Gelfoam in the defect followed by placement of Otomimix closes the leak primarily. Then Duragen is placed over the dural defect and tenting sutures are placed in the dura and the craniotomy closed. Results: All patients had preoperative high resolution temporal bone CT for identification of leak location. Eighteen patients with follow-up data have had identical surgical technique for leak closure and all leaks were successfully closed with no recurrence of the leak on 3- to 6-month follow-up. Discussion: Various surgical techniques have been used for management of postoperative middle cranial fossa CSF leaks due to tegmen defects. It is not uncommon for the mastoidectomy cavity to be filled with an abdominal fat graft followed by glue. More complex options include autologous temporalis fascia, split calvarial bone grafts, cellulose grafts, or auricular cartilage are also often used. There is a paucity in the literature comparing the statistical outcomes of these various techniques. Our technique using Otomimix, however, has 100% efficacy in treating CSF leaks. Otomimix is a hydroxyapatite bone cement initially designed for repair of the ossicles within the middle ear. It has the benefits of easy preparation, rapidly hardening in a wet environment, as well as osseointegration into bone for a permanent effect, making it ideal for the application of tegmen defects. While it has been documented to have roughly 5% risk of infection, none of our patients experienced an infection after the use of Otomimix. Our technique using Otomimix is to first place a Gelfoam plug into the middle fossa defect to prevent extrusion of the Otomimix onto the ossicular heads, which would lead to a conductive hearing loss. We then apply the Otomimix over the entire exposed surface of the middle fossa to prevent persistent microdefects from leaking postoperatively. Duragen is

then applied over the dural defect as well as tenting sutures in the dura prior to closure of the craniotomy with a plating system. Conclusions: The described surgical technique for CSF leak closure is simple and effective.

Otolaryngology – Head and Neck Surgery

Shaftel K, **Pawloski J**, **Fadel H**, **Lim S**, **Ray A**, **Eide J**, **Rock J**, **Craig J**, and **Asmaro K**. Bedside Pneumoencephalography in the Era of Modern Endoscopic Endonasal Surgery: Bringing a Century-Old Technique to Today's Practice. *J Neurol Surg B Skull Base* 2024; 85. Full Text

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

Introduction and Objective: The use of expanded endoscopic endonasal approaches (EEA) is an increasingly popular and effective technique for the treatment of skull base tumors. There is an expected risk of temporary postoperative pneumocephalus due to the nature of intradural and subarachnoid dissection. The degree of pneumocephalus can be exacerbated by lumbar drainage, a known modality to aid in skull base reconstruction. This is due to the increased pressure gradient from the CSF flow diversion, leading to increased air accumulation from the skull base defect. Meanwhile, oxygen therapy has been previously described as a therapy to expedite the improvement in pneumocephalus, often monitored with serial CT scans. To date, no published research explores the efficacy of skull X-rays for monitoring pneumocephalus resolution in the postoperative period. The purpose of this proof-of-concept study is (1) to show the efficacy of bedside skull X-rays to monitor for worsening of pneumocephalus in patients requiring postoperative lumbar drainage, (2) show the reliability of high fraction inspired oxygen (FIO) as an effective method of relieving pneumocephalus, and (3) compare the reduction in hospital costs and radiation exposure by using this method instead of repeat CT scans. Methods: Patients from a single surgeon and institution between September 2022 and June 2023 who underwent expanded EEA for skull base pathologies. Inclusion criteria included patients who underwent intradural dissection, required lumbar drain placement postoperatively, experienced moderate to severe postoperative pneumocephalus shown on post-op CT head which was treated with high FIO (delivered via a non-rebreather facemask) and monitored with serial skull X-rays. Hospital costs of inpatient X-ray and CT scans were also examined. Radiation dose delivery of a skull X-ray and head CT were explored. Results: Nine patients who underwent expanded EEA requiring lumbar drain postoperatively had moderate to severe postoperative pneumocephalus, four men and four women between ages 37 and 68. Of these tumors, three were pituitary adenomas, four meningiomas, one tuberoinfundibular pilocytic astrocytoma, and one esthesioneuroblastoma. One patient developed significant agitation and was found to have worsening postoperative pneumocephalus after starting lumbar drainage of CSF as confirmed on bedside skull X-rays. The other patients were treated with post-operative oxygen via nonrebreather mask, and improvement of pneumocephalus was seen in all patients with bedside skull X-rays while undergoing lumbar drainage. An inpatient skull X-ray at this institution cost roughly $203 compared to a CT head costing roughly $1,071, a five-fold increase in cost. Radiation of skull X-ray is 0.1 mSv, which is 20 times less than the 2.0 mSv dose of a head CT. Conclusion: Bedside skull X-rays can aid in monitoring postoperative pneumocephalus status when there is a concern for over drainage and subsequent air being drawn through the surgical defect. Meanwhile, high FIO can aid in accelerating the resorption of trapped gaseous content within the intracranial cavity. The use of bedside X-rays supplants the need for patient transfer to the CT scanner while significantly reducing cost and radiation exposure ([Figs. 1], [2]).

Pathology and Laboratory Medicine

Eide J, **Mason W**, **Mackie H**, **Cook B**, **Ray A**, **Asmaro K**, **Robin A**, **Rock J**, and **Craig J**. Diagnostic Accuracy of Beta-2 Transferrin GEL Electrophoresis for Detecting Cerebrospinal Fluid Rhinorrhea. *J Neurol Surg B Skull Base* 2024; 85. Full Text

J. Eide, Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, Detroit, MI, United States

Background: Unilateral thin clear rhinorrhea (UTCR) is a common presenting rhinologic complaint and may represent a variety of pathologies, the most concerning being cerebrospinal fluid (CSF) rhinorrhea. Assessing for beta-2 transferrin (B2Tf) on gel electrophoresis (GE) has become the preferred initial

noninvasive testing modality for confirming CSF rhinorrhea due to reportedly high sensitivity (87-100%) and specificity (71-100%). However, despite widespread use, there have been relatively few studies assessing its diagnostic accuracy. The purpose of this single-institution study was to determine the accuracy of B2Tf GE in detecting CSF rhinorrhea. Methods: A single-center retrospective review was conducted from 2015 and 2021 for all patients who presented with UTCR and underwent B2Tf GE. Institutional review board approval was obtained for this study. The gold standard for diagnostic confirmation of true and false positives (TP, FP) as well as false negatives (FN) was endoscopic exploration. The gold standard for true negative (TN) was response to medical therapy. A true positive was defined as a positive B2Tf GE result with positive endoscopic exploration and repair. Indeterminate B2Tf GE results were recorded but not included in analyses. Results: A total of 72 patients underwent 100 B2Tf GE tests. Of these, 35 patients (48.6%) were diagnosed with CSF rhinorrhea. Of the 100 B2Tf GE tests, there were 42 TPs, 40 TNs, 12 FPs, and 6 FNs yielding 87.5% sensitivity, 76.9% specificity, 77.8% positive predictive value, and 87% negative predictive value. Conclusion: While this single-institutional data demonstrates sensitivities, specificities, and predictive values within ranges previously reported in the literature, it also demonstrates potential diagnostic limitations. Clinicians should be aware that FP and FN results can occur. On a case-by-case basis, especially if B2Tf GE results deviate from clinical suspicion, one must consider the utility of repeat B2Tf GE versus other forms of confirmatory diagnostic testing. Future studies should explore reasons for erroneous B2Tf GE results and how these may change clinical decision-making.

Pharmacy

Moorhouse W, Calme G, Gladden D, Felice K, and **Ridgeway E**. MANAGEMENT OF DIABETIC KETOACIDOSIS: A BEFORE-AND-AFTER IMPLEMENTATION STUDY OF THE TWO-BAG METHOD. *Crit Care Med* 2024; 52(1):S650. Full Text

W. Moorhouse, Trinity Health - Livonia, United States

INTRODUCTION: Conventional management of diabetic ketoacidosis (DKA) utilizes a variable rate insulin infusion requiring multiple changes to IV fluid contents to resolve hyperglycemia and anion-gap acidosis. The author's institution standardized DKA management by incorporating the two-bag method into a revised orderset in May 2022. The two-bag method has been associated with earlier anion gap closure, faster normalization of blood glucose, and less hypoglycemia. However, not all studies evaluating the twobag method have reached the same conclusion. This study compares conventional management of DKA to the two-bag method. METHODS: This single-center, pre-post study included adults started on an IV insulin infusion while admitted to the emergency department for DKA treatment from July 1st, 2021 to October 31st, 2022. Patients were divided into two-bag or conventional groups based on timing in relation to the two-bag method orderset go-live in May of 2022. The following patients were excluded: age < 18 years, pregnant, and those not meeting DKA diagnostic criteria at the beginning of treatment. The primary outcome was time to anion-gap resolution (≤12mEq/L). Secondary outcomes included ICU and hospital length of stay (LOS), insulin infusion duration, and time to blood glucose ≤250mg/ dL. Safety outcomes included rates of hypoglycemia and hypokalemia during infusion. RESULTS: Time to anion-gap resolution (conventional(n=43): 11 hours vs. two-bag(n=61): 13 hours; p=0.2), median ICU LOS (1.5 days vs. 1.8 days; p=0.3) and hospital LOS (3.7 days vs. 4.0 days; p=0.9) were all similar between groups. Median duration of insulin infusion (19 hours vs. 15 hours; p=0.02) was shorter in the two-bag group while median time to blood glucose ≤250mg/dL (6 hours vs. 8 hours; p=0.03) was longer in the two-bag group. Incidence of hypoglycemia (28% vs. 5%; p=0.001) and hypokalemia (53% vs. 26%; p=0.005) were lower in the twobag group. CONCLUSIONS: The two-bag method was associated with similar efficacy to the conventional method with a potential improvement in the incidence of hypoglycemia and hypokalemia. However, more studies are needed for full evaluation of two-bag method.

Public Health Sciences

Bolderston A, McCuaig C, Kiely E, **Ghosh S**, and McEntee MF. Gender Disparities in Publication Productivity in the Journal of Medical Imaging and Radiation Sciences...RTi3 Conference, March 22-23, 2024, Toronto, Ontario. *J Med Imaging Radiat Sci* 2024; 55(1):S11-S11. Full Text

University of Alberta

Journal of Medical Imaging and Radiation Sciences
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Henry Ford Hospital

Data from healthcare scholarly journals show that there is a significant and persistent gender gap in academic publishing. There has been little research into potential gender disparities in publication productivity in the medical radiation sciences (MRS). The aim of this study, therefore, was to analyse and explain potential gender differences in article authorship and acceptance for publication in the Journal of Medical Imaging and Radiation Sciences (JMIRS) for 5 years (2017-2021). The annual submissions to the JMIRS were assessed with respect to the gender in the categories of first, last and corresponding authors. The proportions of male and female authors in each year were reported, as well as the proportions of rejections and acceptances by gender. Radiation therapy (RT) was also disaggregated from the other MRS disciplines (diagnostic imaging including ultrasound) due to a known significantly higher publication rate. There were 1116 submissions to JMIRS in all MRS disciplines over the period 2017-2021. The number of female first authors (n=501), last authors (n=430) and corresponding authors (n=456) constituted 44.9%, 38.5% and 40.9% of total first, last and corresponding authors. Overall, female authorship in all categories of authorship placement increased over the timeframe reviewed, and the percentage gain in the increase was higher than that for male authorship. However, male authorship started from a higher baseline in 2017, and it has also increased year on year and overall, as well as in each placement category examined. The three largest contributing countries to JMIRS publication were Canada, the UK and Australia, have 72.3%, 76.1% and 68.3% female MRS populations, respectively. The proportion of female authors, therefore, does not reflect the proportions of females in the profession in each country. There were 138 RT submissions. Female RTs have a statistically higher percentage of being the first and last authors of articles published in the journal in this field than for the other specialist areas in MRS. There were no significant differences in rejection rate by gender. Rejection ratios were 54:46 (Female: Male) for the first authors and 46:54 for the last author. Male author citation rates were significantly higher (1.69 Female, 2.16 Male). Despite the rising trend in female authorship over the 5 years overall and in each of the first, last, and corresponding authors places the overall number of male authors as well as the number in each category, consistently exceeds that of female authors showing that the gender publication gap in the journal exists. First and senior authorship rates do not reflect the gender proportions in the profession. Positive trends in female authorship suggest progress, but efforts are needed to address underlying barriers. The higher representation of female authors in RT compared to other MRS disciplines is possibly influenced by various factors, such as the nature of the research or the culture within the RT subfield.

Public Health Sciences

Cirulli GO, **Corsi N**, **Rakic I**, **Finati M**, **Chiarelli G**, **Stephens A**, **Davis M**, **Tinsley S**, Sood A, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Impact of lymphovascular invasion on survival of surgically treated patients with upper tract urothelial carcinoma: A nationwide analysis. *Eur Urol* 2024; 85:S819-S821. Full Text

Introduction & Objectives: Lymphovascular invasion (LVI) is recognized as an adverse prognostic factor in many cancers. However, its utility in upper tract urothelial carcinoma (UTUC) has not been well-defined. Our aim was to assess the prognostic ability of LVI in UTUC as a predictor of overall survival (OS) using a large North American cohort. Materials & Methods: Our cohort included 5,940 cM0 UTUC patients who underwent a radical nephroureterectomy (RNU), between 2010 and 2016, within the National Cancer Database (NCDB). The main variable of interest was LVI status, and its interaction with pathological nodal (pN) status. Kaplan-Meier curves were used to depict the OS also stratifying patients on LVI status. Cox regression analysis tested the impact of LVI status on OS after accounting for the available covariates. Results: Median (IQR) for age at diagnosis was 71 (63 – 78) and most patients had pT1 stage disease (48.6%). Nodal status was pN0, pN1 and pNx in 45.8%, 6.3% and 47.9%, respectively. Overall, 22.1% had LVI. The median (IQR) follow-up time was 32.6 (16. – 53.3) months. At 5-years postoperative follow-up, the estimated OS rate was 28% in patients with LVI vs. 66% in those without LVI ($p<0.001$). When patients were stratified based on nodal status those rates were 32% vs 68% in pN0 patients ($p<0.001$), 23% vs 30% in pN1 patients ($p = 0.8$), and 28% vs 65% in pNx patients ($p<0.001$). On multivariable analysis, the presence of LVI was associated with less favorable OS (HR

1.79, 95% CI: 1.60-1.99, p<0.001). Conclusions: Our study assessed the impact of LVI on OS in UTUC patients in a large North-American nationwide cohort. Our series, as the largest to-date, indicate that LVI is associated with less favorable survival outcomes in UTUC patients after RNU, and this variable could be used as a risk-stratification tool for future adjuvant therapy trials. [Figure presented]

Sleep Medicine
Badhwar A, **Shakaroun D**, **Bugazia S**, **Carlin A**, **Roehrs T**, and **Skiba V**. PREDICTORS OF PAP COMPLIANCE ONE MONTH AFTER BARIATRIC SURGERY. *Sleep* 2024; 47:A248. Full Text

A. Badhwar, Henry Ford Hospital, United States

Introduction: Obesity is a major risk factor for Obstructive sleep apnea (OSA). Bariatric surgery is a popular treatment modality for sustainable weight loss in obese patients with OSA. Metaanalysis of several randomized controlled trials and observational studies showed that bariatric surgery led to improvement in OSA severity but not cure. These patients will likely need continued treatment for OSA to minimize its complications. It is unclear what factors influence positive airway pressure (PAP) therapy adherence and compliance postoperatively. Our study aims to identify predictors of PAP compliance 1 month after bariatric surgery. Methods: Patients who underwent bariatric surgery at our institution between April and October 2023 and had diagnosed obstructive sleep apnea were identified. The 140 patients were followed prospectively through surgery and 30-day post-surgery. Medical health records, polysomnography or home sleep study results, and on-line databases of PAP use were reviewed for each patient. We used Pearson correlation coefficient testing and t-test to examine potential predictors of PAP use in the 30-day post-operative period. Results: There are statistically significant correlations ($p < 0.05$) between post-surgical PAP use and use during 7 days of initial set up ($r = 0.642$), time spent below 90% SpO2 during sleep testing ($r = 0.425$), time spent below 88% SpO2 ($r = 0.246$), preoperative STOP-BANG ($r = 0.200$), and time from sleep testing to surgery ($r = 0.242$). Pre-surgical AHI and having been evaluated by a sleep physician pre-operatively did not show statistically significant association with post-operative PAP use. Conclusion: PAP use during 7 days of initial set up is highly predictive of 1-month post-operative PAP use and may serve as a valuable marker to intervene on those patients with low use to improve long-term PAP use. Patients who were diagnosed with OSA close to their surgery had lower PAP use, suggesting patients may benefit from more time to get used to the treatment before having surgery.

Sleep Medicine
Bayoneto A, **Treger M**, **Fellman-Couture C**, Batra A, **Drake C**, and **Cheng P**. IMPROVING ADHERENCE TO SLEEP RESTRICTION IN DIGITAL CBT-I. *Sleep* 2024; 47:A191. Full Text

A. Bayoneto, Henry Ford Health, United States

Introduction: Treatment adherence has been a proposed barrier to the success of digital CBT-I (dCBT-I). Adherence to sleep restriction may be particularly important for treatment gains. One model of improving treatment adherence is to enhance dCBT-I with a nurse coach. This study compared adherence to sleep restriction between those with and without access to a nurse coach. Methods: 288 individuals with insomnia (DSM-5 diagnostic criteria) were randomized into two conditions: enhanced dCBT-I (access to a nurse coach: n=148) and control (online program only: n=140). Those in the coaching model had an initial consult with the nurse coach focused on motivational enhancement, and then received feedback via email after each session based on sleep diary reports. Those who miss two consecutive sessions were stepped-up to telehealth coaching focused on implementing sleep restriction. All participants included in this preliminary analysis completed at least 3 sleep diary entries per week throughout the study. Sleep restriction was measured with sleep diary data, operationalized as the change in standard deviation of time in bed and wake time before and after the introduction of sleep restriction. Results: Results indicate that those in the coaching group showed a greater mean reduction in the standard deviation of time in bed (coaching group: -53.3 min, control reduction: -35.9 min; Cohen's d = 0.23). Similarly mean changes in standard deviations of wake time was greater in the coaching group compared to the control group (coaching group: -19.0 min, control reduction: 1.2 min; Cohen's d = 0.22). Conclusion: Results provide preliminary support that enhancing dCBT-I with nurse coaching may produce better adherence to sleep

restriction. Future research should include sensitivity analyses, and examine the relationship between adherence to sleep restriction and improvements in symptoms.

Sleep Medicine
Braeckman R, **Drake C**, Gallo D, Vaughn B, and AbdelFattah I. SAFETY AND EFFICACY OF KP1077 IN A PHASE 2, DOUBLE-BLIND, RANDOMIZED TRIAL IN PATIENTS WITH IDIOPATHIC HYPERSOMNIA. *Sleep* 2024; 47:A278. Full Text

R. Braeckman, Zevra Therapeutics, United States

Introduction: KP1077 is under development as an oral medication for the treatment of rare sleep disorders with Excessive Daytime Sleepiness (EDS), including idiopathic hypersomnia (IH). The active ingredient in KP1077 is serdexmethylphenidate (SDX), a prodrug of d-methylphenidate. The objectives of the study were to assess the safety (primary endpoint) and efficacy of KP1077 in patients with IH. Methods: Adult patients with IH began KP1077 treatment in a 5-week open-label (OL) titration period. Possible dose levels were 80, 160, 240 and 320 mg/day SDX. Patients were randomized to receive their daily dose either once per day (just before going to sleep), or twice per day (half the daily dose just before going to sleep and half shortly after awakening). After the titration period, patients in each treatment group were randomized to placebo or continued KP1077 (optimized dose) during a 2-week double-blind (DB) withdrawal period. Assessments of safety were based on adverse events (AEs), physical examinations, clinical laboratory tests, vital signs, electrocardiograms, sleep quality, and suicidal ideation. Efficacy assessments included the Epworth Sleepiness Scale (ESS) and Idiopathic Hypersomnia Severity Scale (IHSS). Patients rated their difficulty of waking up in the morning with the Sleep Inertia Visual Analog Scale (SI-VAS) and brain fog throughout the day with an exploratory Brain Fog Scale (BFS). Results: Safety and efficacy in the OL titration phase were evaluated in an interim analysis when 22 patients completed the study (target: ≥48 completers). KP1077 was well-tolerated for both treatments and all dose levels, with most frequent AEs of insomnia, headache, and nausea. Most AEs were mild, not leading to early discontinuation. Meaningful clinical improvements in scores of ESS, IHSS, SI-VAS, and BFS were observed in both treatment groups. Mean total ESS scores decreased by >9 points after 5 weeks of OL treatment. Results from all patients in the both the OL titration and DB withdrawal periods will be presented. Conclusion: KP1077 was well-tolerated in patients with IH with AEs typical for a central nervous system stimulant. Meaningful clinical improvements of EDS, sleep inertia and brain fog were observed after 5 weeks of OL KP1077.

Sleep Medicine
Bugazia S, **Badhwar A**, **Shakaroun D**, **Carlin A**, **Roehrs T**, and **Skiba V**. PAP THERAPY IMPACT ON BARIATRIC SURGERY COMPLICATIONS: A 30-DAY PRE-OPERATIVE EVALUATION. *Sleep* 2024; 47:A249-A250. Full Text

S. Bugazia, Henry Ford Macomb Hospital, United States

Introduction: The coexistence of obstructive sleep apnea (OSA) and obesity creates an intricate clinical scenario, particularly for individuals pursuing bariatric surgery. OSA increases perioperative risks, including prolonged stay, re-intubation, and cardiovascular events. It is generally recommended that patients with OSA start using Positive Airway Pressure (PAP) therapy before surgery, however studies are mixed on whether use of PAP reduces postoperative or long-term complications, and many include only subjective compliance data. We examined objective pre-operative PAP use among OSA patients undergoing bariatric surgery and its impact in reducing post-operative complications. Methods: Our study included data from 140 individuals who underwent bariatric surgery gathered over a 6-month period, with 79 having verified PAP use in the 30-days before surgery. A correlation analysis was conducted comparing 30-day preoperative PAP use to total operative time, time in the Post- Anesthesia Care Unit (PACU), length of inpatient stay, collective PACU and inpatient time, ED visits within the 30 days post-op. There were no deaths, ICU transfers, respiratory or surgical complications in this sample. Furthermore, PAP use was categorized into tertiles, and an analysis of variances was completed for the following secondary variables: Apnea-Hypopnea Index (AHI), time with oxygen saturation < 88% and < 90%, age, and weight. Mean PAP use in minutes was 376±59 for the highestuse group, 183±61 for intermediate-use

group, and 10±16 for lowest-use group. Results: Our correlation analysis revealed no significant associations between 30-day pre-operative PAP use and abovementioned outcomes. Upon PAP use stratification into tertiles, a statistically significant effect became apparent in relation to PACU time (p = 0.008), with oxygen saturation < 88% as a significant covariate. The PACU time in minutes varied across tertiles, with the highest-use group having a PACU time of 169±106, the intermediate-use group with 217± 156s, and the lowest-use group with 202±129. Conclusion: Overall, complications rates after bariatric surgery were low. Increased PAP use was significantly associated with shorter stays in the PACU, perhaps related to faster time to recovery from anesthesia due to lower number of desaturations, hence mitigating need for continued nursing monitoring which could potentially lower healthcare associated cost.

Sleep Medicine

Caputo D, **Hirata M**, Moreno J, **Drake C**, Walch O, and **Cheng P**. MEASURING SLEEP WITH THE APPLE WATCH: A COMPARISON OF A MACHINE LEARNING VERSUS TRADITIONAL ALGORITHMS TO ACTIWATCH. *Sleep* 2024; 47:A123. Full Text

D. Caputo, Henry Ford Health, Michigan State University Health Sciences, United States

Introduction: Consumer-based actigraphy has seen rapid adoption in the United States and presents an underutilized opportunity and resource for ecologically valid sleep-wake monitoring. Furthermore, with the discontinuation of Philips Actiwatch, a reliable and scalable alternative is required. Apple Watch may be a promising solution, with prior data indicating strong concordance for activity counts derived from the Apple Watch compared to the Actiwtach. The present study extends previous findings to sleep periods as an outcome of interest. Methods: A community sample of 40 adults wore an Actiwatch and Apple Watch for 7 to 14 days with daily completion of the consensus sleep diary. Sleep periods from both wrist-worn devices were calculated and compared with sleep periods reported on the sleep diary. Sleep based on Apple Watch was derived using two approaches: one that mirrored traditional actigraphy (ie, sleep-wake classification using the Cole-Kripke model), and another than utilized machine learning with steps and heart rate as inputs. Agreement of sleep periods between the wrist-worn device and the sleep diary was operationalized as percent overlap. Performance of Apple Watch compared to the Actiwatch was then evaluated using the ratio of percentage overlap with sleep diary. A ratio of 1.00 represents perfect agreement. Results: The agreement between Apple Watch derived sleep periods and sleep diary was comparable to that with Actiwatches. The ratio of percentage overlap between the two devices was 1.00 when using the machine learning algorithm, and 0.97 when using the traditional actigraphy approach. When averaged across the sample, sleep periods derived from Actiwatch overlapped by 80.7% (95% CI [84.1% - 77.3%]) with sleep diary periods, and sleep periods derived from Apple Watch overlapped by 82.0% (95% CI [84.7% - 79.4%]) and 81.2% (95% CI [84.9% - 77.5%]) for the machine learning and traditional actigraphy approaches, respectively. Total sleep period from the Apple Watch produced lower mean absolute errors compared to Actiwatch (machine learning: 24.8 minutes, traditional actigraphy approach: 19.1 minutes). Conclusion: Sleep periods derived from Apple Watch data showed strong agreement with Actiwatch data, with the machine learning algorithm showing slightly stronger performance compared to the Cole-Kripke algorithm.

Sleep Medicine

Cheng P, Clack S, **Bayoneto A**, **Treger M**, **Fellman-Couture C**, **Kalmbach D**, and **Drake C**. INSOMNIA IN STATE MEDICAID ADMINISTRATIVE CLAIMS: MISSED OPPORTUNITY FOR IMPLEMENTATION AND DISSEMINATION? *Sleep* 2024; 47:A158. Full Text

P. Cheng, Henry Ford Health + Michigan State University Health Sciences, United States

Introduction: It is well-established that insomnia is more prevalent in under-resourced communities, which is further exacerbated by the limited access to treatment. To address this health need, essential health care services are made available by the government to those without the financial resources to purchase them (e.g., Medicaid). However, it is unclear if services for insomnia are available and accessible even within these programs. This study aimed to estimate the prevalence and patterns of diagnosis of insomnia among recipients of a state Medicaid program. Methods: We accessed Medicaid administrative data

through the state data warehouse to identify beneficiaries who had a service between 11/1/2019 and 10/31/2023 with a diagnosis code for sleep problems. We calculated the prevalence of sleep-related diagnoses out of the total number of beneficiaries with enrollment during the study period. Results: Of 3.7 million beneficiaries, 310,092 had at least one service during the study period with a sleep problem diagnosis code, for a prevalence of 8.25%. Their most common sleep problem diagnosis codes were G4700-INSOMNIA, UNSPECIFIED (5.65%), F5101-PRIMARY INSOMNIA (1.14%), G479- SLEEP DISORDER, UNSPECIFIED (0.82%), and F5102- ADJUSTMENT INSOMNIA (0.27%). Among beneficiaries with at least one sleep problem diagnosis code, 55.10% had diagnosis codes in the past 6 months indicating a significant mental health condition, substance use disorder, or neurologic condition; and 6.80% had a diagnosis of shift work disorder, free running type and/or restless leg syndrome in the past 48 months. Conclusion: Other health care administrative datasets have estimated the prevalence of insomnia diagnoses at ~30-35%; in comparison, these findings suggest that insomnia may be severely underdiagnosed and treated among Medicaid beneficiaries. This is a significant missed opportunity for implementation and dissemination of insomnia treatment for low-income adults with Medicaid coverage.

Sleep Medicine
Dauvilliers Y, **Roth T**, Thorpy M, Morse A, Kushida C, Harsh J, Ortiz L, and Gudeman J. COMPARISON OF DEMOGRAPHICS AND BASELINE NARCOLEPSY SYMPTOMS BETWEEN PARTICIPANTS WITH NT1 AND NT2 FROM REST-ON. *Sleep* 2024; 47:A276. Full Text

Y. Dauvilliers, University Montpellier, France

Introduction: Narcolepsy is classified into 2 subtypes: narcolepsy type 1 (NT1; with cataplexy) and 2 (NT2; without cataplexy). Limited data are available regarding subtype differences in clinical characteristics and disease severity. In the phase 3 REST-ON trial, once-nightly sodium oxybate (ON-SXB; LUMRYZ™) demonstrated significant improvement in the 3 coprimary endpoints of change from baseline in mean sleep latency on the Maintenance of Wakefulness test (MWT), Clinical Global Impression of Improvement rating, and weekly cataplexy episodes (all P< 0.001) in patients with NT1 and NT2. This post hoc analysis compared baseline characteristics between participants with NT1 and NT2. Methods: REST-ON (NCT02720744) participants were ≥16 years of age with NT1 or NT2, excessive daytime sleepiness, and cataplexy (NT1 only). Use of alerting agents was permitted. Randomization (1:1 to ON-SXB or placebo) was stratified by narcolepsy type; the trial population was oversampled for NT1. Baseline characteristics were compared between narcolepsy types. Results: The safety population included 212 participants (NT1, n=162; NT2, n=50). At baseline, demographic characteristics of participants with NT1 vs NT2 were: mean (SD) age, 32.1 (11.1) vs 28.3 (10.0) years, respectively; sex, 72.8% vs 52.0% female; body mass index, 28.9 (7.5) vs 25.7 (5.6) kg/m2; and use of concurrent alerting agents, 59.2% vs 68.0%. Mean (SD) baseline clinical characteristics in participants with NT1 vs NT2 were: mean sleep latency (MWT), 4.9 (2.9) vs 4.9 (2.9) minutes; Clinical Global Impression rating (CGI-Severity), 5.2 (1.1) vs 4.7 (1.1); ESS scores, 17.6 (4.0) vs 15.4 (3.2); number of sleep stage shifts to lighter stage of sleep or wake measured by polysomnography (PSG), 61.5 (22.2) vs 55.8 (23.5); number of nocturnal arousals by PSG, 81.5 (42.4) vs 73.2 (35.9); sleep quality (visual analog scale [VAS; 1 = did not sleep and 100 = slept very well]), 54.5 (22.0) vs 55.8 (20.8); and refreshing nature of sleep (VAS; 1 = not refreshed and 100 = refreshed), 49.9 (22.6) vs 42.6 (21.6). Conclusion: Limited data are available comparing NT1 and NT2 populations; these data indicate a similar level of disease severity at baseline.

Sleep Medicine
Drake C, **Mahr G**, **Reffi A**, **Son K**, Seymour G, **Sagong C**, **Jankowiak L**, Pawirosetiko J, **Hehr A**, **Cheng P**, **Kalmbach D**, **Roth T**, and **Moore D**. DEVELOPMENT OF THE AFFECTIVE NEUROSCIENCE DREAM RATING SCALE. *Sleep* 2024; 47:A402. Full Text

C. Drake, Henry Ford Health, United States

Introduction: Methods for quantifying emotional dream content have been developed. These approaches have yielded significant insights into dream content, their relation to waking cognition, and mental health. The current dream rating scale was developed to improve upon previous approaches by conceptualizing the scale based on the known fundamental affective neuronal circuits within the brain. Methods: Seventy-

seven items were developed representing fundamental emotions (SEEKING, RAGE, FEAR, LUST, CARE, GRIEF and PLAY). One-hundred dreams were randomly selected from a dream database (www.dream-bank.net). To determine interrater agreement, two raters scored all 77-items for each of the 100 dreams based on if the emotional content was present or not. Items with an interrater agreement (kappa) below .5 were excluded. Nightmares (i.e., extremely unpleasant or disturbing dreams) were independently identified by a sleeptrauma expert and compared to non-nightmares for the 7 scales. Results: Thirty-three items (kappa > 0.5; range .5-.82) were retained for the final scale. Of the items retained, 29 (85%) were endorsed in 10% or more of dreams. The most frequently identified items in the final scale were danger (44%) and fear (45%). Seven emotional dream scales were apriori identified with 3-9 items each being retained in the final scales. Scales were significantly correlated between raters (r = .54 to .88, p< .001). Across the 100 dreams FEAR was the highest endorsed emotion scale while GRIEF was lowest. As expected, nightmares had significantly elevated scores compared to non-nightmares on the FEAR, RAGE, SEEKING and GRIEF scales (p< .001) but not CARE, LUST, or PLAY. Conclusion: This dream rating scale based on mammalian emotional circuits previously identified through affective neuroscience shows promise for quantifying and understanding the emotional content of dreams. Future studies will need to further validate this preliminary affective dream content scale using different populations including individuals exposed to trauma and those with mental health and sleep disorders to determine its clinical utility.

Sleep Medicine
Dunietz L, Olson A, Tittle L, **Kalmbach D**, **Pitts D**, Yang CL, Jansen E, Kerver J, Hirko K, Burgess H, Swanson L, and O'Brien L. SLEEP TIMING AND DEPRESSION RISK IN PREGNANCY. *Sleep* 2024; 47:A311. Full Text

L. Dunietz, University of Michigan, Ann Arbor, United States

Introduction: There is growing evidence that sleep timing is linked to health outcomes. Poorly timed sleep has been associated with metabolic risk factors and mood problems although there is a lack of data in the pregnant population. Emerging data suggest that late sleep timing during pregnancy may be associated with gestational diabetes, gestational hypertension, and preterm birth. However, data on sleep timing and mood during pregnancy are lacking. Methods: Pregnant women were recruited from prenatal clinics at a large Midwestern tertiary referral center. Women were eligible if they were at least 18 years old and pregnant in their second or third trimester with a single fetus. There were no other exclusion criteria. Participants were queried about their sleep including questions about the time they went to bed, the time they woke up and their typical nocturnal sleep duration. Sleep mid-point was calculated as the time midway between bedtime and wake time and a delayed midpoint was defined as being after 4:00am. Demographic information was abstracted from medical records. Women were considered to have depression with a score of 13 or more on the Edinburgh Postnatal Depression Scale (EPDS) or a clinical diagnosis of depression. Results: A total of 1349 women were included in the analysis, of which 15% were classified as having depression. Mean age was 30.7 years (SD 5.6 years) and mean gestational age was 33.8 weeks (SD 4.3 weeks). Overall, 26% of women had a sleep midpoint after 4:00am. In a regression model, women with a delayed sleep midpoint had a significantly increased odds ratio for depression (OR 1.4, 95%CI 1.1-1.8), which did not appreciably change after controlling for age, race, presence of hypertension or diabetes, first pregnancy, marital status, and sleep duration (aOR 1.5, 95%CI 1.1-2.2). Conclusion: We provide initial evidence suggesting a link between self-reported late sleep midpoint and depressive symptoms in pregnancy. Assessment of sleep timing during pregnancy may have potential for identification of women at risk of depression.

Sleep Medicine
Kalmbach D, **Hirata M**, **Iqal J**, **Bayoneto A**, **Cheng P**, **Reffi A**, **Pitts D**, Swanson L, Ong J, Fresco D, O'Brien L, and **Drake C**. CONSTRUCT VALIDATION OF THE PERINATAL RUMINATION SCALE AT NIGHT IN PREGNANT PATIENTS SEEKING INSOMNIA TREATMENT. *Sleep* 2024; 47:A164. Full Text

D. Kalmbach, Henry Ford Health, United States

Introduction: Perseverating on perinatal concerns at night (nocturnal perinatal rumination) increases insomnia, depression, and suicidal ideation (SI) during pregnancy. Poorly sleeping pregnant women identify reducing nocturnal perinatal rumination as critical for alleviating insomnia during pregnancy. However, no validated measures of nocturnal perinatal rumination exist, thereby limiting research in this area. We sought to develop and validate a brief survey to assess nocturnal perinatal rumination. Methods: This study was a cross-sectional analysis of 223 pregnant women seeking insomnia treatment. Our team developed 11 questions to create the Perinatal Rumination Scale-Night (PRS-Night). Participants rated how intensely they experienced intrusive thoughts related to pregnancy while trying to sleep at night. Responses ranged from 0=not at all to 5=extremely (item examples: worry about your pregnancy or baby; have thoughts or concerns about childbirth). We conducted an exploratory factor analysis (EFA) with varimax rotation to identify the number of latent variables in our measure. Finally, we evaluated the measure's internal consistency, convergent validity, and discriminant validity. Results: 159 patients (71.3%) screened positive for clinical insomnia (insomnia severity index [ISI]≥11), 88 patients (39.5%) screened positive for PND (Edinburgh postnatal depression scale [EPDS]≥10), and 161 patients (72.2%) screened positive for high cognitive arousal (pre-sleep arousal scale's cognitive factor [PSASC]≥18). Bartlett's test of sphericity was significant (p<.001) and KMO was >.90, supporting EFA. The scree plot revealed one factor (Eigenvalue=6.10) consisting of all 11 items. Internal consistency was excellent (Cronbach's α=.92). The PRS-Night yielded good convergent validity with the PSASC (r=.56, p<.001), ISI (r=.53, p<.001), EPDS (r=.58, p<.001), and perinatal anxiety questionnaire-revised (r=.54, p<.001). SI rates were elevated for pregnant patients with high rumination (PRSNight median-split high vs low: 19.6% vs 9.5%). The PRS-Night yielded good discriminant validity with the Epworth sleepiness scale (r=.13, ns) and patient-rated chronotype (r=.10, ns). Conclusion: This study supports the psychometric validity of the PRS-Night for assessing nocturnal perinatal rumination. Given patient stakeholder interest in perinatal rumination at night, the PRS-Night has immense potential to help researchers better understand disease processes related to perinatal rumination and evaluate this construct as an important target mechanism in prenatal insomnia care.

Sleep Medicine

Kushida C, Thorpy M, Morse A, Harsh J, Ortiz L, **Roth T**, Dauvilliers Y, and Gudeman J. MAGNITUDE OF IMPROVEMENT IN EXCESSIVE DAYTIME SLEEPINESS WITH THE ONCE-AT-BEDTIME OXYBATE FOR NARCOLEPSY. *Sleep* 2024; 47:A274. Full Text

C. Kushida, Stanford University, United States

Introduction: Safety and efficacy of once-nightly sodium oxybate (ON-SXB; LUMRYZ™) were investigated in the phase 3 REST-ON trial (NCT02720744). Results demonstrated statistically significant improvements in the secondary endpoint of excessive daytime sleepiness (EDS) measured using the Epworth Sleepiness Scale (ESS; P< 0.001 vs placebo) at all doses tested beginning at week 2 (post hoc analysis, ON-SXB 6 g vs placebo at week 2). The objective of this post hoc analysis was to assess the magnitude of improvement in the patient-reported outcome of EDS following treatment with ON-SXB. Methods: Participants aged ≥16 years with narcolepsy type 1 (NT1) or 2 (NT2) were randomized 1:1 to ON-SXB or placebo. Doses were 4.5 g week 1; 6 g weeks 2-3; 7.5 g weeks 4-8; and 9 g weeks 9-13. Median (interquartile range [IQR]) ESS scores were assessed for each dosing period. Results: Mean age of participants was 31.2 years, 68% were female, 75.5% were white, and 76.4% had NT1. The modified intent-to-treat population included 190 participants (ON-SXB, n=97; placebo, n=93). Baseline median (IQR) ESS scores were 17 (14-19) for ON-SXB and 18 (15-21) for placebo. At week 1, median (IQR) ESS scores were 16 (12-18) for ON-SXB 4.5 g vs 17 (13-20) for placebo. At week 3 (ON-SXB 6 g), median (IQR) ESS scores were 14 (10-18) vs 17 (14-20) for placebo. At week 8 (ON-SXB 7.5 g), median (IQR) ESS scores were 12 (8-16) vs 15.5 (12-20) for placebo. At week 13, median (IQR) ESS scores for ON-SXB 9.0 g were 9.5 (6.0-15.0) vs 15 (11-19) for placebo. Conclusion: Treatment with ON-SXB resulted in clinically meaningful improvements in EDS with doses ≥6 g, as median ESS scores were within the range considered normal (≤10) at the end of the trial. ON-SXB is considered an effective intervention in treatment of EDS for patients with narcolepsy with a once-at-bedtime dose.

Sleep Medicine

Miller C, **Hirata M**, Bradley D, Blaine A, Henry A, Hall S, Thomson G, Wood I, **Kalmbach D**, and **Drake C**. UPTAKE OF FULLY AUTOMATED DIGITAL CBT FOR INSOMNIA IN THE HENRY FORD HEALTHCARE SYSTEM: THE FIRST 100 PATIENTS. *Sleep* 2024; 47:A192. Full Text

C. Miller, Big Health, United States

Introduction: Despite Cognitive Behavioral Therapy for Insomnia (CBT-I) being first line treatment for insomnia, primary care physicians typically treat insomnia with sleep hygiene or pharmacotherapy, but are unsatisfied with these approaches (Ulmer et al., 2017). Physicians may also lack knowledge about CBT-I (Dyas et al., 2010), or find it difficult to refer patients to receive therapist-delivered treatment due to a lack of trained providers (Haycock et al., 2021). Fully automated (without therapist support) digital CBT-I provides a solution with immediate, standardized, and convenient access for patients. This implementation project aims to embed evidenced-based digital treatment (Sleepio) in real world clinical practice within a large health care system (Henry Ford Health) and evaluate a novel clinical workflow. Methods: Patients with insomnia who may benefit from CBT-I determined by their treating practitioner are offered Sleepio via the Epic electronic health records system at HFH Academic Internal Medicine (AIM) and Sleep clinics. Normalization Process Theory (May et al., 2016) was used to provide a framework to help embed digital CBT-I access. We report rates of electronic orders and Sleepio sign-ups for implementation and workflow acceptability. Leaflets and digital assets were distributed. Training sessions were also provided for clinicians at both the AIM and Sleep clinics. Email reminders helped promote access over time. Results: As of December 13, 2023, N=565 electronic orders were placed by treating practitioners, and n=214 (38%) patients signed-up to start Sleepio (n=140 female, mean age=52.9 [range: 18-88]). The majority (84%) of patients were from sleep clinics. Adapting the electronic order process enabled clinicians to provide immediate digital access for patients. Senior staff training sessions at the sleep clinics were associated with a higher order rate across the Sleep clinics compared with the AIM clinic. Conclusion: Fully-automated digital CBT for insomnia can be delivered as part of routine clinical care and electronic workflows with limited disruption to clinical practice. Normalization Process Theory enabled low-lift non-disruptive changes to clinical workflow over time allowing patients to obtain access to Sleepio. Training and reminding clinicians on how to introduce patients to a digital treatment helped increase uptake.

Sleep Medicine

Ortiz L, **Roth T**, Morse A, Thorpy M, Harsh J, Kushida C, Gudeman J, and Dauvilliers Y. COMPOSITE RESPONSE WITH ONCE-NIGHTLY SODIUM OXYBATE: SYMPTOM IMPROVEMENT IN PARTICIPANTS WITH NARCOLEPSY TYPE 1. *Sleep* 2024; 47:A272-A273. Full Text

L. Ortiz, Johns Hopkins Medical Institutions, Johns Hopkins All Children's Hospital, United States

Introduction: A novel once-nightly formulation of sodium oxybate (ON-SXB; LUMRYZ™) was investigated in patients with narcolepsy type 1 (NT1) and 2 (NT2) in the phase 3 REST-ON trial (NCT02720744). ON-SXB treatment resulted in statistically significant improvements vs placebo for the coprimary endpoints of change from baseline in mean sleep latency on the Maintenance of Wakefulness test (MWT), Clinical Global Impression-Improvement (CGI-I) rating, and number of weekly cataplexy attacks, as well as the secondary endpoint of improved excessive daytime sleepiness (EDS) using the Epworth Sleepiness Scale (ESS; all P< 0.001 vs placebo). The objective of this post hoc analysis was to assess the proportion of participants with NT1 achieving clinically significant improvement on a composite of these endpoints. Methods: Participants (aged ≥16 years with NT1 or NT2) who had continuing presence of EDS (sleep latency < 11 min on the MWT and ESS score >10) and continuing cataplexy (average of 8 episodes/week) were randomized 1:1 to ON-SXB or placebo. Doses were 4.5 g week 1; 6 g weeks 2-3; 7.5 g weeks 4-8; and 9 g weeks 9-13. Clinically significant improvement thresholds per the 2021 American Academy of Sleep Medicine Clinical Practice Guidelines for each endpoint were defined as follows: MWT (2-min improvement), CGI-I (1-point improvement), cataplexy (25% decrease), or ESS (2-point improvement) and examined for each dose. Results: Mean age of participants with NT1 was 32.1 years, 72.8% were female, and 76.5% were white. The modified intent-to-treat population included 145 participants with NT1 (ON-SXB, n=73; placebo, n=72). At week 13 (9 g), more participants treated with

ON-SXB vs placebo had clinical improvement in ≥2 endpoints (87.3% vs 62.9%; P< 0.01), ≥3 endpoints (76.4% vs 43.5%; P< 0.001), and in all 4 endpoints (47.3% vs 14.5%; P< 0.001). Similar results were observed at all doses. Conclusion: These data support the robust clinical efficacy of ON-SXB, a once-at-bedtime oxybate for treatment of cataplexy or EDS in adults with narcolepsy, using multiple disease state metrics compared with placebo.

Sleep Medicine
Paniccia G, Habash S, **Drake C**, Walch O, and **Cheng P**. PERSONALIZED LIGHT THERAPY FOR NIGHT SHIFT WORK: A PRECISION MEDICINE APPROACH TO REDUCING INSOMNIA AND SLEEPINESS. *Sleep* 2024; 47:A11-A12. Full Text

G. Paniccia, Henry Ford Health, Michigan State University Health Sciences, United States

Introduction: Night shift workers experience symptoms of excessive sleepiness and insomnia due to misalignment between their circadian clock and work schedule. Circadian misalignment can be corrected using exposure to bright light delivered in accordance with a phase response curve. Our prior data indicate that a light schedule personalized to an individual's melatonin rhythms produces greater reductions in circadian misalignment compared to a one-schedule-fits-all approach. This randomized controlled trial extends prior findings by examining the effect of personalized light therapy on symptoms of shift work disorder. Methods: Individuals with shift work disorder (ICSD-3 diagnostic criteria) were randomized into two conditions: personalized light therapy (n = 14), or a non-personalized light therapy control (n = 7). Personalized light schedules were based on estimates of dim light melatonin onset (DLMO) derived from mathematical modeling of data collected via an Apple Watch. Light schedules were delivered through a mobile app (Arcashift) that updated in accordance with real-time estimates of DLMO. Estimates were confirmed with in-lab DLMO. Participants were provided light blocking glasses and a light box as source of bright light at night. Sleepiness (Karolinska Sleepiness Scale) and insomnia (Insomnia Severity Index) were assessed before and after treatment, and analyses evaluated change scores from pre- to post-treatment. Results: Those in the personalized light therapy group demonstrated decreased insomnia symptoms during daytime sleep (mean = -4.64, SD = 8.03) compared to those in the nonpersonalized control (mean = 3.57, SD = 5.38), p < 0.05. The personalized light therapy group also achieved a decrease in peak sleepiness (mean = -0.21, SD = 0.68) compared to the control (mean = 0.77, SD = 0.76), p < .001. Conclusion: Preliminary results suggest that personalizing light therapy according to the individual's specific circadian phase may be more effective in improving symptoms of insomnia and sleepiness by delivering treatment. Future research should examine other occupational and health outcomes associated with a personalized approach to light therapy.

Sleep Medicine
Roth T, Schweitzer P, Thorpy M, Gudeman J, and Dauvilliers Y. COMPARISON OF BASELINE NARCOLEPSY CHARACTERISTICS AMONG PARTICIPANT AGE GROUPS: ANALYSIS FROM REST-ON. *Sleep* 2024; 47:A275-A276. Full Text

T. Roth, Sleep Disorders and Research Center, Henry Ford Health System, United States

Introduction: Narcolepsy is a chronic disease with symptom onset frequently occurring between the ages of 10-25 years. Efficacy and safety of once-nightly sodium oxybate (ON-SXB; LUMRYZ™) were demonstrated in the phase 3 REST-ON trial. The objective of this post hoc analysis was to compare baseline narcolepsy characteristics among 3 age groups from REST-ON. Methods: Participants aged ≥16 years with narcolepsy type 1/2 were enrolled in the randomized, double-blind, placebocontrolled REST-ON trial (NCT02720744). Baseline data were trichotomized post hoc by age subgroups (years, youngest: 16-25; middle: 26-34; oldest: 35-72). Results: The safety analysis included 212 participants who received ≥1 dose of study drug (youngest, n=73; middle, n=70; oldest, n=69). For youngest, middle, and oldest participants, respectively, mean age was 20.6, 29.6, and 44.0 years; 63.0%, 68.6%, and 72.5%, were female. Respective mean baseline values for excessive daytime sleepiness (EDS) measures were similar across the youngest, middle, and oldest age groups (range of group means, mean sleep latency on the Maintenance of Wakefulness Test: 4.5-5.1, 4.6-5.0, 4.9-5.1 minutes; Clinical Global Impression of Severity for sleepiness rating: 4.8-5.3, 5.1-5.3, 5.1 [both treatment arms]; Epworth Sleepiness Scale

score: 16.7-16.9, 15.2-17.9, 17.6-18.1). For objective disrupted nighttime sleep (DNS) measures determined by polysomnography, the middle group (range of group means, 58.1-68.2) and oldest group (63.4-66.3) had more sleep stage shifts to lighter stage of sleep/wake compared to the youngest group (50.5-56.3). The oldest group experienced a higher number of nocturnal arousals (range of group means, 83.5- 87.2) compared to the middle (77.6-83.2) and youngest groups (65.4-80.7). Subjective DNS measures were similar across age groups (range of group means, visual analog scale [VAS] sleep quality, 1=did not sleep/100=slept very well: 48.3-60.7; VAS refreshing nature of sleep, 1=not refreshed/100=refreshed: 44.2-53.2). Conclusion: Baseline measures of EDS were similar among age groups of participants with narcolepsy in the REST-ON trial. Objective but not subjective DNS measures were worse in older participants, suggesting DNS may increase with age.

Sleep Medicine
Russell J, Habash S, **Drake C**, and **Cheng P**. A PILOT STUDY EXAMINING THE RELATIONSHIP BETWEEN WORK PRODUCTIVITY AND CIRCADIAN MISALIGNMENT IN NIGHT SHIFT WORK. *Sleep* 2024; 47:A3-A4. Full Text

J. Russell, Henry Ford Health + Michigan State University Health Sciences, United States

Introduction: There has been general agreement that circadian misalignment is a primary driver of poor outcomes associated with night shifts, such as insomnia, excessive sleepiness, and impaired work productivity. However, few studies have utilized gold-standard measures of circadian rhythms (eg, dim light melatonin onset and offset; DLMO and DLMOff) in examining its association with outcomes. This pilot data aimed to examine the magnitude of the relationship between circadian misalignment and work productivity in night shift workers. Methods: Participants were fixed night shift workers, engaging in at least three shifts per week with their shift beginning between 18:00 and 02:00 and lasting 8 to 12 hours. DLMO and DLMOff were assessed in-lab with 24 hourly salvia collections. Work productivity was measured with the Endicott Work Productivity Scale (EWPS). Circadian misalignment was operationalized as any overlap of DLMO and DLMOff during the participant's work shift. Insomnia and excessive sleepiness were operationalized as a score of 10 or greater on the Insomnia Severity Index (ISI; referenced to daytime sleep) and the Epworth Sleepiness Scale (ESS). Results: Night shift workers with circadian misalignment reported an EWPS score of 43.2 (SD=12.1), while those without circadian misalignment scored 39.6 (SD=15.6). The Cohen's d effect size was 0.26. In contrast, those with insomnia reported an average EWPS score of 43.9 (SD=13.6) compared to 36.1 (SD=8.5) for those without insomnia (Cohen's d = 0.69). Furthermore, those with excessive sleepiness had an average EWPS score of 44.7 (SD=14.2), versus 39.1 (SD=10.7) for those without excessive sleepiness (Cohen's d = 0.44). Conclusion: These results suggest that the association between circadian misalignment and work productivity in night shift workers may be smaller than anticipated. Instead, work productivity in night shift worker may be more strongly associated with symptoms of shift work disorder. These data are consistent with evidence that insomnia in non-shift workers are associated with higher absenteeism and presenteeism. This is also consistent with our prior research indicating that symptoms of shift work disorder can be influenced by various factors, including sleep reactivity.

Sleep Medicine
Thorpy M, **Roth T**, Kushida C, Morse A, Harsh J, Ortiz L, Gudeman J, and Dauvilliers Y. CONSISTENT EFFICACY OF ONCE-NIGHTLY SODIUM OXYBATE ACROSS PATIENT DEMOGRAPHIC AND BASELINE DISEASE CHARACTERISTICS. *Sleep* 2024; 47:A268. Full Text

M. Thorpy, Montefiore Medial Center, United States

Introduction: Once-nightly sodium oxybate (ON-SXB; LUMRYZ™) was investigated in patients with narcolepsy type 1 (NT1) or 2 (NT2) in the phase 3 REST-ON trial; treatment with 6, 7.5, and 9 g demonstrated significant improvements vs placebo (all P< 0.001) for the coprimary endpoints of change from baseline in mean sleep latency on the Maintenance of Wakefulness Test (MWT), Clinical Global Impression-Improvement (CGI-I) rating, and weekly number of cataplexy episodes (NCA), and the secondary endpoint Epworth Sleepiness Scale (ESS) score. This post-hoc analysis assessed ON-SXB efficacy in various subgroups. Methods: REST-ON (NCT02720744) participants aged ≥16 years with NT1

or NT2 were randomized 1:1 to ON-SXB (4.5 g, 1 week; 6 g, 2 weeks; 7.5 g, 5 weeks; 9 g, 5 weeks) or placebo for 13 weeks. Least squares mean differences (LSMDs) in changes from baseline for ON-SXB vs placebo for mean sleep latency on MWT, NCA (NT1 only), and ESS, and odds ratios for much / very much improved on CGI-I, were compared among baseline demographic (age, sex, race, body mass index [BMI] category) and narcolepsy disease characteristic (NT1/NT2; concomitant alerting agent use) subgroups. Results: The modified intent-to-treat population included 190 participants (ON-SXB, n=97; placebo, n=93). LSMDs for ON-SXB 9 g vs placebo in change from baseline on the MWT at week 13 revealed significant improvements (P< 0.05) for subgroups based on age, sex, race, BMI, narcolepsy type, and alerting agent/no alerting agent use. Odds ratios were significant in favor of ON-SXB 9 g vs placebo for much or very much improved on CGI-I at week 13 (P< 0.05) for both low/high age, female sex, white/non-white, high BMI, NT1, and alerting agent/no alerting agent use. LSMDs were significant in favor of ON-SXB 9 g vs placebo for change from baseline in NCA (P< 0.05) in all subgroups, except non-white and male. For the ESS, all subgroups exhibited significant improvements (P< 0.05) with ON-SXB 9 g vs placebo, except NT2. Comparable differences were found with the 6-g dose at Week 3 and the 7.5-g dose at Week 8. Conclusion: Post-hoc subgroup analyses demonstrate the robust efficacy of ON-SXB across demographic and clinical subgroups.

Sleep Medicine
Van Dongen H, Leary E, Eglit G, **Drake C**, Bogan R, and Jaeger J. SOLRIAMFETOL ON COGNITION IN OBSTRUCTIVE SLEEP APNEA WITH EXCESSIVE DAYTIME SLEEPINESS AND IMPAIRED COGNITION. *Sleep* 2024; 47:A433. Full Text

H. Van Dongen, Sleep and Performance Research Center, Washington State University, Spokane, WA, United States

Introduction: Cognitive impairment is a burdensome symptom in many patients with excessive daytime sleepiness (EDS) associated with obstructive sleep apnea (OSA). Solriamfetol (Sunosi) is a dopamine/norepinephrine reuptake inhibitor, with agonistic properties at TAAR1 and serotonin 1A receptors, approved to treat EDS associated with OSA (37.5-150 mg/day). We evaluated the effect of solriamfetol on subjective cognitive function by examining overall scores and individual cognitive complaint and functional items of the British Columbia-Cognitive Complaints Inventory (BC-CCI). Methods: SHARP was a randomized, double-blind, placebocontrolled, crossover trial in participants with impaired cognition associated with OSA and EDS. Participants received solriamfetol for 2 weeks (75 mg for 3 days, then 150 mg/day), and placebo for 2 weeks, separated by a 1-week wash out. Items of the BC-CCI included forgetfulness/memory problems, slow thinking speed, trouble expressing thoughts, trouble finding the right word, poor concentration, trouble figuring things out, and vocational, family/friends, and social/recreational functioning. Mixed models with repeated measures were used to examine differences in changes from baseline between placebo and solriamfetol. Results: The SHARP study enrolled 59 participants (ages 52.2±10.7y; 36% female). Baseline overall BC-CCI scores were 11.4±2.5 (mean±SD); scores were comparable in participants randomized to the solriamfetol/placebo (n=30; mean=11.4) versus placebo/solriamfetol (n=29; mean=11.4) crossover sequences. Overall BC-CCI scores showed greater reduction from baseline (ie, more improvement in subjective cognitive function) after solriamfetol compared with place bo (P=0.002; Cohen's d=0.45). Baseline scores on individual BC-CCI items were generally similar for participants randomized to solriamfetol/ placebo versus placebo/solriamfetol. Solriamfetol led to greater reductions from baseline compared with placebo in poor concentration (P=0.007; d=0.37), slow thinking speed (P=0.009; d=0.36), trouble finding the right word (P=0.042; d=0.28), trouble figuring things out (P=0.030; d=0.30), and forgetfulness/ memory problems (P=0.013; d=0.34). Trouble expressing thoughts approached significance (P=0.077; d=0.24). No significant differences were found for vocational, family/friends, and social/recreational functioning (P>0.05). Conclusion: Consistent with previous reports showing improvement on objective cognitive measures, solriamfetol led to significant subjective improvements overall, and particularly in subjective cognitive domains that may be related to memory, executive functioning, and processing speed. Solriamfetol can improve subjective cognitive functioning in participants with impaired cognition associated with OSA and EDS.

Sleep Medicine

Yaqoob Z, **Jaffery S**, and **Bazan L**. PRESSURE INJURY OF THE FACE AFTER AN OVERNIGHT TITRATION STUDY. *Sleep* 2024; 47:A517. Full Text

Z. Yaqoob, Henry Ford Health, United States

Introduction: We present a case of facial pressure injury related to a CPAP mask occurring within 24 hours of an overnight titration study, an uncommon finding. Report of case(s): Patient is a 69-year-old man with prior history of OSA who presented to the Henry Ford Sleep Medicine Clinic for reevaluation. His past medical history included class III obesity, diabetes mellitus, hypertension, coronary artery calcification, dyslipidemia and 88 pack-year history of smoking, he quit in 2010. When he was first diagnosed with OSA, he was treated with PAP therapy for 4 years without any reported skin adverse effects. He stopped using PAP therapy for 5 years prior to presentation to our clinic. A home sleep apnea test showed severe OSA with sleep related hypoxia. He underwent a titration study with the use of F&P Evora full face. CPAP was transitioned to BiPAP during the titration due to persistent hypoxia. He felt as though the plastic edge of the mask had cut into his skin during the study. Within 24 hours he noticed facial puffiness, tenderness, redness and facial wounds with increasing purulent discharge. He was seen in the sleep clinic the following day and was prescribed sulfamethoxazole-trimethoprim for a 7-day course for unstageable pressure injury to the face, which soon resolved. Patient was seen by allergy and an allergic reaction to the mask was ruled out. Further work up of hypoxia showed restrictive lung disease on pulmonary function testing and sniff test showed right diaphragmatic weakness. Conclusion: Pressure injury to the face within 24 hours of using a mask is an uncommon complication of overnight titration studies. To our knowledge, this is the first reported case after using the F&P Evora full face mask which could have been the triggering factor for this type of injury. We suggest proper mask fitting during titration to minimize facial pressure injuries in the sleep lab.

Surgery

Badhwar A, **Shakaroun D**, **Bugazia S**, **Carlin A**, **Roehrs T**, and **Skiba V**. PREDICTORS OF PAP COMPLIANCE ONE MONTH AFTER BARIATRIC SURGERY. *Sleep* 2024; 47:A248. Full Text

A. Badhwar, Henry Ford Hospital, United States

Introduction: Obesity is a major risk factor for Obstructive sleep apnea (OSA). Bariatric surgery is a popular treatment modality for sustainable weight loss in obese patients with OSA. Metaanalysis of several randomized controlled trials and observational studies showed that bariatric surgery led to improvement in OSA severity but not cure. These patients will likely need continued treatment for OSA to minimize its complications. It is unclear what factors influence positive airway pressure (PAP) therapy adherence and compliance postoperatively. Our study aims to identify predictors of PAP compliance 1 month after bariatric surgery. Methods: Patients who underwent bariatric surgery at our institution between April and October 2023 and had diagnosed obstructive sleep apnea were identified. The 140 patients were followed prospectively through surgery and 30-day post-surgery. Medical health records, polysomnography or home sleep study results, and on-line databases of PAP use were reviewed for each patient. We used Pearson correlation coefficient testing and t-test to examine potential predictors of PAP use in the 30-day post-operative period. Results: There are statistically significant correlations ($p < 0.05$) between post-surgical PAP use and use during 7 days of initial set up ($r = 0.642$), time spent below 90% SpO2 during sleep testing ($r = 0.425$), time spent below 88% SpO2 ($r = 0.246$), preoperative STOP-BANG ($r = 0.200$), and time from sleep testing to surgery ($r = 0.242$). Pre-surgical AHI and having been evaluated by a sleep physician pre-operatively did not show statistically significant association with post-operative PAP use. Conclusion: PAP use during 7 days of initial set up is highly predictive of 1-month post-operative PAP use and may serve as a valuable marker to intervene on those patients with low use to improve long-term PAP use. Patients who were diagnosed with OSA close to their surgery had lower PAP use, suggesting patients may benefit from more time to get used to the treatment before having surgery.

Surgery

Bugazia S, **Badhwar A**, **Shakaroun D**, **Carlin A**, **Roehrs T**, and **Skiba V**. PAP THERAPY IMPACT ON BARIATRIC SURGERY COMPLICATIONS: A 30-DAY PRE-OPERATIVE EVALUATION. *Sleep* 2024; 47:A249-A250. Full Text

S. Bugazia, Henry Ford Macomb Hospital, United States

Introduction: The coexistence of obstructive sleep apnea (OSA) and obesity creates an intricate clinical scenario, particularly for individuals pursuing bariatric surgery. OSA increases perioperative risks, including prolonged stay, re-intubation, and cardiovascular events. It is generally recommended that patients with OSA start using Positive Airway Pressure (PAP) therapy before surgery, however studies are mixed on whether use of PAP reduces postoperative or long-term complications, and many include only subjective compliance data. We examined objective pre-operative PAP use among OSA patients undergoing bariatric surgery and its impact in reducing post-operative complications. Methods: Our study included data from 140 individuals who underwent bariatric surgery gathered over a 6-month period, with 79 having verified PAP use in the 30-days before surgery. A correlation analysis was conducted comparing 30-day preoperative PAP use to total operative time, time in the Post- Anesthesia Care Unit (PACU), length of inpatient stay, collective PACU and inpatient time, ED visits within the 30 days post-op. There were no deaths, ICU transfers, respiratory or surgical complications in this sample. Furthermore, PAP use was categorized into tertiles, and an analysis of variances was completed for the following secondary variables: Apnea-Hypopnea Index (AHI), time with oxygen saturation < 88% and < 90%, age, and weight. Mean PAP use in minutes was 376±59 for the highestuse group, 183±61 for intermediate-use group, and 10±16 for lowest-use group. Results: Our correlation analysis revealed no significant associations between 30-day pre-operative PAP use and abovementioned outcomes. Upon PAP use stratification into tertiles, a statistically significant effect became apparent in relation to PACU time ($p = 0.008$), with oxygen saturation < 88% as a significant covariate. The PACU time in minutes varied across tertiles, with the highest-use group having a PACU time of 169±106, the intermediate-use group with 217± 156s, and the lowest-use group with 202±129. Conclusion: Overall, complications rates after bariatric surgery were low. Increased PAP use was significantly associated with shorter stays in the PACU, perhaps related to faster time to recovery from anesthesia due to lower number of desaturations, hence mitigating need for continued nursing monitoring which could potentially lower healthcare associated cost.

Surgery

Chamseddine H, **Kabbani L**, **Shepard A**, **Kavousi Y**, **Weaver M**, **Nypaver T**, **Onofrey K**, **Boules T**, and Hoballah JJ. Temporal Trends in Infrainguinal Bypass Outcomes: A Comparative Analysis Across Three Eras. *J Vasc Surg* 2024; 79(6):e262-e263. Full Text

Objectives: The declining volume of infrainguinal bypass (IIB) has raised concerns over contemporary outcomes compared to earlier periods. This study compares the outcomes of IIB in the contemporary era to earlier periods when IIB was more widely practiced. Methods: Patients undergoing IIB for peripheral artery disease (PAD) between 2003-2021 were identified in the Vascular Quality Initiative (VQI). Patients were stratified into three groups based on treatment era: early era (2003-2007, E1), intermediate era (2009-2013, E2), and contemporary era (2015-2019, E3). Mantel-Haenszel (MH) test for linear trend was used to test for a linear relationship between era and outcomes. Multivariate Cox regression was used to evaluate the independent association of treatment era with the outcomes of primary patency, reoperation, major amputation, and mortality. Results: A total of 39,538 patients received IIB during this time period. The average number of IIB performed per center dropped from 47.8 IIB/year to 25.3 IIB/year between 2003-2020 (Fig 1). Patients in the latter period (E3) were more likely to have a previous ipsilateral infrainguinal peripheral vascular intervention (P <.001), ipsilateral minor amputation (P <.001), and undergo emergent surgery (P <.001). Over the three time periods, there was a significant decrease in venous conduit use (E1, 71.3%; E2, 60.8%; E3, 55.2%; P <.001). Worse outcomes at 1-year for primary patency (E1, 88.6%; E2, 86.1%; E3, 84.4%; P <.001) and higher rates of reintervention (E1, 12.4%; E2, 15.0%; E3, 15.8%; P =.002) and major amputation (E1, 9.4%; E2, 9.1%; E3, 10.4%; P =.009) were observed. On multivariate Cox- regression, compared to E1 patients, higher hazard of loss of primary patency was observed for both E2 (HR, 1.72; 95% CI, 1.51-1.95) and E3 (HR, 3.67; 95% CI, 3.23-4.17)

patients (Table I). In addition, higher re-intervention was observed for both E2 (HR, 1.38; 95% CI, 1.17-1.62) and E3 (HR, 1.41; 95% CI, 1.21-1.66) patients. No difference was seen regarding major amputation and 30-day mortality between the three eras. Conclusions: There is a decline in the mean rate of IIB performed across the centers in the VQI. Patients undergoing IIB for lower extremity PAD in the contemporary era have decreased primary patency compared to those in earlier eras. This decline may stem from decreased technical proficiency associated with lower bypass volume, increased complexity of disease, and decreased use of vein conduits. This study emphasizes the need for further investigation into the factors contributing to the changing landscape of IIB outcomes.

Surgery

Chamseddine H, **Kadiyala D**, **Shepard A**, **Nypaver T**, **Weaver M**, **Kavousi Y**, **Onofrey K**, **Peshkepija A**, **Miletic K**, and **Kabbani L**. Endovascular Electrocautery Septostomy During Thoracic Endovascular Aortic Repair for Type B Dissection Provides a Suitable Sealing Zone. *J Vasc Surg* 2024; 79(6):e151. Full Text

Objectives: Thoracic endovascular aortic repair (TEVAR) is prone to type Ib endoleak when treating chronic type B aortic dissection (cTBAD) and residual TBAD (rTBAD) after type A aortic dissection repair. Fenestration of the dissection flap proximal to the distal landing zone can provide a good seal zone to land the TEVAR in and reduce the risk of retrograde false lumen perfusion. This study aims to describe the outcomes of this technique, particularly the outcome of type Ib endoleak. Methods: A prospective registry of all patients receiving a distal dissection flap fenestration with septostomy using electrocautery during TEVAR at a quaternary medical center between 2019 and 2023 was queried. Medical records were reviewed. All aortic measurements were made using computed tomography scans. Descriptive statistics were used to describe the patient population. The primary outcome was the occurrence of type Ib endoleak. Results: A total of 16 patients (14 males, 2 females) with mean age 58 ± 9 years were included. Three were cTBAD, and 13 were rTBAD. The mean maximal aortic diameter was 57 ± 12 mm, and mean aortic diameter at the aortic hiatus was 45 ± 12 mm. All procedures were performed in the elective setting. No patients required conversions to open repair. In most patients, crossing the dissection septum was made using a sheathed 0.14 wire that was bent in the middle, sheathed on both ends so that only the middle section was in contact with the septum, and connected to an electric cautery. The septum was transected using the cut setting on the cautery. The average length of septostomy was 9 cm (range, 3-27 cm). All patients had a distal end of the septostomy in aortic zone 5. Fluoroscopy time was 58 ± 20 minutes, and contrast used was 171 ± 93 mL. Median follow-up time was 16 months. On follow-up, the mean maximal aortic diameter decreased by 2 mm, whereas the mean aortic diameter at the aortic hiatus increased by 1 mm. Occurrences of endoleaks are presented in Table I. There were three type Ib endoleaks – two were attributed to aortic degeneration at the distal landing zone and required graft extension, and one persisted despite re-ballooning and required coiling of the false lumen. Conclusions: Electrocautery septostomy is a feasible and safe method to optimize a distal landing zone for TEVAR. Despite good exclusion of the false lumen, close follow-up is required because distal seal zone degeneration may occur.

Surgery

Chamseddine H, **Kavousi Y**, **Kabbani L**, **Weaver M**, **Nypaver T**, **Peshkepija A**, **Lee A**, **Musili N**, **Nguyen T**, and **Shepard A**. Outcomes of Cryopreserved Allografts for Arterial Reconstruction in Infected and Contaminated Fields. *J Vasc Surg* 2024; 79(6):e289-e290. Full Text

Objectives: Limited literature exists on cryopreserved allograft (CPA) complication rates, specifically in terms of reinfection, aneurysmal degeneration, and rupture. This study aims to assess outcomes of CPA in the setting of infection/contamination. Methods: A retrospective review of all patients in a quaternary medical center who received CPA for arterial reconstruction in the setting of infection/contamination between 2000-2023 was performed. Exclusions included patients receiving CPA for venous reconstruction, dialysis access, or lower extremity bypass surgery for reasons other than infection. Demographics, indications, procedural details, and outcomes were analyzed. Primary outcomes included CPA reinfection, rupture, aneurysmal degeneration, stenosis, and thrombosis. Kaplan-Meier estimates were used for event rate estimation and subgroup comparisons. Results: Seventy-one patients (49 males, 22 females) with mean age of 64 years met inclusion criteria. Indications for CPA included 49 central

artery infections (16 primary, 33 secondary) and 22 peripheral artery infections (7 primary, 15 secondary). Positive intraoperative cultures were found in 73% (52/71) of patients. Median follow up was 25.2 months. Thirty-day, 1-year and 5-year survival rates were 91%, 76%, and 54%, respectively. Early (30-day) CPA-related complications were observed in 7% (n = 5) of patients and included graft rupture, anastomotic dehiscence from persistent infection, and graft thrombosis (Table I). One-year CPA-related complications affected 20% (n = 12) of the patients and included graft aneurysmal degeneration, graft rupture, graft stenosis, graft thrombosis, and graft infection (Table I; Fig 1). Ninety percent (17/19) of all graft-related complications occurred within the first postoperative year. Complications were not associated with implant site (central vs peripheral), infection type (primary vs secondary), or type of organism cultured. Freedom from graft-related reintervention at 1 and 5 years was 83% and 80%, respectively. Reinterventions at 1 year included procedures for rupture (3), aneurysmal degeneration (1), anastomotic dehiscence (2), stenosis (2), occlusion (3), and uretero-graft limb fistula (1). Conclusions: Cryopreserved allografts are an acceptable conduit for arterial reconstruction in infected or contaminated fields. Graft reinfection is low at 7%. All three graft ruptures happened within the first year, with causes of rupture attributed to graft degeneration in two patients and infection from a ureteral injury and pancreatitis in one patient. Aneurysmal degeneration occurred in 6% of patients, whereas graft thrombosis and stenosis occurred in 7% and 3% of patients, respectively. This study revealed that the rate of major CPA complications is highest in the first 12 months post implantation. Aggressive early surveillance is mandatory for optimal outcomes when using this graft in contaminated or infected fields.

Surgery

Chamseddine H, **Shepard A**, **Kavousi Y**, **Weaver M**, **Nypaver T**, **Onofrey K**, **Peshkepija A**, **Boules T**, Hoballah JJ, and **Kabbani L**. National Trends in Pedal Bypass Surgery: Are We Offering Every Chance to Patients with Critical Limb Ischemia? *J Vasc Surg* 2024; 79(6):e264-e265. Full Text

Objectives: Pedal bypass (PB) has been shown to increase limb salvage in chronic limb- threatening ischemia (CLTI). However, increased use of endovascular modalities coupled with the technical challenges of PB jeopardizes its potential as a valuable revascularization modality. This study aims to assess the temporal trends in the use of PB and to compare its outcomes between high and low-volume centers. Methods: The Vascular Quality Initiative (VQI) infrainguinal bypass (IIB) module was queried for all procedures performed between 2003 and 2020. Pedal bypass was defined as a bypass to the dorsalis pedis artery, the posterior tibial artery at the ankle, or the tarsal and plantar arteries. The annual ratio of PB to IIB was calculated and trended for 18 years. The annual rate of PB performed at each center was also calculated, and centers were stratified into high-volume (≥4 PB/year) and low-volume (≤2 PB/year) centers. Multivariate Cox regression analysis was done to evaluate the independent association of center volume with the outcomes of primary patency, re-operation, major amputation, and mortality. Results: The rate of PB surgery dropped from 14% in 2003 to 4% in 2020 (Fig 1). Only 7% (19/267) of participating centers were high volume, while 15% (40/267) of participating centers did not perform any PB surgery. Compared to all IIB patients, patients undergoing PB were more likely to be diabetic, have tissue loss, and have a previous ipsilateral infrainguinal peripheral vascular intervention (Table I). The average primary patency of PB at 1-year was 85%. High-volume centers achieved higher 1-year primary patency (88% vs 81%; P =.003) and lower 1-year re-intervention (14% vs 19%; P =.04) compared to low-volume centers. On multivariate Cox regression, patients in high-volume centers had a 40% decrease in the hazard of loss of primary patency (HR, 0.62; 95% CI, 0.48-0.81) and a 30% decrease in the persistence of ischemic symptoms (HR, 0.68; 95% CI, 0.53-0.87) compared to those in low- volume centers. Conclusions: PB is not frequently utilized, even though it has an excellent 1-year 85% patency rate. High-volume PB centers have better patency rates than low-volume centers. The rate of PB in North America is declining, a finding that raises the concern as to whether CLTI patients are being offered every limb salvage option. Patients with CLTI may benefit from evaluation at centers offering PB before being subjected to other revascularization modalities or a major limb amputation.

Surgery

Chamseddine H, **Shepard A**, **Weaver M**, **Kavousi Y**, **Nypaver T**, **Onofrey K**, **Peshkepija A**, **Miletic K**, and **Kabbani L**. Comparative Analysis of Stroke Rates in Arch TEVAR: Total Endovascular Repair Plagued by High Stroke Rates. *J Vasc Surg* 2024; 79(6):e289. Full Text

Objectives: Endovascular stent-grafting extending into the ascending aorta (zone 0) is becoming more prevalent in the treatment of aortic arch disease. This study aims to evaluate the risk of stroke in patients undergoing zone 0 thoracic endovascular aortic repair (TEVAR) for aortic arch disease, considering various techniques of head vessel revascularization. Methods: Patients undergoing zone 0 TEVAR covering all arch vessels were identified in the Vascular Quality Initiative (VQI) between 2014-2023. Exclusions included cases of aortic rupture or trauma. Patients were categorized based on head vessel revascularization technique: a) open revascularization (OR) of all head vessels, b) endovascular revascularization (ER) of all head vessels during TEVAR, and c) hybrid revascularization (HR) defined as endovascular repair of at least one head vessel with open debranching of the others. Univariate analysis was performed to compare stroke rates among the three groups. Kaplan-Meier (KM) analysis and long-rank test were used to estimate and compare survival. Results: Among 382 patients receiving Zone 0 TEVAR involving the head vessels, 201 (53%) underwent OR, 76 (20%) underwent ER, and 105 (27%) underwent HR. The rate of OR dropped from 83% to 31% between 2013-2023, while that of HR increased from 4% to 54% (Fig 1). OR patients were younger (OR 63 ± 12 years, ER 70 ± 10 years, HR 69 ± 12 years; P <.001) and more likely to be symptomatic at presentation (P =.002). Otherwise, the groups exhibited similar baseline characteristics, pathologies, and distal landing zones. Hospital stay (P =.267) and ICU stay (P =.117) were comparable. The overall perioperative stroke and 30-day mortality rates were 12.5% and 10.1%, respectively. ER showed the highest incidence of stroke (ER 22.4%, OR 11.4%, HR 7.6%; P =.010). Postoperative myocardial infarction was least in patients undergoing OR (OR 1.5%, ER 11.8%, HR 10.5%; P <.001), and no difference in pneumonia rates was observed (P =.878). KM estimates of 30-day mortality (OR 9.1%, ER 10.4%, HR 11.7%) and 1-year mortality (OR 16.5%, ER 16.6%, HR 21.3%) were similar (Fig 2). Conclusions: TEVAR covering the arch vessels is associated with high stroke and mortality rates. Total endovascular revascularization of the head vessels after TEVAR has more than 2- fold higher stroke rate compared to open or hybrid revascularization with no improvement in morbidity or mortality. Using current technology, ER is overshadowed by high perioperative stroke rates, and thus open or hybrid revascularization of the head vessels should be favored (or strongly considered) whenever feasible.

Surgery

Chamseddine H, **Shepard A**, **Weaver M**, **Nypaver T**, **Kavousi Y**, **Onofrey K**, and **Kabbani L**. A Novel Amputation-Specific Index for the Prediction of Major Amputation Despite a Patent Infrainguinal Bypass. *J Vasc Surg* 2024; 79(6):e263-e264. Full Text

Objectives: While lower extremity limb salvage parallels infrainguinal bypass (IIB) graft patency, some patients who receive an IIB for peripheral artery disease still end up with a major amputation even with a patent bypass graft. This study aims to derive the risk factors associated with major amputation despite bypass patency and develop a weighted index for the prediction of this outcome. Methods: The Vascular Quality Initiative (VQI) IIB module was queried for all patients between 2003 and 2021. Patients with an occluded IIB were excluded. Patients receiving a major amputation with documentation of a patent bypass graft at the time or after the amputation date were included. The outcome of interest was major amputation. Univariate and multivariate analyses were used to identify variables associated with amputation. A risk predictive logistic model was derived using a 70% derivation cohort and validated on the remaining 30%. Finally, the amputation-specific index (ASI) was created and assessed with discrimination and calibration abilities. Results: A total of 21,973 patients (mean age, 66.3 years) were included. Of the full cohort, 1536 (7.0%) patients received an amputation despite a patent IIB. The most important predictors of the primary outcome on multivariate analysis included Black race (OR, 1.58; 95% CI, 1.33-1.87), dialysis (OR, 1.64; 95% CI, 1.26-2.12), non-ambulatory status (OR, 1.64; 95% CI, 1.28-2.12), emergency surgery (OR, 1.58; 95% CI, 1.34-1.86), rest pain (OR, 2.35; 95% CI, 1.80-3.06), tissue loss (OR, 3.92; 95% CI, 3.06-5.03), prosthetic graft (OR, 1.50; 95% CI, 1.29-1.75), infra-popliteal target (OR, 2.44; 95% CI, 2.08-2.86), prior ipsilateral IIB (OR, 1.88; 95% CI, 1.58-2.23), and persistence of ischemic symptoms (OR, 4.46; 95% CI, 3.82-5.20). The final ASI model encompassed the 10 predictors with different weights assigned to each predictor. The ASI performance and calibration testing provided an area under receiver operator curve (AUROC) of 80% and 77% on derivation and validation cohorts, respectively (Fig 1), with a calibration R-squared = 0.99 and proper goodness of fit. To better display the ASI index, values were divided into ranges and grouped into four risk stages, for which the risk of amputation was calculated (Table I). Conclusions: Seven percent of patients who undergo IIB may need

an amputation despite a patent graft. While wound, ischemia, and foot infection prove to be important determinants of limb salvage, our risk index had a similar predictive value to the WIfI classification system, and can accurately predict amputation risk in patients planned for IIB based on preoperative and operative characteristics.

Surgery
Choi WJ, **Ivanics T**, Rajendran L, Li Z, Jones O, Gravely A, Claasen M, Yoon P, 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 C, Englesakis M, 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. *HPB (Oxford)* 2024; 26:S48-S49. Full Text

Introduction: Solitary hepatocellular carcinoma (HCC) measuring ≤3 cm represent approximately 30% of HCC cases, yet treatment guidelines lack robust evidence. This study compares oncologic outcomes following ablation, resection, and liver transplantation (LT) for solitary, small HCC. Methods: We systematically searched databases up to February 7, 2022, for studies including adults with solitary, small HCC (≤3 cm) treated by any ablation, resection, or LT. We excluded non-HCC cancers, recurrent/metastatic diseases, and alternative therapies. A frequentist network meta-analysis assessed 5-year overall survival (OS) and recurrence-free survival (RFS) using only adjusted effect estimates while accounting for bias risk. Results: We identified 81 studies (four RCTs, 73 retrospectives, and four prospective cohorts) with 28,333 patients. In the network meta-analysis for 5-year OS (26 studies), LT had the best outcome (HR 0.47 [95% CI 0.31-0.73, referenced to resection]), followed by resection (reference), while ablation had the least favorable outcome (HR 1.32 [95% CI 1.16-1.49, referenced to resection]). For 5-year RFS (19 studies), LT had the best outcome (HR 0.36 [95% CI 0.20-0.63, referenced to resection]), followed by resection (reference), with ablation showing the least favorable outcome (HR 1.67 [95% CI 1.45-1.93, referenced to resection]). Conclusion: This network meta-analysis provides the highest-level evidence for comparing treatment modality outcomes for solitary, small HCC. LT emerges as the superior choice for achieving a better 5-year OS, followed by resection, then ablation. When feasible to preserve liver function, resection can be prioritized. Ablation with close surveillance should be reserved for individuals unfit for surgical or LT procedures.

Surgery
Huttler JJ, Rodriguez PP, Dandu C, Piazza G, **Kabbani L**, Kashyap V, Slade M, Zwibelman H, Guzman RJ, and Ochoa Chaar CI. Comparative Outcomes of Peripheral Vascular Intervention in Patients Discharged on Clopidogrel in Combination With Factor Xa Inhibitors or Aspirin. *J Vasc Surg* 2024; 79(6):e290-e292. Full Text

Objectives: Dual antiplatelet therapy with clopidogrel and aspirin (DAPT) is commonly prescribed following peripheral vascular interventions (PVI) for peripheral arterial disease (PAD). Although clopidogrel is frequently used after PVI for various indications, its use in combination with Factor Xa inhibitors (FXaI) has not been assessed. While societal guidelines provide mixed support for combination antithrombotic regimens in patients with PAD, the utility of FXaI and clopidogrel (FXaI+C) in comparison to DAPT following PVI remains unexplored. This study aims to investigate outcomes of PVI for PAD in patients discharged on FXaI+C compared with those receiving traditional DAPT. Methods: The Vascular Quality Initiative-PVI (VQI-PVI) database was used. For patients with multiple PVI in the database, only the index procedure was analyzed. Patients with a history of atrial fibrillation or absent follow-up data were excluded. All remaining patients discharged on DAPT or FXaI+C without aspirin were included. Nearest neighbor logistic regression propensity score matching was used to generate patient populations with similar comorbidities and procedural characteristics. Patient demographics, procedural details, and outcomes following PVI were compared. Cox proportional hazard regression and Kaplan-Meier curves were used to assess patient survival outcomes. Results: A total of 225,514 PVI were reviewed, and 161,550 patients undergoing primary PVI were included. Following index PVI, 50.9% (n = 82,255) of patients received DAPT and 3.3% (n = 5291) received FXaI+C at discharge. Excluding individuals with a history of atrial fibrillation, 52,584 patients were discharged on either DAPT (30.7%; n = 49,571) or FXaI+C (1.9%; n = 3013). After four-to-one matching, 8356 patients receiving DAPT were compared with 2089 patients taking FXaI+C. Patient demographics, procedural indication, and urgency were comparable

between the matched groups (Table). After mean follow-up of 400 days, patients discharged on FXaI+C had significantly higher rates of reintervention (20.4% vs 15.9%; P <.001) and 1-year mortality (13.3% vs 11.3%; P <.001) compared with patients discharged on DAPT (Table). Kaplan-Meier analysis demonstrated that patients discharged on DAPT had improved survival compared with those discharged on FXaI+C (Fig). Cox proportional hazard regression analysis showed that discharge on FXaI+C was independently associated with increased mortality compared with DAPT (HR, 1.22; 95% CI, 1.01-1.47), but was not significantly associated with combined amputation or death (HR, 1.11; 95% CI, 0.85-1.45) after PVI. Conclusions: Discharge regimens of FXaI in combination with clopidogrel after PVI seem to be associated with worse outcomes compared to traditional DAPT. Further research is needed to determine the optimal combination of antithrombotic medications for patients with PAD undergoing PVI.

Surgery

Lehman H, **Hans S**, and **Kaur S**. Brachial Artery to Axillary Vein Dialysis Graft Creation for Salvage After Failed Upper Extremity Dialysis Access. *J Vasc Surg* 2024; 79(6):e180. Full Text

Objectives: Maintaining hemodialysis (HD) access can be challenging in patients with a history of multiple accesses in the ipsilateral extremity. Much effort has been directed at finding reliable alternative access, one of which being a brachial artery to axillary vein graft. Certain techniques have described the axillary vein as the point of outflow in arteriovenous graft (AVG) creation, but questions have been raised in relation to the precise anatomic location of the venous anastomosis. In this clinical case series, we report 20 patients who underwent brachial artery to anatomic axillary vein graft creation with venous outflow medial to the teres major for HD access following failed fistulas and recorded their primary and secondary patencies. Methods: This is a single-institution case series of patients undergoing dialysis graft creation from the brachial artery to the anatomic axillary vein operated on by a single practitioner from 1990 to 2020. The technique of axillary vein exposure required an infraclavicular incision with division of the pectoralis minor tendon. Patient demographics and comorbidities were recorded, and frequency distributions were constructed and presented in the form of percentages. Kaplan-Meier analyses were performed on (a) primary patency (n = 20), and (b) secondary patency (n = 13). Results: The primary patency of brachial artery to axillary vein grafts was 62% at 6 months, 45.7% at 12 months, and 17.1% at 24 months (Fig 1). The secondary patency was 79.3% at 6 months, 51% at 12 months, and 24% at 24 months (Fig 2). On average, patients undergoing this brachial artery axillary vein graft creation had 3.3 ± 0.56 interventions after AVG creation. Conclusions: Brachial artery to axillary vein grafts provide a proximal option for dialysis access when considering an access in the contralateral extremity or a HERO graft. As this technique has been performed in a small series, further data is needed to extrapolate outcomes on a prospective basis.

Surgery

Li Z, Magyar CT, Jones O, Claasen MP, **Ivanics T**, Bucur R, Rukavina N, Sayed BA, Selzner N, Ghanekar A, Cattral M, and Sapisochin G. Survival benefit of living donor availability in a large North American Center. An intention-to-treat analysis. *HPB (Oxford)* 2024; 26:S65-S66. Full Text

Background: Living-donor liver transplantation (LDLT) offers superior survival than staying on the waiting list, even at low MELD-Na of 11. We sought to evaluate the benefits of LDLT through an intention-to-treat-analysis from the time of listing. Methods: Liver transplant candidates listed at the University Health Network (2000-2021) were categorized as pLDLT (with a potential live donor who had undergone health screening) or pDDLT (without an identified live donor). Employing Cox proportional-hazard regression, we evaluated pLDLT's survival impact through a risk-adjusted analysis (age, sex, MELD-Na at listing, primary etiology, presence of HCC). Furthermore, we assessed pLDLT's effect across the spectrum of MELD-Na. Results: Of 4,553 candidates, 1,504 (33%) had potential living donors. Median age was 57 years, 68% were male and median MELD-Na was 15. Common etiologies included hepatitis C (29.5%) and alcoholic liver disease (29.1%), with 35.8% having HCC. The pDDLT group had a higher waitlist dropout (45%vs.21%, P<0.001) and waitlist mortality (19%vs.10%, P<0.001) overall, while the pLDLT group experienced a shorter median waiting time (4.8vs.6.2 months, P=0.003). The pLDLT group demonstrated superior survival outcomes at 1- (88.7%vs.82.4%), 5- (75.4%vs.64.4%), and 10-year (66.5%vs.54.5%) from listing (log-rank P<0.001)(Figure 1A) with a 36% reduced risk of death (adjusted hazard ratio 0.64, 95% CI 0.57-0.72, P<0.001). Moreover, predicted hazard ratios consistently remained below 1 across the

MELD-Na range 12-39 (Figure 1B). Conclusion: Potential living donors enhance survival for end-stage liver disease patients with MELD-Na as low as 12, emphasizing LDLT's significance for those awaiting liver transplants.

Surgery
Lu AK, **Hans SS**, and **Serra GP**. Coverage of Exposed Femoral-Femoral Crossover Graft With Rectus Femoris Muscle Flap. *J Vasc Surg* 2024; 79(6):e85. Full Text

Background: We demonstrate a rectus femoris muscle flap coverage of a nonhealing groin wound. Patient had undergone femoral-femoral crossover bypass graft 6 weeks prior.

Surgery
Magyar CTJ, Li Z, Claasen MP, **Ivanics T**, Bucur R, Rukavina N, Selzner N, Ghanekar A, Cattral M, Sayed BA, and Sapisochin G. Temporal evolution of living donor liver transplantation recipient outcomes – a UNOS registry study. *HPB (Oxford)* 2024; 26:S528-S529. Full Text.

Background: Living donor liver transplantation (LDLT) is a curative treatment option for several liver diseases and has the potential to eliminate the wait list duration and its associated mortality. We aim to evaluate (1) temporal changes of overall survival (OS), (2) independent predictors for mortality and (3) differences of risk factors over time. Methods: Adult LDLT patients from the United Network for Organ Sharing (UNOS) registry up to 2020 were included. Groups in 5 year intervals were formed. Kaplan-Meyer and multivariate stepwise backward elimination logistic regression analysis were performed. Results: 5,506 LDLT patients (median age 54.0years, 56% male, 81% non-Hispanic White, BMI 26.1kg/m2, 47% blood type O and MELD of 15 at time of transplant) were selected. The cold ischemic time was 1.5hours with in 86.4% a right lobe graft used. The median follow-up was 4.0years. The OS was significantly different between time periods (log-rank p<0.001) (Figure 1). Comparing 1996-2000 to 2016-2020 OS has relatively improved at 1-year by +13% and at 3-year by +17%. Temporal significant changes of the independent predictors for mortality of recipient and donor age, hepatocellular carcinoma with cirrhosis, cholangiocarcinoma, previous transplantation, creatinine, albumin, INR, encephalopathy and length of stay were noted. Conclusions: LDLT is a safe procedure with good short-, middle- and long-term survival rates. Its efficacy has significantly improved despite a temporal increase of risk parameters. These findings suggest that the limit for LDLT in the United States has yet to be met, as this evolving therapeutic option pushes its boundaries.

Surgery
Rajendran L, Perez CFM, Magyar C, Brar A, Claasen M, Yoon P, Li Z, **Ivanics T**, Miranda ES, Haider M, and Sapisochin G. The role of sarcopenia on waitlist and post-transplant outcomes in liver transplantation for hepatocellular carcinoma. *HPB (Oxford)* 2024; 26:S531. Full Text

Introduction: Sarcopenia is common in patients with hepatocellular carcinoma (HCC); however, research on its role in waitlist and post-transplant outcomes for this population is limited. Our study aimed to assess this relationship at a large North American transplant institution. Methods: Adults with HCC listed for liver transplantation at Toronto General Hospital were retrospectively analyzed. Third lumbar vertebrae (L3) skeletal muscle index (SMI) and psoas muscle index (PMI) were calculated from the most recent scan prior to de-listing. Sarcopenia was defined by literature-established cut-offs for L3SMI and L3PMI. Primary outcomes included: overall survival (intention-to-treat), waitlist mortality, and post-transplant survival. Secondary outcomes included: 90-day complications and HCC recurrence. Results: Of 439 patients, 248(57%) were classified in the sarcopenia group by L3SMI cut-off, and 120(28%) by L3PMI cut-off. Intention-to-treat analysis demonstrated no survival difference between patients with or without sarcopenia from time of listing (L3SMI p=0.23, L3PMI p=0.99) or post-transplant (L3SMI p=0.43, L3PMI p=0.92). On competing risk analysis, sarcopenia was not associated with waitlist mortality (L3SMI p=0.30, L3PMI p=0.64). There were no differences in post-transplant overall 90-day complications or recurrence-free survival between groups. However, in patients stratified beyond Milan criteria pre-transplant, sarcopenia was associated with worse post-transplant survival (p=0.008) (FIGURE 1) and increased risk of death (HR 3.00 [95% CI 1.41-6.38], p=0.004). Conclusion: There was no association between sarcopenia and survival from time of listing or post-transplant in HCC patients, except in the beyond Milan

criteria population. Sarcopenia is one factor that may help refine transplant criteria, especially for populations beyond Milan criteria.

Urology

Cirulli GO, **Corsi N**, **Rakic I**, **Finati M**, **Chiarelli G**, **Stephens A**, **Davis M**, **Tinsley S**, Sood A, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Impact of lymphovascular invasion on survival of surgically treated patients with upper tract urothelial carcinoma: A nationwide analysis. *Eur Urol* 2024; 85:S819-S821. Full Text

Introduction & Objectives: Lymphovascular invasion (LVI) is recognized as an adverse prognostic factor in many cancers. However, its utility in upper tract urothelial carcinoma (UTUC) has not been well-defined. Our aim was to assess the prognostic ability of LVI in UTUC as a predictor of overall survival (OS) using a large North American cohort. Materials & Methods: Our cohort included 5,940 cM0 UTUC patients who underwent a radical nephroureterectomy (RNU), between 2010 and 2016, within the National Cancer Database (NCDB). The main variable of interest was LVI status, and its interaction with pathological nodal (pN) status. Kaplan-Meier curves were used to depict the OS also stratifying patients on LVI status. Cox regression analysis tested the impact of LVI status on OS after accounting for the available covariates. Results: Median (IQR) for age at diagnosis was 71 (63 – 78) and most patients had pT1 stage disease (48.6%). Nodal status was pN0, pN1 and pNx in 45.8%, 6.3% and 47.9%, respectively. Overall, 22.1% had LVI. The median (IQR) follow-up time was 32.6 (16. – 53.3) months. At 5-years postoperative follow-up, the estimated OS rate was 28% in patients with LVI vs. 66% in those without LVI ($p<0.001$). When patients were stratified based on nodal status those rates were 32% vs 68% in pN0 patients ($p<0.001$), 23% vs 30% in pN1 patients ($p = 0.8$), and 28% vs 65% in pNx patients ($p<0.001$). On multivariable analysis, the presence of LVI was associated with less favorable OS (HR 1.79, 95% CI: 1.60-1.99, $p<0.001$). Conclusions: Our study assessed the impact of LVI on OS in UTUC patients in a large North-American nationwide cohort. Our series, as the largest to-date, indicate that LVI is associated with less favorable survival outcomes in UTUC patients after RNU, and this variable could be used as a risk-stratification tool for future adjuvant therapy trials.