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Henry Ford Health Publication List – August 2025

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 biomedical databases PubMed, Embase, Web of Science, and CINAHL during the month, and then imported into EndNote for formatting. There are 296 unique citations listed this month, including 149 articles and 147 conference abstracts.

Articles are listed first, followed by conference abstracts. Due to various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health authors.

Note to authors: To help facilitate scholarly activity tracking, please include "Henry Ford Health" and your department/location in your author affiliation when submitting to a journal.

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If your published work has been missed, please use this form *to notify us for inclusion on next month's list. All articles and abstracts listed here are deposited into* Scholarly Commons*, the Henry Ford Health institutional repository.*

Articles

Administration
Allergy and Immunology
Anesthesiology
Behavioral Health Services/ Psychiatry/Neuropsychology
Cardiology/Cardiovascular Research
Center for Health Policy and Health Services Research
Center for Individualized and Genomic Medicine Research
Clinical Quality and Safety
Dermatology
Diagnostic Radiology
Emergency Medicine
Endocrinology and Metabolism
Gastroenterology
Global Health Initiative
Graduate Medical Education
Hematology-Oncology
Hospital Medicine
Infectious Diseases
Internal Medicine
Nephrology
Neurology
Neurosurgery
Nursing
Obstetrics, Gynecology and Women's Health Services
Ophthalmology and Eye Care Services
Orthopedics/Bone and Joint Center
Otolaryngology – Head and Neck Surgery
Pathology and Laboratory Medicine
Pharmacy
Public Health Sciences
Radiation Oncology
Rehabilitation Services/Physical Therapy/Occupational Health
Research Administration
Sleep Medicine
Surgery
Urology

Conference Abstracts

Administration
Anesthesiology
Cardiology/Cardiovascular Research
Dermatology
Emergency Medicine
Gastroenterology
Hematology-Oncology
Hospital Medicine
Internal Medicine
Nephrology
Neurology
Neurosurgery
Nursing
Ophthalmology and Eye Care Services
Otolaryngology – Head and Neck Surgery
Palliative Medicine
Pathology and Laboratory Medicine
Pharmacy
Plastic Surgery
Public Health Sciences
Pulmonary and Critical Care Medicine
Radiation Oncology
Surgery

Articles

Administration
Kemper K, Abebe W, Bastos LSL, Berha AB, Bozza FA, Kesteman T, Llor C, Nasir N, Okorie M, **Parke DM**, Parker SK, Pattanaik D, Sarele TV, Sartino C, Jawed B, Sila F, Suleyman G, and Cummins N. Best Practices for Addressing Differences in Antimicrobial Resistance Through Quality Improvement Projects in Antimicrobial Stewardship in Low-Resource Settings. *Mayo Clin Proc* 2025; Epub ahead of print. PMID: 40888787. Full Text

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Fundação Oswaldo Cruz, Rio de Janeiro, Brasil.
University of Oxford, Oxford, United Kingdom.
University Institute in Primary Care Research Jordi Gol, Barcelona, Spain.
Aga Khan University, Karachi, Pakistan.
University of Sussex, Brighton and Sussex Medical School, Brighton, United Kingdom.
Henry Ford Health, Detroit, MI.
Children's Hospital Colorado/University of Colorado School of Medicine, Aurora, CO.
VA Medical Center, Memphis, TN.
AIDS Healthcare Foundation, Maseru, Lesotho.
Indiana University (IU) Health, Indianapolis, Indiana.
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Administration
Wu B, **Yang M**, Hu D, **Zhang R**, **Liu B**, **Hochstadt S**, **Lanfear DE**, Witonsky J, Kumar R, Hollenbach JA, Burchard EG, Ziv E, and **Williams LK**. HLA variation associated with peanut allergy and anaphylaxis among non-Hispanic Black individuals. *J Allergy Clin Immunol Glob* 2025;4(3):100485. PMID: 40476093. Full Text

Center for Individualized and Genomic Medicine Research, Department of Internal Medicine, Henry Ford Health, Detroit, Mich.
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Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, Ill.
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BACKGROUND: Peanut is a major cause of food allergy. HLA genes have been consistently associated with peanut allergy in association studies. To date, however, there have been very few genetic studies of peanut allergy in non-Hispanic Black (Black) individuals, a group disproportionately affected by food allergy. OBJECTIVE: Our aim was to study the relationship between HLA alleles and peanut allergy among Black individuals. METHODS: The analysis consisted of Black participants from the Study of Asthma-Related Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE), a large cohort of individuals from metropolitan Detroit. At the time of enrollment, participants provided detailed food allergy histories, including symptoms. Four-digit resolution HLA allele calls were made using whole genome sequence data. RESULTS: The cases consisted of 119 individuals with reported peanut allergy and 59 individuals with peanut-related anaphylaxis; the comparison group consisted of 2640 individuals without reported food allergy. HLA-DRB1∗13:02 was the most significant allele associated with peanut

allergy (adjusted odds ratio = 1.94 [95% CI = 1.28-2.93]), and HLA-DQA1∗01:02 was the top association with peanut-related anaphylaxis (aOR = 1.67 [95% CI = 1.14-2.44]). Amino acid polymorphisms at position 71 in the binding groove of HLA-DRB1 were associated with peanut allergy and estimated to affect peanut allergen binding affinity. CONCLUSIONS: In a cohort of Black individuals, this study independently identified the same associations of peanut allergy and HLA that were previously observed in non-Hispanic White individuals. Our findings suggest that specific HLA binding groove amino acid polymorphisms may confer similar peanut allergy risk across population groups and HLA alleles.

Administration

Zhang R, **Liu B**, **Yang M**, **Wu B**, **Hochstadt S**, **Lanfear DE**, Witonsky J, Kumar R, Burchard EG, Ziv E, and **Williams LK**. Socioenvironmental factors associated with shrimp allergy and shrimp sensitization in a large and diverse patient population and cohort study from metropolitan Detroit. *J Allergy Clin Immunol Glob* 2025;4(3):100492. PMID: 40502543. Full Text

Center for Individualized and Genomic Medicine Research (CIGMA), Department of Internal Medicine, Henry Ford Health, Detroit, Mich.
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BACKGROUND: Earlier studies have demonstrated significant differences in food allergy by race and ethnicity, particularly for seafood and shrimp. Shrimp allergy is particularly interesting given the potential for cross-reactive sensitization from other arthropods. OBJECTIVES: We characterized risk factors for shrimp allergy and shrimp sensitization. METHODS: Data from electronic health records were abstracted for food allergies among patients who sought care at a large health system between October 1, 2010, and April 1, 2024. Geocoded addresses were linked to US Census data to identify characteristics associated with shrimp allergy. Non-Hispanic Black participants from the Study of Asthma-Related Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE) were assessed for allergic sensitization using an IgE array, and survey data collected from participants were evaluated for association with shrimp, cockroach, and dust mite sensitization. RESULTS: Among 2,975,183 health system patients, 4,709 individuals reported shrimp allergy. Compared to White individuals, rates of shrimp allergy were significantly higher in Black, Asian/Pacific Islander, Native American, and Latino individuals. Shrimp allergy was higher with increasing age, female sex, and asthma, and it was inversely related to median household income. Among SAPPHIRE participants, sensitization to shrimp, cockroach, and dust mite was positively associated with total IgE levels and proportion of African ancestry, but inversely associated with head of household level of education. CONCLUSIONS: Both shrimp allergy and sensitization were associated with sociodemographic factors, suggesting that environmental exposures leading to cross-reactive sensitization may be important risk factors. Nevertheless, sensitization was also associated with ancestry, highlighting the potential importance of group-specific genetic risk factors.

Allergy and Immunology

Moore CM, Secor EA, Everman JL, Fairbanks-Mahnke A, Jackson N, Pruesse E, Diener K, Morin A, Arbes SJ, Bacharier LB, Bendixsen CG, Calatroni A, Dupont WD, Furuta GT, Gebretsadik T, Gruchalla RS, Gupta RS, Khurana Hershey GK, Kattan M, Liu AH, Lussier SJ, Murrison LB, Numata M, O'Connor GT, River-Spoljaric K, Phipatanakul W, Rothenberg ME, Seroogy CM, **Zoratti EM**, Castina S, Jackson DJ, Camargo CA, Jr., **Johnson CC**, Ethridge R, Ramratnam S, Stelzig L, Teach SJ, Togias AG, Fulkerson PC, Hartert TV, and Seibold MA. The common cold is associated with protection from SARS-CoV-2 Infections. *J Infect Dis* 2025; Epub ahead of print. PMID: 40795882. Full Text

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BACKGROUND: Adults and children often respond differently to SARS-CoV-2 infection, with adults facing a higher risk of symptomatic and severe illness. We hypothesize that children's protection from symptomatic SARS-CoV-2 may be due to more frequent respiratory viral infections, which prime their airway antiviral defenses. METHODS: Using case-cohort and case-control analyses in the Human Epidemiology and Response to SARS-CoV-2 cohort, we evaluated whether infection with common respiratory viruses protects against SARS-CoV-2 infections and investigated airway molecular mechanisms by which this protection is achieved. We tested 10,493 longitudinal nasal swabs from 1,156 participants for 21 respiratory pathogens. We performed RNA-sequencing on 147 swabs (N=144 participants) collected prior SARS-CoV-2 infection and 391 swabs (N=165 participants) during and before rhinovirus infection. RESULTS: Participants with rhinovirus infection in the previous 30 days were at 48% lower risk of SARS-CoV-2 infection (aHR:0.52, p=0.034). Among participants with SARS-CoV-2 infection, recent rhinovirus infection was associated with 9.6-fold lower SARS-CoV-2 viral load (p=0.0031). Higher pre-infection expression of 57 genes was associated with lower SARS-CoV-2 viral load, including 24 antiviral defense genes; 22 of these were induced by rhinovirus infections. Relative to adults, children expressed higher levels of the antiviral gene signature (p=0.014) and were at 2.2-fold increased risk for rhinovirus infections. CONCLUSIONS: Rhinovirus infections, which trigger increased expression of antiviral airway genes, are linked to a lower risk of SARS-CoV-2 infection. Frequent rhinovirus infections may enhance this protective gene profile, partially explaining why children experience milder SARS-CoV-2 infections compared to adults. TRIAL REGISTRATION NUMBER: NCT04375761.

Anesthesiology
Ye T, Sun H, Harman AE, Deiner SG, **Mitchell JD**, and Macario A. Anesthesiology Milestones 1.0: Residents' Learning Trajectories and Training Outcomes. *Anesth Analg* 2025; Epub ahead of print. PMID: 40815157. Full Text

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BACKGROUND: The Accreditation Council for Graduate Medical Education (ACGME) requires anesthesiology training programs to submit Milestones ratings for each resident every 6 months, starting in the 2014 to 2015 academic year. We aimed to understand how anesthesiology residents progress through the Milestones evaluations from residency entry to graduation. METHODS: Anesthesiology Milestones 1.0 included 25 subcompetencies in 6 core competencies of Patient Care, Medical Knowledge, Systems-Based Practice, Practice-Based Learning & Improvement, Professionalism, and Interpersonal & Communication Skills. Milestones data from all anesthesiology residency programs from July 2015 to June 2019 were used to (1) assess the prevalence of straight-lining (ie, percentage of residents who received the same rating for all 25 subcompetencies for each program per reporting period), (2) describe residents' progression trajectories in each subcompetency, including the baseline at 6-month training, growth rate (ie, rate increase every 12 months), and outcomes on graduation (ie, percentage of residency graduates who received at least 1 Level 4 [target for graduation] or above subcompetency rating, and percentage of graduates who did not reach Level 4 for at least 1 subcompetency), and (3) use 3-level linear mixed-effect models to examine individual resident growth in each subcompetency over time while accounting for clustering effect of residency programs. RESULTS: The analyses included 11,691 residents from 153 training programs. Among 6696 clinical anesthesia year 3 residents, 98.3% received at least 1 Level 4 or above rating on graduation; 28.8% to 36.8% of the graduating cohort did not reach Level 4 for at least 1 subcompetency among the 6 core competencies. One hundred and thirty-six programs (88.9% of 153) had straight-lining for at least 1 reporting period. For the multilevel linear mixed-effect models, the fixed intercept estimates were close to 1.0 for Professionalism and Interpersonal & Communication Skills subcompetencies while those for Patient Care subcompetencies were <0.75; the fixed slope estimates were near 1.0 for all 25 subcompetencies. Across all subcompetencies, residency programs accounted for 63% to 84% of between-resident variability in the baseline ratings and 60% to 92% of between-resident variability in the growth rates. CONCLUSIONS: We found a high prevalence of straight-lining in Anesthesiology Milestones 1.0 ratings. This raises concerns about whether Milestones evaluations reflect individual resident performance in specific domains. The programs explained most of the between-resident variability in both baseline ratings and growth rates. Future studies are needed to promote standardization and consistency of Milestones evaluations, allowing learners to track their progress and target specific areas to improve performance.

Behavioral Health Services/Psychiatry/Neuropsychology

Magidson JF, Bradley VD, Anane JS, Kleinman MB, **Felton JW**, Hines AC, Baskar R, Greenblatt AD, Dean D, Anvari MS, Fitzsimons H, Bennett ME, and Belcher AM. "HEAL together": a randomized, hybrid type 1 effectiveness-implementation trial protocol of a peer-delivered behavioral activation intervention to improve methadone treatment retention. *Front Public Health* 2025;13:1637846. PMID: 40756389. Full Text

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BACKGROUND: Although medications exist to effectively treat opioid use disorder (OUD), treatment retention is a pressing challenge. Peer recovery specialists (PRSs) may play an important role in OUD treatment retention, yet few evidence-based interventions to support OUD retention have been developed specifically for PRS delivery. Behavioral activation is a brief, reinforcement-based intervention with empirical support for improving depression and substance use outcomes, delivered typically by specialist mental health providers. Informed by key stakeholder feedback, our team adapted a behavioral activation and problem-solving intervention for PRS delivery ("Peer Activate") to improve methadone treatment retention. Building on a successful open-label pilot trial demonstrating initial feasibility, acceptability, and preliminary effectiveness of Peer Activate, the current type 1 hybrid randomized controlled trial evaluates

the effectiveness of Peer Activate compared to treatment as usual on six-month methadone retention (primary) and longer-term implementation outcomes. METHODS: The trial is being conducted at a large methadone treatment program in Baltimore City, Maryland. We are enrolling 200 patients who recently initiated methadone treatment or are experiencing challenges with methadone adherence in a randomized 1:1 ratio to receive Peer Activate plus treatment as usual (PA + TAU) or TAU only. Additionally, we are recruiting 12 stakeholders to provide feedback on implementation and sustainability. Peer Activate consists of four core intervention sessions delivered by a PRS with relevant lived experience and training in the intervention. Sessions focus on problem-solving barriers to retention and behavioral activation-increasing value-driven, substance-free activities-and continued skill practice and relapse prevention. Assessments are administered at baseline, post-treatment (approximately 3 months), and 6 months. The primary effectiveness outcome is methadone retention over 6 months, measured using chart review. Implementation outcomes are defined based on Proctor's model, including feasibility, acceptability, and fidelity of the intervention. DISCUSSION: This trial will provide insight as to whether a PRS-delivered intervention may be effective and feasible for improving methadone treatment retention and other behavioral health outcomes. If findings are promising, Peer Activate may provide a platform on which to incorporate an evidence-based behavioral activation approach into PRS training nationally. CLINICAL TRIAL REGISTRATION: NCT05299515.

Behavioral Health Services/Psychiatry/Neuropsychology
Meram ED, **Kammo S**, **Repins S**, and **Mahr GC**. Severe Anemia From Vitamin B12 Deficiency Presenting With a Craving for Bleach Powder: An Odd Case of Pica. *Case Reports in Psychiatry* 2025; (1):8779524. PMID: 40894376. Full Text

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Pica, the ingestion of nonnutritive substances, represents a complex and poorly understood phenomenon. Although it is inherently a psychiatric condition, it has an intricate relationship with other psychiatric, physiological, and pathological states, suggesting a highly multifactorial etiology. Recognizing and addressing pica in acute settings is crucial, as it poses significant health risks for patients, including the potential of toxic ingestion. Our presentation highlights the case of a 36-year-old woman with a complex psychiatric history who presented to the emergency department (ED) with severe symptomatic anemia. Her anemia was found to be macrocytic and a result of autoimmune-induced vitamin B12 deficiency. Further inquiry uncovered that, prior to admission, the patient exhibited a craving for smelling bleach powder that progressed to mouthing the toxic substance for more than a month. This is the first report of a case of bleach craving in a patient with vitamin B12 deficiency absent coexisting iron-deficiency. This unique presentation underscores the importance of psychiatric consultations as a part of comprehensive clinical assessments in emergency medical settings. We also suggest that pica presentations may be nuanced and thus it is critical to understand the biopsychosocial factors driving this behavior and target interventions in the appropriate medical domains.

Behavioral Health Services/Psychiatry/Neuropsychology
Miller-Matero LR, **Pappas C**, **Christopher B**, **Grossi R**, **Vanderziel A**, Barnett NP, Moore RS, **Hamann A**, **Carlin AM**, **Varban OA**, and **Braciszewski JM**. A technology-based intervention to reduce alcohol use after metabolic and bariatric surgery: feasibility, acceptability, and preliminary outcomes. *Surg Obes Relat Dis* 2025; Epub ahead of print. PMID: 40885652. Full Text

Henry Ford Health, Behavioral Health, Detroit, Michigan; Henry Ford Health, Center for Health Policy and Health Services Research, Detroit, Michigan. Electronic address: Lmatero1@hfhs.org.
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BACKGROUND: Patients who undergo metabolic and bariatric surgery (MBS) are at increased risk for an alcohol use disorder. A technology-based intervention, rooted in motivational interviewing, could broadly reach patients after MBS and has the potential to reduce alcohol use. OBJECTIVE: Examine the feasibility, acceptability, and preliminary outcomes of a technology-based intervention to reduce alcohol use delivered after MBS. SETTING: Health system. METHODS: Participants (N = 60) who were 3-18 months post-MBS were randomized to the intervention or treatment-as-usual control group. The tailored intervention consisted of 2 (15-minute) sessions of interactive web-based content followed by 3-months of daily text messaging. Participants completed baseline and a postintervention assessment (91.7% retention). RESULTS: Participants were primarily female (90%), White (55.0%) or Black (43.3%), with a mean age of 44.6 years (SD = 10.4). Of those randomized to the intervention (n = 24), 83.3% (n = 20) began the intervention and 95% (n = 19) completed it. The majority of participants rated all intervention components positively and 100% agreed that other patients would use the intervention. The intervention group reported a significant increase in level of motivation to avoid alcohol use from baseline to postintervention (P = .02), whereas the control group did not show a significant change (P = .73). At the postintervention, the intervention group had significantly fewer participants endorsing alcohol use than the control group (43.5% versus 75%; X(2) = 5.63, P = .02). CONCLUSION: A technology-based intervention delivered after MBS was feasible, acceptable, and showed promising preliminary outcomes for increasing motivation to avoid alcohol use as well as reducing alcohol use.

Behavioral Health Services/Psychiatry/Neuropsychology
Pflaum-Carlson J, **Redding A**, **Murphy D**, **MacLean L**, **Hamilton J**, and **Santarossa S**. Recruitment, retention and recouperation: lessons learned from a study aimed at assessing burnout mitigation in physician learners. *BMC Res Notes* 2025;18(1):376. PMID: 40890847. Full Text

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Behavioral Health Services/Psychiatry/Neuropsychology
Ponton-Almodovar A, **Udumula MP**, Khullar V, **Rashid F**, **Rattan R**, **Bernard JJ**, and **Horibata S**. GPT2 mediates glutamine metabolism-driven metabolic alterations in platinum-resistant ovarian cancer cells. *Sci Rep* 2025;15(1):30528. PMID: 40835655. Full Text

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Metabolic reprogramming is recognized as a hallmark of cancer frequently associated with drug resistance in ovarian cancer. This is problematic as ovarian cancer is one of the deadliest gynecologic cancers with platinum resistance contributing to poor survival. However, the mechanism by which ovarian cancer cell metabolism contributes to platinum resistance is not well understood. Herein, metabolic signatures were determined in platinum-resistant ovarian cancer cell lines compared to the more platinum-sensitive parental lines. Chemoresistant ovarian cancer cells showed increased oxidative phosphorylation (OXPHOS) compared to chemosensitive cells. This was associated with elevated levels of glutaminolysis and tricarboxylic acid (TCA)-related metabolites supporting their dependence on OXPHOS. Key enzymes involved in glutaminolysis, specifically, glutamic-pyruvic transaminase 2 (GPT2), were upregulated in chemoresistant compared to chemosensitive cells. Interestingly, high GPT2 gene expression is associated with worse prognosis in ovarian cancer patients, adding translational relevance to the pre-clinical findings. GPT2 knockout in chemoresistant cells restored the metabolic phenotype to that of the sensitive cells and reversed drug resistance. These data suggest that GPT2 is a critical link between glutaminolysis, the TCA cycle, and OXPHOS and is a potential target to attenuate the increased metabolic activity associated with a chemoresistant phenotype.

Cardiology/Cardiovascular Research
Al Jebbawi L, and **Khan A**. Non-Pulmonary Vein Triggers-Does Sex Matter? *JAMA Netw Open* 2025;8(8):e2529535. PMID: 40875236. Full Text

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Cardiology/Cardiovascular Research
Al-Abdouh A, Kumar S, Jabri A, Mhanna M, Alhuneafat L, Paul TK, **Villablanca P**, and Khalife W. The Use of Protamine in Transcatheter Aortic Valve Replacement: A Meta-analysis. *Am J Ther* 2025; Epub ahead of print. PMID: 40795122. Full Text

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Cardiology/Cardiovascular Research
Al-Mhanna SB, Poon ET, Franklin BA, Tarnopolsky MA, Hawley JA, Jakicic JM, Stamatakis E, Little JP, Pescatello LS, Riebe D, Thompson WR, Skinner JS, Colberg SR, **Ehrman JK**, Metsios GS, Douda HT, Omar N, Alghannam AF, and Batrakoulis A. Comparative effectiveness of high-intensity interval training and moderate-intensity continuous training on cardiometabolic health in patients with diabesity: a systematic review and meta-analysis of randomized controlled trials. *Diabetol Metab Syndr* 2025;17(1):331. PMID: 40804647. Full Text

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OBJECTIVE: To evaluate the effects of high-intensity interval training (HIIT) on cardiometabolic health-related outcomes in patients with type 2 diabetes mellitus and concurrent overweight/obesity (diabesity). DESIGN: Systematic review and meta-analysis of randomized controlled trials (RCTs). DATA SOURCES: PubMed, Web of Science, Scopus, Science Direct, Cochrane Library, and Google Scholar databases were searched from inception up to January 31, 2025. ELIGIBILITY CRITERIA FOR SELECTING STUDIES: RCTs comparing HIIT alone ≥ 2 weeks in duration with moderate-intensity continuous training (MICT). Participants were adults with diabesity. RESULTS: A total of 26 RCTs qualified, involving 790 patients (50/50 female/male ratio; age: 59.8 ± 12.9 years; body mass index: 28.9 ± 4.2 kg/m(2)). HIIT revealed a significant reduction in fasting insulin [standardized mean differences (SMD) - 0.43, 95% CI - 0.82 to - 0.05] and homeostatic model assessment for insulin resistance (HOMA-IR; SMD - 0.52, 95% CI - 0.97 to - 0.07) compared to MICT. Additionally, HIIT significantly increased cardiorespiratory fitness (VO_2max; SMD 0.53, 95% CI 0.14 to 0.91) compared to MICT. Other clinically relevant cardiometabolic outcomes, including body composition, lipid profile, fasting blood glucose, glycated hemoglobin, and blood pressure, showed comparable changes between HIIT and MICT. Subgroup analyses of studies reporting comorbidities indicated a significant increase in high-density lipoprotein cholesterol (SMD 0.49, 95% CI 0.04 to 0.95) and a decrease in HOMA-IR (SMD - 0.83, 95% CI - 1.62 to - 0.04) for HIIT compared to MICT. However, these findings are limited by very low certainty evidence and non-robust sensitivity analyses. CONCLUSIONS: The present findings suggest that HIIT may serve as an adjunctive non-

pharmaceutical management solution for patients with diabesity. Open Science Framework registry: https://osf.io/9by24.

Cardiology/Cardiovascular Research
Basala T, Seth M, Madder RD, Wanamaker B, **Fuller B**, Shlofmitz E, Daher E, Tucciarone M, Alraies C, Kaki A, Rao SV, Gurm HS, and Sukul D. Safety and Effectiveness of Intracoronary Imaging-Guided PCI in Contemporary Practice: Insights From BMC2. *Circ Cardiovasc Interv* 2025;e014886. Epub ahead of print. PMID: 40827405. Full Text

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BACKGROUND: Studies suggest percutaneous coronary intervention (PCI) guided by intracoronary imaging (ICI) results in larger balloon/stent diameters and longer stents. Whether this occurs in real-world PCI is poorly understood. METHODS: De novo PCIs performed at 48 nonfederal Michigan hospitals between July 2019 and June 2022 were evaluated with regression modeling to evaluate associations between ICI-guided PCI and balloon/stent dimensions. The association between ICI-guided PCI and coronary dissection/perforation was assessed using adjusted odds ratios. RESULTS: ICI was used in 16 777 (22.5%) PCI-treated lesions and increased from 11.2% of cases in July 2019 to 32.1% in June 2022. Compared with angiography alone, the average patient/procedural-adjusted treatment effect of ICI use included: +0.19 mm stent diameter (95% CI +0.16 to +0.22), +0.45 mm maximum balloon diameter (95% CI +0.40 to +0.51), and +3.51 mm stent length (95% CI +2.54 to +4.48). These findings persisted when controlling for the operator. ICI use was associated with a higher risk of dissections (adjusted odds ratio, 2.55 [95% CI, 2.05-3.16]) and perforations (adjusted odds ratio, 2.25 [95% CI, 1.74-2.91]); however, increased use of ICI and larger stent/balloon sizes over the study period (P<0.001 for trend for both) was not associated with a concomitant increase in rates of dissection or perforation (P=0.78 and P=0.33 for trend, respectively). CONCLUSIONS: In real-world practice, ICI-guided PCI was associated with larger stent/balloon diameters and longer stents. While ICI use was associated with dissections and perforations, there was no significant increase in the rate of these complications despite significant increases in ICI use and stent/balloon sizes during the study period. Further research is needed to evaluate the association between ICI use and procedural complications.

Cardiology/Cardiovascular Research
Cowger JA, and Potapov E. To build a better VAD: What is needed to make MCS truly competitive with cardiac transplantation for long-term outcomes? *JHLT Open* 2025;9:100325. PMID: 40808827. Full Text

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While average survival in patients undergoing durable left ventricular assist device (dLVAD) support now approximate 6 years, the application of therapy remains limited across the globe. Herein we highlight important deficiencies common to present technology and propose device innovations and field

corrections that will be necessary to improve acceptance of dLVAD support by both patients and medical providers caring for patients with end-stage heart failure. Pragmatic trials will also be needed to help identify the therapeutic strategy (permanent dLVAD support vs heart transplant vs dLVAD as a bridge to transplant) that affords the best outcomes for a patient's risk profile and total survival goals.

Cardiology/Cardiovascular Research

El Sabbagh A, Hibbert B, Bangalore S, Fong P, Zlotnick D, El-Sabawi B, Zhang R, Zwischenberger B, Mourad A, Palatnic L, Sayfo S, Gilyard S, Younes S, Younes A, Ingrassia J, Cheema M, Hammadah M, Prasad A, Hamid N, Voudris K, **Villablanca P**, Kaki A, Qintar M, Baloch Z, Patton M, Dominguez A, Akhtar Y, Panaich S, Lugo-Fagundo N, Yucel E, Hodge DO, Rosenfield K, Baddour L, Sorajja P, Moriarty J, Parikh SA, and Sethi SS. Outcomes of Percutaneous Mechanical Aspiration in Right-Sided Infective Endocarditis: A Multicenter Registry. *J Am Coll Cardiol* 2025; Epub ahead of print. PMID: 40864007. Full Text

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BACKGROUND: Catheter-based percutaneous mechanical aspiration (PMA) is an emerging acute intervention for debulking infective vegetations in right-sided infective endocarditis (RSIE); however, its outcomes and safety remain undefined. OBJECTIVES: The authors sought to assess early clinical outcomes and safety of PMA in patients with RSIE. METHODS: The CLEAR-IE (Cardiac Lesion Extraction and Aspiration Registry for Infective Endocarditis) is a large multicenter retrospective registry of consecutive patients with RSIE who have undergone PMA. Procedural success was defined as a ≥70% reduction in site-reported vegetation size or a residual size ≤1 cm on intraprocedural echocardiography,

which included transesophageal echocardiography (TEE), intracardiac echocardiography (ICE), and transthoracic echocardiography (TTE), selected at the operator's discretion to guide the intervention. The primary endpoint was a composite of in-hospital mortality, new pulmonary embolism (PE), or emergency surgery. Secondary endpoints included each component of the primary endpoint and in-hospital worsening tricuspid regurgitation (TR). RESULTS: Between January 2014 and January 2024, 256 patients from 19 institutions were included. Median age was 43 years; 43% were women, and 51% had history of injection drug use. Acute PE (50.8%) and shock (27%) were frequent at presentation. Tricuspid valve involvement was present in 70%, with a median site-reported vegetation size of 2.4 cm (Q1-Q3: 0.6-9 cm). Severe TR was noted in 31.3% at baseline. Staphylococcus aureus was the predominant pathogen (73.8%). Procedural success was achieved in 89.4%, with a median residual vegetation size of 0.7 cm (Q1-Q3: 0.2-1.1 cm). Overall, 86.9% completed the procedure free from procedure-related complications. The primary endpoint occurred in 18% (mortality: 9.8%; new PE: 8.3%; emergency surgery: 3.1%). Among those without baseline severe TR, worsening TR occurred in 16.9%. On univariate analysis, shock (OR: 2.27; 95% CI: 1.15-4.43; P = 0.03) and hypoxia (OR: 3.62; 95% CI: 1.83-7.17; P < 0.001) were significantly associated with the primary endpoint, whereas worsening TR was not. On multivariate analysis, hypoxia (OR: 2.76; 95% CI: 1.34-5.73; P = 0.006) remained significantly associated with the primary outcome. CONCLUSIONS: PMA of RSIE is feasible with high procedural success. Adverse events were acceptable and largely driven by underlying RSIE. Randomized trials are warranted to confirm the clinical impact and safety of PMA in RSIE.

Cardiology/Cardiovascular Research
Fang JX, **Villablanca PA**, **Frisoli TM**, Giustino G, **Lai LKL**, **Lee JC**, **Engel Gonzalez P**, **Zweig B**, **Alrayes H**, **Fram GK**, **Nguyen F**, Jabri A, **Andrews T**, **Abdelhai O**, **Rangavajla G**, **O'Neill WW**, and **O'Neill BP**. Transjugular Approach for Evoque Transcatheter Tricuspid Valve Replacement in Patients With Challenging Anatomy. *Circ Cardiovasc Interv* 2025;e015276. Epub ahead of print. PMID: 40827406. Full Text

Center for Structural Heart Disease, Henry Ford Health System, Detroit, MI (J.X.F., P.A.V., T.M.F., L.K.L.L., J.C.L., P.E.G., B.Z., H.A., G.K.F., F.N., T.A., O.A., G.R., W.W.O.N., B.P.O.N.).
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BACKGROUND: The Evoque system is the first commercially available transcatheter tricuspid valve replacement (TTVR) system in the United States. However, challenging anatomy in real-world patients could preclude successful transfemoral Evoque TTVR. We aim to investigate the feasibility of the transjugular Evoque TTVR in anatomy unsuitable for a transfemoral approach. METHODS: Eleven patients with challenging anatomy underwent transjugular Evoque TTVR at a high-volume center in the United States from February 2024 to January 2025, following an unsuccessful transfemoral attempt (n=9) or anatomic unsuitability (n=2). Procedural characteristics, intraprocedural success, periprocedural outcomes, echocardiographic findings, and 30-day clinical outcomes were assessed using the Tricuspid Valve Academic Research Consortium definitions. The procedural technique is provided in the accompanying supplement. RESULTS: Intraprocedural success was achieved in all 11 patients, with reasonable procedural time and no major procedural complications, except for 1 pacemaker implantation. At 30 days, the clinical success rate was 100%. Tricuspid regurgitation was reduced to none-to-trivial in 8 patients, mild in 2 patients, and moderate in 1 patient. There was no stroke, mortality, or rehospitalization. Nine out of 11 patients experienced an improvement in New York Heart Association functional class. CONCLUSIONS: In the largest single-center cohort of patients reported to date, transjugular Evoque TTVR demonstrated favorable intraprocedural, periprocedural, and short-term clinical outcomes, and was found to be a feasible alternative for patients with anatomy unsuitable for transfemoral Evoque TTVR.

Cardiology/Cardiovascular Research
Jamal L, Syeda R, **Jamal F**, **Kasmikha Z**, and **Crawford J**. The atrial mass without an auscultatory "plop": renal cell carcinoma presenting with cardiac syncope-a case report. *AME Case Rep* 2025;9:95. PMID: 40761210. Full Text

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BACKGROUND: Renal cell carcinoma (RCC) presenting with extension of tumor thrombus into the inferior vena cava (IVC) and right atrium is a rare, life-threatening condition that requires surgical treatment with the simultaneous involvement of multiple surgical subspecialties. CASE DESCRIPTION: We present a case of a 65-year-old male who presented to the hospital with syncope, and was subsequently diagnosed with a level four cavoatrial sinus tumor thrombus extending from a primary renal mass. The patient had no concerning physical exam and electrocardiogram (EKG) findings, however, transthoracic and transesophageal echocardiography revealed severely reduced systolic function with a hyperechoic, vascular, and cystic mass extending from the IVC into the right atrial cavity that originated from a renal mass that involved the right renal vein and IVC. CONCLUSIONS: The purpose of this case is to highlight the critical importance of early recognition and timely intervention in patients who present with nonspecific symptoms, such as syncope, which may signal underlying fatal conditions. This case illustrates RCC with tumor thrombus extending into the IVC and right atrium. This rare but serious manifestation highlights the need for a high index of suspicion and comprehensive evaluation when faced with vague clinical presentations. Early recognition not only facilitates appropriate management but can also alter the patient's prognosis and survival outcomes.

Cardiology/Cardiovascular Research
Lai LKL, **Fram G**, **Alrayes H**, **Apostolou D**, **Alter J**, **Zweig B**, **Dawdy J**, **Parikh S**, **O'Neill BP**, **Villablanca PA**, **Gonzalez PE**, **O'Neill WW**, **Lee JC**, and **Frisoli TM**. Percutaneous Closure of Left Ventricular Outflow Tract to Left Atrium Fistula With 3-Dimensional Printing Simulation. *JACC Case Rep* 2025;30(26):104889. PMID: 40912839. Full Text

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Case Summary: We present a case of a 31-year-old man with a history of aortic valve endocarditis and surgical aortic intervention. Computed tomography revealed a complex serpiginous fistula with 2 openings between the left ventricular outflow tract and the left atrium. Using 3-dimensional printing simulation for device fit testing and planning, the “mother-in-daughter” system, multimodality guidance with computed tomography angiography C-arm prediction, and 3-dimensional transesophageal echocardiogram guidance successfully guided an 18-mm Cribriform Amplatzer device deployed via a retrograde approach. Take-Home Message: Three-dimensional printing simulation significantly enhances preprocedural planning and device selection for this complex fistula closure, facilitating successful percutaneous repairs in high-risk patients.

Cardiology/Cardiovascular Research
Lurz P, Hahn RT, Kodali S, Makkar R, Sharma RP, Davidson CJ, **O'Neill BP**, Yadav P, Zahr F, Chadderdon S, Eleid MF, Szerlip M, Smith R, Whisenant B, Garcia S, Kister T, Kipperman RM, Lim S, Saxon J, Kapadia S, Hermiller J, Mishell JM, Rassi A, Herrmann HC, Szeto W, Hausleiter J, Babaliaros V, Barker CM, Lindman BR, Latib A, Muhammad K, von Bardeleben RS, Summers M, Chetcuti S, Ailawadi G, Russo M, Rinaldi M, Chehab BM, Nickenig G, Stinis C, Inglessis-Azuaje I, Dhoble A, Chhatriwalla AK, Petrossian G, Shah P, Staniloae C, Williams M, Nores M, McCabe JM, Singh G, Baldus S, Rudolph V, Barb I, Klodell C, Gray W, Strote J, Sannino A, Grayburn P, Mack MJ, Leon MB, and Thourani VH. Tricuspid valve replacement outcomes by baseline tricuspid regurgitation severity: the TRISCEND II trial. *Eur Heart J* 2025; Epub ahead of print. PMID: 40878717. Full Text

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BACKGROUND AND AIMS: The TRISCEND II trial demonstrated superior clinical benefits for patients with ≥severe tricuspid regurgitation (TR) treated with the EVOQUE transcatheter tricuspid valve replacement (TTVR) system plus medical therapy versus medical therapy alone. This work reports 1-year and 18-month outcomes in patients stratified by baseline TR severity. METHODS: The multicentre, prospective TRISCEND II trial enrolled 400 patients with symptomatic, ≥severe TR and randomised 2:1 to TTVR (n=267) or control (n=133). In a post-hoc analysis, patients were stratified into severe TR (n=172) and massive/torrential TR (n=220) cohorts. Clinical and quality-of-life outcomes were reported at 1 year, with Kaplan-Meier estimates for all-cause mortality and heart failure (HF) hospitalisation assessed at 18 months. Study oversight included an independent echocardiographic core laboratory, clinical events committee, and data safety monitoring board. RESULTS: One year after TTVR, TR was ≤mild in 95.2% of severe TR and 95.3% of massive/torrential TR patients. The primary safety and effectiveness endpoint (win ratio) favoured TTVR over control regardless of baseline TR severity: severe (1.64 [95% CI: 1.11, 2.43]) and massive/torrential (2.20 [1.55, 3.14]). At 18 months, TTVR patients had similar mortality to controls (rate difference: severe 0.2% [-11.6, 11.9], massive/torrential -5.8% [-17.6, 6.0], whereas HF

hospitalisation rates favoured TTVR in the massive/torrential cohort (vs. control, severe 9.8% [-3.0, 22.7], massive/torrential -15.2% [-28.9, -1.5]). CONCLUSIONS: Patients with ≥severe TR benefit from TTVR, experiencing improvements in TR severity, functional capacity, and quality of life regardless of baseline TR severity, with a signal for greater benefit in patients with more advanced disease.

Cardiology/Cardiovascular Research
Madanat L, Mazumder S, **Kheyrbek M**, Foglesong A, Baqain R, Kutinsky I, and Bloomingdale R. Impact of Coronary Dominance on Atrioventricular Node Ablation Approach. *Am J Cardiol* 2025;257:60-62. PMID: 40763887. Full Text

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Persistent atrial fibrillation often requires atrioventricular node (AVN) ablation when conventional rhythm - or rate-control strategies are unsucessful, but procedural outcomes may be influenced by anatomic variability. We hypothesized that coronary artery dominance affects AVN positioning and the preferred ablation approach. In this retrospective study, 132 patients who underwent AVN ablation and coronary CTA were analyzed. Right coronary dominance was present in 78.8% of patients, left in 13.6% and co-dominant in 7.6%. Patients with left or co-dominant circulation had significantly higher odds of requiring a left-sided approach compared with right-dominant patients (21.4% vs 1.9%, p<0.001), and demonstrated longer mean procedure time (50 vs 34 minutes, p = 0.044). These findings suggest that coronary dominance may influence AVN localization and ablation strategy. Incoroporating coronary dominance assessment into preprocedural imaging may enhance procedural planning, shorten duration and reduce radiation exposure.

Cardiology/Cardiovascular Research
Mansoor T, Ismayl M, Agarwal S, **Gupta K**, **Parikh S**, Brubaker A, Minhas AMK, Gupta V, and Koshy SKG. Comparative outcomes of percutaneous coronary intervention in ST-elevation myocardial infarction: an analysis by infarct-related coronary artery. *Proc (Bayl Univ Med Cent)* 2025;38(5):787-792. PMID: 40821466. Full Text

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Cardiology/Cardiovascular Research
Mansoor T, Ismayl M, **Parikh S**, Nambi V, Virani SS, Mehta A, Jia X, and Minhas AMK. Emerging pharmacological strategies in lipoprotein(a) reduction. *Proc (Bayl Univ Med Cent)* 2025;38(5):783-786. PMID: 40821459. Full Text

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BACKGROUND: Lipoprotein(a) (Lp(a)) is an low-density lipoprotein (LDL)-like particle whose elevation is considered a causal risk factor for atherosclerotic cardiovascular disease (ASCVD) and calcific aortic valve stenosis. Currently, there are no published clinical trials showing whether Lp(a) lowering in conjunction with optimal LDL cholesterol control reduces ASCVD risk. METHODS: Clinicaltrials.gov, an online database for clinical research studies, was used to identify ongoing clinical trials studying targeted Lp(a) lowering pharmacotherapy as of May 2025. Twelve clinical studies met the criteria and were included in this summary. RESULTS: The three large, multicenter phase 3 outcome trials evaluating clinical cardiovascular disease endpoints of major adverse cardiac event (MACE) are Lp(a)HORIZON (NCT04023552), OCEAN(a) (NCT05581303), and ACCLAIM-Lpa(a) (NCT06292013), which investigate pelacarsen, olpasiran, and lepodisiran, respectively. Other phase 2 and phase 3 trials are also under way. CONCLUSION: Results from upcoming trials will inform us whether Lp(a) reductions translate to improved cardiovascular clinical outcomes.

Cardiology/Cardiovascular Research

Mansoor T, Jabbar ABA, Ismayl M, Yu D, **Gupta K**, **Parikh S**, Brubaker A, Khan Minhas AM, Abramov D, Kalavakunta J, Gupta V, Virani SS, and Koshy SKG. Cardiogenic Shock With Acute Myocardial Infarction Among Older Adults in the United States. *JACC Adv* 2025;4(9):102078. PMID: 40834806. Full Text

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BACKGROUND: Characteristics and outcomes associated with cardiogenic shock (CS) with acute myocardial infarction (AMI) in older patients have not been well characterized. OBJECTIVES: The purpose of this study was to investigate characteristics and outcomes of older patients admitted with CS with AMI. METHODS: We used the National Inpatient Sample database to evaluate clinical characteristics of hospitalizations, clinical outcomes, and health care utilization of hospitalizations of older patients ≥80 years with CS and AMI from 2003 to 2021. We also compared data from older patients with a reference relatively younger patient population (18-79 years). RESULTS: During the study period, 207,333 hospitalizations of older patients ≥80 years and 675,491 hospitalizations of patients 18 to 79 years were identified. Between the first 4 years of the study period (2003-2006) and the final 4-year interval of the study period (2016-2019), there was an increase in the number of hospitalizations of older patients with AMI and CS (39,220-51,640). On adjusted analysis, there were increases in the percentage of older patients undergoing treatment with percutaneous coronary intervention (19.2% to 34.1%; P < 0.001) and encounters for palliative care (2.0% to 32.4%; P < 0.001) alongside a decline in in-hospital mortality (61.4% to 49.0%; P < 0.001) over the study period. Compared to patients 18 to 79 years of age, those aged ≥80 years had greater in-hospital mortality (51.8% vs 33.0%; P < 0.001). CONCLUSIONS: From 2003 to 2021, for older patients with CS and AMI, hospitalizations increased, and mortality decreased.

Cardiology/Cardiovascular Research
McDermott MM, Kadian-Dodov D, **Aronow HD**, Beckman JA, Creager MA, Gornik HL, Leeper NJ, Ross E, and Bonaca MP. Response to: 'A call for patient involvement in peripheral artery disease research priority setting'. *Vasc Med* 2025; Epub ahead of print. PMID: 40845014. Full Text

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Cardiology/Cardiovascular Research
Multani NS, **Affas ZR**, and **Alexander PB**. LIMA-LAD Steal Syndrome as a Cause of Post-CABG Angina. *JACC Case Rep* 2025;30(25):104828. PMID: 40883084. Full Text

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BACKGROUND: Coronary steal from unligated side branches of the left internal mammary artery (LIMA) after coronary artery bypass grafting may lead to recurrent angina. CASE SUMMARY: A 64-year-old man presented with recurrent angina 2 years after coronary artery bypass grafting. Imaging showed perfusion defects in the territory of the left anterior descending artery (LAD). Coronary angiography revealed a large patent LIMA side branch. A percutaneous vascular plug successfully occluded the side branch, with symptom resolution. DISCUSSION: There is conflicting evidence regarding the diagnosis and treatment of coronary steal syndrome from LIMA graft. Despite the lack of formal guidelines, reversible anterior wall defects on stress testing may help identify patients with clinically significant symptoms. TAKE-HOME MESSAGES: The side branches of the LIMA when unligated represent a relatively common anatomical variation that could have clinical implications. Large, unligated side branches when accompanied by anterior wall ischemia may indicate a diagnosis of LIMA-LAD steal amenable to percutaneous intervention.

Cardiology/Cardiovascular Research
O'Neill B, **Halboni A**, Giustino G, **Engel P**, **Fram G**, **Frisoli T**, Fang JX, **O'Neill W**, **Villablanca P**, and Wang DD. Treatment Patterns of Patients With Mitral Valve Disease and Critical Neo-LVOT Obstruction. *Catheter Cardiovasc Interv* 2025; Epub ahead of print. PMID: 40793929. Full Text

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BACKGROUND AND AIMS: Among patients with severe mitral valve (MV) disease and predicted high-risk of left ventricular outflow track obstruction (LVOTO), the patterns of treatment and clinical outcomes have not previously described. The aim of this study was to explore outcomes of this patient population. METHODS: We conducted a single-center study including all consecutive patients with severe MV disease who were evaluated by a multidisciplinary structural heart disease team for MV therapies between 2018 and 2023. All patients underwent pre-procedural contrast cardiac computed tomography

(CT). We defined high risk for LVOTO as a post-transcatheter mitral valve replacement (TMVR) predicted neo-LVOT < 150 mm(2). RESULTS: A total of 157 patients with a median Neo-LVOT of 0 (IQR 0-80.4) were included. Median age was 79 (72-83), and most were females (89.2%). A total of 59 patients (37.6%) had severe mitral stenosis, 48 (30.6%) had severe mitral regurgitation, and 98 (58%) had both. The median STS score was 22.6 (17-29.6). Most patients were in NYHA class III or IV (77.1%), and the median KCCQ-12 was 48.9 (IQR: 29-68.7). Overall, the majority of patients were assigned to medical therapy (54.1%). There were a total of 41 deaths (26.1%) at a median follow-up time of 247 days (IQR: 70-568). When separated into non-severe MAC and severe MAC, patients with severe MAC had higher rates of all-cause mortality at 1 year (unadjusted HR: 2.44; 95% CI: 1.13-5.24; p = 0.02). Severe MAC patients were more likely to be assigned to medical therapy. Treatment allocation was not independently associated with a higher or lower risk of death. CONCLUSIONS: Patients with severe MV disease at high-risk for LVOTO (LVOT < 150 mm(2)) after TMVR were overwhelmingly female and were most frequently assigned to medical therapy. Patients with severe MAC had higher rates of death. Treatment allocation was not independently associated with mortality. Novel transcatheter therapies are needed to definitively treat this high-risk population.

Cardiology/Cardiovascular Research
Oska N, **Peterson D**, Brothers K, **Maramraju R**, **Ayyad A**, and **Hohmann B**. Isolated Facial Vein Thrombophlebitis Caused by Fusobacterium nucleatum: A Lemierre-Variant Case. *Case Rep Infect Dis* 2025;9938125. PMID: 40860904. Full Text

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Background: Lemierre's syndrome is an uncommon yet potentially fatal infection, classically secondary to bacterial pharyngeal infections. It is typically characterized by bacteremia, most frequently due to Fusobacterium necrophorum and internal jugular vein thrombophlebitis. If untreated, septic embolization may result, potentially damaging the lungs, liver, brain, or other organs. This report describes a variant of Lemierre's syndrome in a young woman with streptococcal pharyngitis, who developed Fusobacterium nucleatum bacteremia and isolated facial vein thrombophlebitis, highlighting the importance of early diagnosis and treatment. Case Presentation: A 33-year-old woman with no significant past medical history presented with sore throat, chills, and right-sided facial and neck pain. Initially diagnosed with streptococcal pharyngitis at an urgent care clinic, she presented to the emergency department soon afterwards due to the development of severe rigors and fever. Blood cultures revealed growth of Fusobacterium nucleatum, raising suspicion for Lemierre's syndrome in the setting of worsening facial and neck pain despite negative initial imaging of the soft tissue of the neck. A subsequent CT venogram confirmed isolated thrombosis of the right facial vein. The patient was treated and discharged in stable condition on a 4 week course of metronidazole and 2 weeks of ceftriaxone. Conclusion: This case emphasizes the importance of maintaining suspicion for Lemierre's syndrome in patients with bacterial pharyngitis, especially when atypical symptoms such as facial pain occur. Although the internal jugular vein is most commonly affected, facial vein thrombosis may also occur. Early antibiotic treatment is critical for preventing severe complications including septic shock and embolization.

Cardiology/Cardiovascular Research
Rangavajla G, **Patel R**, **Nguyen F**, **Vickers B**, **Abdelhai O**, **La Starza B**, **Ilg K**, **Maskoun W**, **Ebinger M**, **Lahiri M**, **Khan A**, **Greenberg J**, **Fram G**, **Alrayes H**, **Lok Lai LK**, **Wyman J**, **Parikh S**, **Zweig B**, **Dawdy J**, **Bowerman N**, **Engel Gonzalez P**, **O'Neill W**, **Villablanca P**, **Lee J**, **O'Neill BP**, **Raad M**, and **Frisoli TM**. Atrioventricular Block After EVOQUE Transcatheter Tricuspid Valve Replacement. *Struct Heart* 2025;9(9):100701. PMID: 40822378. Full Text

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•Based on a real-world study of 106 Evoque transcatheter tricuspid valve replacement (TTVR) recipients, a total of 14 (25%) cases of new atrioventricular (AV) block occurred after Evoque implantation in the 55

patients without prior pacemakers who met study inclusion criteria. This incidence is similar to that reported in the TRISCEND II clinical trial.•New AV block occurred in a median of 26 hours after Evoque TTVR (interquartile range: 5-60 hours), but there were cases of new AV block that occurred as late as 7 days after the procedure.•Of the 14 new cases of AV block, 12 were treated successfully with implantation of a leadless pacemaker (Micra) under fluoroscopic guidance without procedural complications or compromising the valve implantation.•The institutional strategy of 48-hour post-Evoque inpatient monitoring for all patients followed by mobile cardiac outpatient telemetry identified 11 of 14 cases of new AV block as before discharge from the hospital and 1 case as an outpatient before symptom onset.

Cardiology/Cardiovascular Research

So KC, Stolz L, Fam N, Ong G, Cheung A, Boone R, **Villablanca P**, **Jabri A**, Lam YY, Tchétché D, Oliva O, De Backer O, Møllller JE, Latib A, Scotti A, Coisne A, Sudre A, Dreyfus J, Nejjari M, Favre PE, Cruz-Gonzalez I, Estévez-Loureiro R, Barreiro-Perez M, Makkar R, Patel D, Leurent G, Donal E, Modine T, and Hausleiter J. Transjugular Transcatheter Tricuspid Valve Replacement in Patients With Cardiac Implantable Electronic Devices. *JACC Asia* 2025; Epub ahead of print. PMID: 40884522. Full Text

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BACKGROUND: Cardiac implantable electronic device (CIED)-related tricuspid regurgitation (TR) is common. Transcatheter tricuspid valve replacement (TTVR) is feasible with CIEDs in the right ventricle; however, data in this population are limited. OBJECTIVES: This study retrospectively analyzed patients undergoing compassionate-use transjugular TTVR with the LuX-Valve Plus for symptomatic TR with CIEDs from January 2022 to August 2024 at 17 international centers. METHODS: The primary endpoint was procedural TR reduction. Secondary endpoints included TR reduction, survival at 30 days, New York Heart Association functional class changes, and CIED function at follow-up. Non-CIED group was used for comparison. RESULTS: Of 99 patients, 36 (36.4%) had CIEDs. Baseline characteristics were similar, though the CIED group had a higher EuroSCORE (European System for Cardiac Operative Risk Evaluation) II score and more comorbidities. Procedural success (CIED vs non-CIED: 91.7% vs 95.2%; P = 0.781), 30-day mortality (5.6% vs 4.8%; P > 0.999), TR reduction (≤1+: 83.8% vs 84.9%; P > 0.999), and NYHA functional class I/II (80.8% vs 83.7%; P = 0.89) were comparable. The CIED cohort exhibited a higher numerical incidence of conversion to surgery (8.3% vs 1.6%) and tricuspid reintervention (11.5% vs 3.3%) within 6 months; however, these differences did not reach statistical significance (P = 0.267 and P = 0.160, respectively). Of the 22 patients with postoperative interrogation (median of 3.3 months), 9.1% of CIED patients exhibited worsening device parameters, with no need for lead replacement or extraction. CONCLUSIONS: Transjugular TTVR is safe and effective for managing TR and heart failure in patients with CIEDs. Due to the small sample size, these findings highlight the need for larger, prospective studies to validate these outcomes.

Cardiology/Cardiovascular Research

Stolz L, Fam N, Ong G, **Villablanca P**, **Jabri A**, de Backer O, Møllller JE, Tchétché D, Oliva O, So KC, Lam YY, Latib A, Scotti A, Coisne A, Sudre A, Dreyfus J, Nejjari M, Cruz-Gonzalez I, Estévez-Loureiro R, Barreiro-Perez M, Leurent G, Donal E, Bonnet G, Modine T, Makkar R, Patel D, Kresoja KP, Lurz P, and Hausleiter J. Transcatheter tricuspid valve replacement using the LuX-Valve Plus system: 1-year compassionate use outcomes. *Eur J Heart Fail* 2025; Epub ahead of print. PMID: 40879890. Full Text

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Cardiology/Cardiovascular Research
Strepkos D, Alexandrou M, Mutlu D, Carvalho PEP, Sara JDS, Ser OS, **Alaswad K**, **Basir MB**, Khelimskii D, Jaffer F, Rafeh NA, Chandwaney R, Cevik C, Ahmad Y, Mastrodemos O, Rangan BV, Jalli S, Voudris K, Sandoval Y, Burke MN, and Brilakis ES. Multiple Versus Single Vessel CTO PCI in the Same Hospitalization: Data From the PROGRESS-CTO Registry. *Am J Cardiol* 2025;257:77-83. PMID: 40759244. Full Text

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Percutaneous coronary intervention (PCI) of multiple chronic total occlusions (CTOs) during a single procedure is infrequently performed and remains understudied. We compared the characteristics and outcomes of patients who underwent multiple versus single CTO PCIs during the same procedure. We analyzed data from 16,550 patients (16,876 CTO PCIs) from a large, multicenter registry. PCI of multiple CTOs was attempted in 626 lesions (3.7%) in 304 patients: 289 patients (95.1%) underwent PCI of 2 CTOs, 15 patients underwent PCI of 3 CTOs (4.9%) and 1 of 4 CTOs. Single CTO PCI was attempted in 16,246 patients. These patients had more comorbidities and more complex lesions, with higher prevalence of moderate or severe calcification and tortuosity, higher PROGRESS-CTO scores (1.56 vs 1.22, p <0.001), but similar J-CTO scores (2.46 vs 2.38, p = 0.110). Technical (84.7% vs 87.3%, p = 0.215) and procedural (83.0% vs 86.0%, p = 0.163) success were similar. Patients who underwent PCI of multiple CTOs required longer procedure and fluoroscopy times and higher contrast volume and use of percutaneous ventricular assistance devices (pVAD) (9.2% vs 1.8%, p <0.001). The incidence of major adverse cardiovascular events (MACE) was similar (2.6% vs 1.9%, p = 0.372). In patients who underwent PCI of multiple CTOs during the same procedure, subsequently treated CTOs had higher complexity compared with the initially treated CTO. Despite higher complexity, attempting PCI of multiple CTOs during the same procedure was associated with similar outcomes, but higher use of radiation, contrast and pVAD compared with PCI of single CTOs.

Cardiology/Cardiovascular Research
Waggoner T, Garcia S, Chakravarty T, Makar M, Latib A, Kipperman RM, Zahr F, Hanson I, Sinha AK, Sharma RP, Depta JP, Castellanos JA, Kodali S, Krishnaswamy A, Whisenant B, Menees D, Lim DS, Gilani F, Sanchez CE, Gheewala N, Gada H, Kapadia S, Ramanathan PK, Shah PB, Renard B, Theodos G, Yaryura R, Gardner B, Steinberg DH, Gnall E, Kaddissi G, Chhatriwalla AK, Frangieh AH, Eleid MF, Généreux P, Saxon JT, **Villablanca P**, Matar F, Agarwal H, Chetcuti S, Frisoli T, and Makkar R. Early

U.S. Commercial Experience With a Novel Transcatheter Edge-to-Edge Repair System: Insights From Real-World Data. *JACC Cardiovasc Interv* 2025;18(16):2036-2046. PMID: 40866033. Full Text

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BACKGROUND: The PASCAL Precision transcatheter valve repair system provides a new option for treating prohibitive surgical risk patients with significant, symptomatic degenerative mitral regurgitation (DMR). OBJECTIVES: The authors report early U.S. commercial experience with the PASCAL Precision system. METHODS: Patients with DMR treated with the PASCAL Precision system in the United States were analyzed from the STS/ACC TVT Registry. Procedural, clinical, echocardiographic, functional, and quality-of-life outcomes to 30 days were assessed. All outcomes, including echocardiographic assessments, were site-assessed. RESULTS: In 1,995 DMR patients, the median age was 81.6 years, and 57.0% were male. Median STS-PROM for mitral valve repair was 3.6%, and 69.4% were in NYHA functional class III/IV. Mixed etiology (DMR + other etiology) was present in 11.4%, and 66.9% had complex anatomy (annular/leaflet calcification, mitral valve area <4 cm(2), bileaflet flail/prolapse/tethering,

or mitral stenosis). The device was successfully implanted in 97.7%. MR reduction was significant at 30 days with 94.2% achieving ≤moderate MR and 72.6% ≤mild MR (P < 0.001 vs baseline). Patients experienced significant functional and quality-of-life improvements with a mean 21.0-point increase in Kansas City Cardiomyopathy Questionnaire score and 84.6% in NYHA functional class I/II (all P < 0.001). Mitral valve reintervention and single-leaflet device attachment rates were 0.4% and 0.5%, respectively, and all-cause mortality, cardiovascular mortality, and heart failure readmission rates were 2.2%, 1.2%, and 2.6%, respectively, at 30 days. CONCLUSIONS: Early U.S. STS/ACC TVT Registry commercial experience confirms the safety and effectiveness of the novel PASCAL Precision system in the treatment of a broad population of real-world DMR patients.

Cardiology/Cardiovascular Research
Zalawadiya S, Abraham J, Rathman L, Bhatt K, **Grafton G**, Chuang J, Johnson N, Connolly A, and Lindenfeld J. Early Reduction of Pulmonary Artery Pressures Is Associated With Improved Mortality Among Medicare Beneficiaries With Heart Failure. *JACC Heart Fail* 2025;13(10):102589. PMID: 40811935. Full Text

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BACKGROUND: The early hemodynamic trajectories of heart failure patients receiving implantable pulmonary artery pressure monitor and the clinical implications of those trajectories are unknown in a contemporary real-world population. OBJECTIVES: This study aims to determine whether baseline pulmonary artery diastolic pressure (PAD) and its early trajectories predict risk of mortality. METHODS: Patients in Merlin.net implanted with the CardioMEMS sensor between 2017 and 2022 were linked to Medicare claims. Patients were categorized by PAD being acceptable (≤20 mm Hg) or elevated (>20 mm Hg). Multivariable regression was used to evaluate the impact of baseline PAD (cohort A) and its early changes at 90 days (cohort B) on long-term mortality. RESULTS: In cohort A (N = 9,579), baseline PAD was elevated in 64.1%. The 2-year risk of mortality was lower for those with acceptable vs elevated PAD at baseline (HR: 0.68 [95% CI: 0.62-0.73]; P < 0.001). In cohort B (N = 8,452), 63.3% had elevated PAD at baseline; of those, 24.0% improved to having acceptable PAD (Δ: -6.5 ± 4.3 mm Hg), and 76.0% remained persistently elevated at 90 days despite experiencing a reduction (ΔPAD: -1.6 ± 4.3 mm Hg). Those with improved PAD (acceptable at 90 days from elevated at baseline) had lower mortality compared with those with persistently elevated PAD (HR: 0.72 [95% CI: 0.64-0.81]; P < 0.001). Lower baseline PAD and no history of chronic obstructive pulmonary disease or atrial arrhythmia were associated with higher odds of improved PAD. CONCLUSIONS: Among Medicare beneficiaries, CardioMEMS-guided management was associated with a reduction in PAD. Achieving acceptable PAD within 90 days of implant was associated with better survival. Our study highlights the need to develop novel strategies, including standardization of management algorithms that target elevated PAD.

Center for Health Policy and Health Services Research
Hall SV, Pangori A, Tilea A, Zivin K, Platt IS, **Vance AJ**, and Dalton VK. Birth outcomes among pregnant people with treated and untreated perinatal mood and anxiety disorder (PMAD). *Gen Hosp Psychiatry* 2025;96:251-252. PMID: 40784100. Full Text

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Center for Health Policy and Health Services Research
Kaljee LM, **Ahmedani B**, **Srinivasan S**, Wells E, Ruprecht MT, **Ahmed Y**, **Randall S**, Beckwith C, and Keuten J. Feasibility of implementation of the zero suicide model in community-based organizations serving Afghan refugees resettled in Michigan. *BMC Public Health* 2025;25(1):2769. PMID: 40814037.
Full Text

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BACKGROUND: Pioneered at HFH Behavioral Health Services in 2001, the Zero Suicide (ZS) model is comprised of several evidence-based approaches including suicide screening and assessment, caring contacts, care coordination, and suicide specific psychotherapies. The ZS model has been successfully introduced in more than twenty countries; however, to date the model has been primarily introduced in higher income countries within large health systems. It is important to understand the feasibility of this approach in a range of other settings. In the current project, a feasibility study was conducted, and a pilot program is currently underway to adapt the model for use in Community-based Organizations (CBOs) serving refugee populations. METHODS: This feasibility study focused on Afghan refugees arriving in Michigan as a part of the U.S. government "Operation Allies Welcome" program. The qualitative study included interviews with social, health, and behavioral health providers and staff at CBOs serving refugee and asylum-seeking populations in Michigan and behavioral health specialists at HFH and Wayne State University. A Stakeholders' Advisory Board was established including HFH and CBO partners. RESULTS: Afghan refugees encountered challenges on arrival and during their settlement into life in Southeastern Michigan, including linguistic, social, economic, medical, and behavioral health barriers. The data include specific recommendations made by the respondents for adaptations to the Zero Suicide model. CONCLUSION: While the need for behavioral health services for refugee communities is recognized, challenges remain in the implementation of accessible, acceptable, and adaptable programs. Within Michigan, CBOs have developed strong relationships with refugees and asylum seekers resettled into the state. The current project was designed to build on these existing infrastructures within CBOs and determine the feasibility of integrating an evidence-based suicide prevention program. Through the feasibility study, it was evident that CBOs were interested in including the Zero Suicide model as a part of their health services. However, it was clear that adaptations were needed to support the introduction of the model and that those adaptations would have to account for diverse refugee communities and varied resources and structures within each CBO.

Center for Health Policy and Health Services Research

Lindahl A, **Hill T**, **Mazier E**, **Patel M**, **Kahn G**, **Zhou Y**, and **Day CS**. "Patient-Specific" Cost and Quality Value Comparison of Endoscopic Carpal Tunnel Release in Two Surgical Settings. *J Hand Surg Glob Online* 2025;7(5):100802. PMID: 40837494. Full Text

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PURPOSE: Prior studies have demonstrated that transitioning surgeries from a hospital outpatient department (HOPD) to an ambulatory surgical center (ASC) lowers costs. With 500,000 carpal tunnel release (CTR) surgeries annually, CTR offers an opportunity to determine the value of one of the most performed upper-extremity surgeries. We aim to quantify the value of an endoscopic CTR in a HOPD compared to an ASC by analyzing differences in costs and patient outcomes. We hypothesize the ASC will provide greater value by lowering costs while maintaining patient outcomes. METHODS: Total costs were comprised of time-driven activity-based labor costs (TDABC), activity-based supply costs, and claims-based facility costs. Differences in preoperative Patient-Reported Outcome Measure (PROM) Information System Upper Extremity (UE) and Pain Interference (PI) scores and 3-month postoperative PROM Information System UE and PI scores were calculated to determine PROM Information System Quality-Adjusted Life Years (QALY(UE/PI)). Total costs were divided by QALYs for each PROM to calculate the Value(UE/PI) of each cohort. The magnitude of the difference in value between cohorts was elucidated by calculating incremental cost-effectiveness ratios. RESULTS: A total of 25 patients comprised each cohort. The ASC generated 28% lower costs compared to the HOPD ($3,370.73 ± $128.80 vs $4,654.75 ± $140.19). Average QALY(UE) and QALY(PI) gain was not significantly greater for patients at the ASC compared to the HOPD (QALY(UE) 1.06 vs 0.89; QALY(PI) 1.22 vs 0.92). The ASC demonstrated 40% to 45% greater value, represented by a lower cost/QALYs, compared to the HOPD (Value(UE) $3,168.81/QALY vs $5,242.78/QALY, Value(PI) $2,759.90/QALY vs $5,038.04/QALY). CONCLUSIONS: We observed between 40% to 45% greater value by performing CTRs in the ASC. Although ASCs lowered costs by 28%, costs alone do not fully explain the value differential. Patient-reported outcomes serve a valuable role in providing a holistic picture of the value being delivered to patients. Providers can use this information to guide patient decision-making regarding operative treatment options for carpal tunnel syndrome. TYPE OF STUDY/LEVEL OF EVIDENCE: Economic/Decision Analysis II.

Center for Health Policy and Health Services Research

Miller-Matero LR, **Pappas C**, **Christopher B**, **Grossi R**, **Vanderziel A**, Barnett NP, Moore RS, **Hamann A**, **Carlin AM**, **Varban OA**, and **Braciszewski JM**. A technology-based intervention to reduce alcohol use after metabolic and bariatric surgery: feasibility, acceptability, and preliminary outcomes. *Surg Obes Relat Dis* 2025; Epub ahead of print. PMID: 40885652. Full Text

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BACKGROUND: Patients who undergo metabolic and bariatric surgery (MBS) are at increased risk for an alcohol use disorder. A technology-based intervention, rooted in motivational interviewing, could broadly reach patients after MBS and has the potential to reduce alcohol use. OBJECTIVE: Examine the feasibility, acceptability, and preliminary outcomes of a technology-based intervention to reduce alcohol use delivered after MBS. SETTING: Health system. METHODS: Participants (N = 60) who were 3-18 months post-MBS were randomized to the intervention or treatment-as-usual control group. The tailored

intervention consisted of 2 (15-minute) sessions of interactive web-based content followed by 3-months of daily text messaging. Participants completed baseline and a postintervention assessment (91.7% retention). RESULTS: Participants were primarily female (90%), White (55.0%) or Black (43.3%), with a mean age of 44.6 years (SD = 10.4). Of those randomized to the intervention (n = 24), 83.3% (n = 20) began the intervention and 95% (n = 19) completed it. The majority of participants rated all intervention components positively and 100% agreed that other patients would use the intervention. The intervention group reported a significant increase in level of motivation to avoid alcohol use from baseline to postintervention (P = .02), whereas the control group did not show a significant change (P = .73). At the postintervention, the intervention group had significantly fewer participants endorsing alcohol use than the control group (43.5% versus 75%; X(2) = 5.63, P = .02). CONCLUSION: A technology-based intervention delivered after MBS was feasible, acceptable, and showed promising preliminary outcomes for increasing motivation to avoid alcohol use as well as reducing alcohol use.

Center for Health Policy and Health Services Research

Tao MH, **Wu T**, **Gordon SC**, **Zhou Y**, **Rupp LB**, **Trudeau S**, Schmidt MA, Daida YG, and **Lu M**. Antiviral treatment Reduces Risk of Development of Lung Cancer and non-Hodgkin Lymphoma in Patients with Chronic Hepatitis C. *Cancer Epidemiol Biomarkers Prev* 2025; Epub ahead of print. PMID: 40874910. Full Text

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BACKGROUND: Antiviral treatment for hepatitis C virus (HCV) has been shown to reduce risk of liver cancer, but there are few studies on its impact on the risk of non-liver cancers. We used a large cohort of HCV patients with extensive follow-up to investigate whether receipt of antiviral therapy affects the risk of extrahepatic cancers. METHODS: 17,485 HCV patients were followed until incidence of lung cancer, non-Hodgkin lymphoma (NHL), breast or prostate cancer, death, or last follow-up. We used multivariable modeling with time-varying covariates and propensity scores to adjust for treatment selection bias; we also applied generalized estimating equations (GEE) with a multinominal link function for discrete time-to-event data. Death was considered a competing risk. RESULTS: After 15 years of follow-up, we identified 408 incident cases of cancers, including 140 lung, 72 NHL, 81 breast (female), and 115 prostate. Compared to no treatment, patients who receive either direct-acting antivirals (DAA) or interferon-based (IFN) treatment had significantly lower risk of lung cancer (hazard ratio [HR]= 0.35, 95% CI 0.24-0.52 for achieving sustained virological response [SVR]; HR= 0.34, 95% CI 0.21-0.55 for treatment failure). Risk of NHL was reduced only among patients who achieved SVR. There were no significant associations between antiviral therapy and risks of breast and prostate cancer. CONCLUSIONS: Antiviral treatment for HCV independently reduced the risk of lung cancer, while the protective association with NHL was limited to patients achieving SVRs. IMPACT: Our findings support the importance of timely initiation antiviral therapy in patients with chronic HCV.

Center for Individualized and Genomic Medicine Research

Wu B, **Yang M**, Hu D, **Zhang R**, **Liu B**, **Hochstadt S**, **Lanfear DE**, Witonsky J, Kumar R, Hollenbach JA, Burchard EG, Ziv E, and **Williams LK**. HLA variation associated with peanut allergy and anaphylaxis among non-Hispanic Black individuals. *J Allergy Clin Immunol Glob* 2025;4(3):100485. PMID: 40476093. Full Text

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BACKGROUND: Peanut is a major cause of food allergy. HLA genes have been consistently associated with peanut allergy in association studies. To date, however, there have been very few genetic studies of peanut allergy in non-Hispanic Black (Black) individuals, a group disproportionately affected by food allergy. OBJECTIVE: Our aim was to study the relationship between HLA alleles and peanut allergy among Black individuals. METHODS: The analysis consisted of Black participants from the Study of Asthma-Related Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE), a large cohort of individuals from metropolitan Detroit. At the time of enrollment, participants provided detailed food allergy histories, including symptoms. Four-digit resolution HLA allele calls were made using whole genome sequence data. RESULTS: The cases consisted of 119 individuals with reported peanut allergy and 59 individuals with peanut-related anaphylaxis; the comparison group consisted of 2640 individuals without reported food allergy. HLA-DRB1∗13:02 was the most significant allele associated with peanut allergy (adjusted odds ratio = 1.94 [95% CI = 1.28-2.93]), and HLA-DQA1∗01:02 was the top association with peanut-related anaphylaxis (aOR = 1.67 [95% CI = 1.14-2.44]). Amino acid polymorphisms at position 71 in the binding groove of HLA-DRB1 were associated with peanut allergy and estimated to affect peanut allergen binding affinity. CONCLUSIONS: In a cohort of Black individuals, this study independently identified the same associations of peanut allergy and HLA that were previously observed in non-Hispanic White individuals. Our findings suggest that specific HLA binding groove amino acid polymorphisms may confer similar peanut allergy risk across population groups and HLA alleles.

Center for Individualized and Genomic Medicine Research
Zhang R, **Liu B**, **Yang M**, **Wu B**, **Hochstadt S**, **Lanfear DE**, Witonsky J, Kumar R, Burchard EG, Ziv E, and **Williams LK**. Socioenvironmental factors associated with shrimp allergy and shrimp sensitization in a large and diverse patient population and cohort study from metropolitan Detroit. *J Allergy Clin Immunol Glob* 2025;4(3):100492. PMID: 40502543. Full Text

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BACKGROUND: Earlier studies have demonstrated significant differences in food allergy by race and ethnicity, particularly for seafood and shrimp. Shrimp allergy is particularly interesting given the potential for cross-reactive sensitization from other arthropods. OBJECTIVES: We characterized risk factors for shrimp allergy and shrimp sensitization. METHODS: Data from electronic health records were abstracted for food allergies among patients who sought care at a large health system between October 1, 2010, and April 1, 2024. Geocoded addresses were linked to US Census data to identify characteristics associated with shrimp allergy. Non-Hispanic Black participants from the Study of Asthma-Related Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE) were assessed for allergic sensitization using an IgE array, and survey data collected from participants were evaluated for association with shrimp, cockroach, and dust mite sensitization. RESULTS: Among 2,975,183 health system patients, 4,709 individuals reported shrimp allergy. Compared to White individuals, rates of shrimp allergy were significantly higher in Black, Asian/Pacific Islander, Native American, and Latino individuals. Shrimp allergy was higher with increasing age, female sex, and asthma, and it was inversely related to median household income. Among SAPPHIRE participants, sensitization to shrimp, cockroach, and dust mite was positively associated with total IgE levels and proportion of African ancestry, but inversely associated with head of household level of education. CONCLUSIONS: Both shrimp allergy and sensitization were associated with sociodemographic factors, suggesting that environmental exposures leading to cross-reactive sensitization may be important risk factors. Nevertheless, sensitization was also associated with ancestry, highlighting the potential importance of group-specific genetic risk factors.

Clinical Quality and Safety
Hole MK, Letchuman S, Gates J, and **Berry LL**. What Adult Medical Care Can Learn from Pediatrics: Creating Comfort, Connection, and Joy in the Hospital. *Mayo Clin Proc Innov Qual Outcomes* 2025;9(5):100650. PMID: 40822860. Full Text

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Clinical Quality and Safety
Prascius S, **Wells A**, **Collier AM**, **Renard A**, **Hooper D**, and **Stein T**. Reduction of Hospital-Onset Methicillin-Resistant Staphylococcus aureus (MRSA) Bacteremia with the Use of Twice Daily Alcohol-Based Nasal Antiseptic in Intensive Care Units. *Am J Infect Control* 2025; Epub ahead of print. PMID: 40840818. Full Text

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BACKGROUND: A 191-bed hospital within a Midwest healthcare system experienced an increase in hospital acquired Methicillin-resistant Staphylococcus aureus (MRSA) bacteremia. In response, the hospital sought a targeted intervention for MRSA prevention within two intensive care units using an alcohol based nasal antiseptic. METHODS: In August 2021, Infection Prevention and Control (IPC) partnered with Nursing and the alcohol-based nasal antiseptic product vendor to implement the product in the two units. Nasal antiseptic was administered twice daily. To measure process adherence, a report was created within the electronic medical record to track compliance. Patient tracking and communication of data reports to nurse leadership by IPC began shortly afterward. RESULTS: MRSA standardized infection ratios (SIR) declined with an SIR of 1.18 in 2021 to an SIR of 0.90 in 2023. The total number of MRSA cases decreased from 2021 to 2022 with four cases and one case, respectively. DISCUSSION: Barriers were identified, including personnel permitted to administer alcohol-based antiseptic, product location, and administration documentation. As these were addressed, compliance in administration began to increase. Manually tracking compliance was later replaced with an automated report for sustainability purposes. Options available to analyze the data were limited due to lack of control data.

Clinical Quality and Safety
Steffensen KD, and **Berry L**. Shared Decision Making Can-and Should-Actively Involve Family Caregivers. *JCO Oncol Pract* 2025; Epub ahead of print. PMID: 40802917. Full Text

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Dermatology
Armstrong A, Strober B, Gisondi P, Orroth KK, Cordey M, Kent ST, Deignan C, Jardon S, Hernandez RK, Brookhart MA, and **Stein Gold L**. Benefits of Earlier Apremilast Initiation in Patients with Psoriasis and Limited Skin Involvement: Results from a Real-World Retrospective Study. *Dermatol Ther (Heidelb)* 2025; Epub ahead of print. PMID: 40767996. Full Text

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INTRODUCTION: Many patients with psoriasis remain on topical therapy despite meeting criteria for systemic therapy. Our objective was to estimate the effect of earlier initiation of apremilast on attaining body surface area (BSA) treatment targets in patients with psoriasis in a real-world setting. METHODS: This retrospective cohort study conducted in the OM1 database analyzed patients with psoriasis and a BSA value between ≥ 1 and ≤ 10% (on index date) who had initiated apremilast or a topical treatment. Relative risks were used to compare achieved BSA targets across treatment groups. Confounding, selection bias, and missing data may have been present, but measures were taken to limit their impact. RESULTS: Of 3589 apremilast initiators, 2073 (57.8%) initiated early (≤ 6 months after index date) and 1516 (42.2%) initiated late (> 6 months); separately, 9777 patients initiated their second or later topical treatment (topical users). Compared with early initiators, late initiators had higher BSA values at treatment initiation. Early apremilast initiators were more likely than topical users to achieve BSA ≤ 1% or ≥ 75% improvement in BSA (BSA-75) at 6 and 12 months after treatment initiation: for early apremilast initiators, the relative risks of achieving BSA ≤ 1% and BSA-75 compared with topical users were 1.54 (95% confidence interval [CI]: 1.27, 1.87) and 1.52 (95% CI: 1.21, 1.89), respectively, at 6 months, and 1.49 (95% CI: 1.23, 1.80) and 1.50 (95% CI: 1.22, 1.85), respectively, at 12 months. CONCLUSIONS: Earlier initiation of apremilast, an oral systemic treatment, was associated with lower cumulative disease burden and increased likelihood of attaining BSA goals compared with topical users.

Dermatology
Bitterman D, **Pandher K**, and **Shwayder TA**. A Persistent Papular Eruption on the Cheek of a Young Woman. *JAMA Dermatol* 2025; Epub ahead of print. PMID: 40864453. Full Text

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A woman in her 20s presented with a 9-year history of skin-colored papules with a background of hyperpigmentation on her left cheek. Before presentation, treatment with desonide and ammonium lactate was unsuccessful. What is your diagnosis?
eng

Dermatology
Bouazzi D, Nielsen SM, Hagan PG, Botvid S, Hove LS, Prens EP, Christensen R, Jemec GBE, Knecht-Gurwin K, Szepietowski JC, Anaba EL, Chehad AS, Zobiri S, Serradj A, Bhuiyan MSI, Noor T, Guillem P, Parvizi MM, Saki N, Alpsoy E, Vardar C, Kanni T, Giamarellos-Bourboulis EJ, Frew JW, Al Maharbi WHA, van Huijstee JC, Aarts P, Dewi ST, Febriana SA, Indrastuti N, Suryawati N, Pangastuti M, Adji A, Akhyar G, Nopriyati N, Hazlianda CP, Reyes-Baraona F, Matas C, Saeed H, Moodley A, Binamer Y, Kamil MAA, Jocic I, Mijuskovic Z, Mallawaarachchi K, Gangani C, Tusheva I, Boshkovski VB, Hu D, Geng S, Medianfar CE, Saunte DML, Chandran NS, van der Zee HH, Zouboulis CC, Benhadou F, Villumsen B, Alavi A, Ibekwe PU, **Hamzavi IH**, Ingram JR, Naik HB, Garg A, and Boer J. Prevalence of Hidradenitis Suppurativa: A Meta-Analysis of Global Hidradenitis Suppurativa Atlas Studies. *JAMA Dermatol* 2025; Epub ahead of print. PMID: 40864454. Full Text

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IMPORTANCE: Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease with a substantial burden. Standardized global prevalence estimates and data on associated sociodemographic and risk factors are lacking. OBJECTIVE: To estimate the global prevalence of HS and study differences in prevalence by age, sex, geographical location, body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), smoking status, gross domestic product (GDP), and Human Development Index (HDI). DATA SOURCES AND STUDY SELECTION: Included studies were conducted using the standardized Global Hidradenitis Suppurativa Atlas methodology with finalized data collection before May 19, 2023. Studies were required to use a population-based sampling method and conduct clinical confirmation of HS diagnosis following a screening questionnaire. DATA EXTRACTION AND SYNTHESIS: Data were independently extracted from relevant studies by 2 reviewers (D.B. and C.E.M.) using a standardized form. Extracted variables included geographic location, age, sex, BMI (median and BMI >30), smoking status, HS prevalence estimates (with 95% CIs), GDP, and HDI. A proportional meta-analysis using a random-effects model was conducted on the included studies. MAIN OUTCOMES AND MEASURES: The primary outcome was the point prevalence of HS, confirmed by clinical examination. Secondary outcomes included differences in HS prevalence by sex, age, BMI category, smoking status, and country-level socioeconomic indicators (GDP and HDI). All outcomes were prespecified before data analysis. RESULTS: The sample included 22 743 participants, identifying 247 patients with HS, across 25 studies in 23 countries spanning 6 continents. The median proportion of female patients with HS was 55.6%, and the median age was 34.5 years. While the prevalence estimates showed considerable inconsistency ($I^2 > 75\%$; $\tau^2 = 0.747$), the overall random-effects global prevalence of HS was 0.99% (95% CI, 0.67%-1.46%). Female sex was the only factor observed to be associated with the prevalence estimates ($\beta = 1.02$; 95% CI, 1.01-1.03). CONCLUSIONS AND RELEVANCE: In this meta-analysis, an estimated global prevalence of HS between 0.67% and 1.46% surpassed previous global estimates. Substantial global variations in HS prevalence were also observed. Female sex was the only factor associated with prevalence in this sample. Future studies assessing genetic, environmental, and etiological factors are warranted to explain the heterogeneity in prevalence.

Dermatology
Clark M, Xue GR, **Powers M**, and Nassim JS. Eyelash Serums: A Consumer Analysis of the Rising Demand for Topical Eyelash Enhancement Products. *Dermatol Surg* 2025; Epub ahead of print. PMID: 40833018. Full Text

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Dermatology
Clark MM, and Que SKT. In vivo parallel relaxing incisions for scalp defect repairs. *Dermatol Online J* 2025;31(3). PMID: Not assigned. Full Text

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Dermatology
Jiang X, Mortlock RD, Pironon N, Zhou J, Hu R, Liu W, Acosta A, **Shwayder TA**, Hovnanian A, Lifton RP, and Choate KA. A recurrent de novo damaging variant in EMP2 causes progressive symmetric erythrokeratoderma. *Proc Natl Acad Sci U S A* 2025;122(32):e2509896122. PMID: 40758889. Full Text

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Genetic investigation in Mendelian skin disorders featuring generalized or localized skin scaling and redness, known as the ichthyoses, has revealed novel pathways relevant to epidermal integrity, barrier function, and desquamation. Here, we show that a recurrent de novo missense variant in EMP2 (epithelial membrane protein 2), which encodes a cell surface tetraspan protein in the growth-arrest specific 3 (GAS3)/peripheral myelin protein 22 (PMP22) family, is associated with a Mendelian skin disorder in the progressive symmetric erythrokeratoderma spectrum. The disorder features severely thickened, red, and scaly skin at sites of wound healing or repetitive movement including on the face, genitals, flexural areas, and the palms and soles. EMP2 has previously been shown to directly associate with focal adhesion kinase, which links cell junction forces to signaling pathways relevant to proliferation, migration, and wound healing. Using single-cell spatial transcriptomics in affected tissue, we found ectopic suprabasal activation of signaling pathways downstream of receptor tyrosine kinases including epidermal growth factor receptor (EGFR), which we confirmed with western blotting in affected cells, supporting a gain-of-function mechanism for mutant EMP2. Remarkably, treatment with erlotinib, an EGFR inhibitor, led to marked clinical improvement underscoring the key role of EMP2 in epidermal differentiation and proliferation.

Dermatology
Kircik LH, Harper JC, Gold M, **Gold LS**, Draelos ZD, Guenin E, Choi SY, Wroblewski K, Baldwin H, Callender VD, Hebert AA, and Weiss JS. Safety and Tolerability of Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel for Truncal Acne. *J Drugs Dermatol* 2025;24(8):803-809. PMID: 40773616. Full Text

BACKGROUND: Truncal acne is underdiagnosed and undertreated, and it can lead to scarring and postinflammatory hyperpigmentation. However, applying topical treatments to larger skin surface areas introduces additional safety/tolerability concerns. Clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% (CAB) gel is the only fixed-dose, triple-combination topical for acne and has demonstrated favorable efficacy/safety in participants with facial acne. METHODS: Data were pooled from one phase 2

(NCT04892706) and two phase 3 (NCT04214639, NCT04214652), double-blind, 12-week studies. Participants aged ≥9 years (≥12 years, phase 2) with moderate to severe facial acne were randomized to once daily CAB or vehicle gel. Truncal acne treatment was optional, and efficacy was not the main outcome. Truncal treatment-emergent adverse events (TEAEs) and truncal cutaneous safety/tolerability were evaluated through week 12. Only participants treating both face and trunk were included in this post hoc analysis (CAB, n=118; vehicle, n=101). RESULTS: Through week 12, TEAE rates on the trunk were higher with CAB vs vehicle (5.9% vs 1.0%). Most TEAEs were mild, none were serious, and only 1 participant (CAB-treated) discontinued due to TEAEs. Mean truncal cutaneous safety/tolerability scores with CAB were <0.5 (1=mild) at all visits. Severe (grade 3) ratings postbaseline occurred in <1% of CAB-treated participants for erythema, hyperpigmentation, and burning (n=1 each). CONCLUSIONS: In this pooled analysis, fixed-dose CAB gel was well tolerated over 12 weeks in participants treating their truncal acne. The lack of safety signals combined with the favorable safety/tolerability profile of CAB shows that it is a safe treatment option for truncal and facial acne.

Dermatology
Passeron T, Liu W, Morita A, Goh CL, Alexis A, Dreno B, Kang HY, Ly F, Puig S, Schalka S, Ocampo Candiani J, Demessant-Flavigny AL, Le Floc'h C, Kerob D, Krutmann J, **Lim H**, Taieb C, and Ezzedine K. Stigmatization in patients with pigmentation disorders: the ISPOT study. *Clin Exp Dermatol* 2025; Epub ahead of print. PMID: 40796152. Full Text

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Dermatology
Rinck JA, **Boothby-Shoemaker W**, and **Friedman BJ**. Solitary Cutaneous Xanthogranuloma With DNMT3A Mutation Arising Postallogenic Transplant in a Patient With T-Cell Acute Lymphoblastic Leukemia. *Am J Dermatopathol* 2025; Epub ahead of print. PMID: 40762954. Full Text

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The development of a mature histiocytic neoplasm after an immature lymphoproliferative disorder is rare but well documented. Previous studies have demonstrated clonal relationships between these entities-often through T- and B-cell receptor clonality analyses-supporting the concept of transdifferentiation. We

report a unique case of a solitary, subtle xanthogranuloma identified during routine comprehensive skin examination in a patient with a history of T-cell acute lymphoblastic lymphoma, postallogeneic stem cell transplant. Next-generation sequencing of the skin lesion revealed the presence of a DNMT3A mutation identical to that found in the patient's prior lymphoma, despite the patient being in both morphologic and molecular remission in the peripheral blood and bone marrow. This case underscores the importance of vigilant surveillance and highlights a potential mechanistic link through clonal evolution or transdifferentiation.

Dermatology

Schlesinger T, Chapman MS, Tu JH, Cohen JL, Strasswimmer J, Zeitouni NC, Torres A, Jazayeri SS, Goldman MP, Ibrahim SF, Lain EL, Couvillion MP, Bruce S, Laquer VT, Hanke CW, **Ozog DM**, Schneider J, Markowitz O, Berman B, Nestor MS, Gold MH, Munavalli GS, Forsha DW, Siegel DM, Mrohs D, Schmitz B, Schäning R, Pospiech N, Lyons J, Foguet M, Lübbert M, Lübbert H, and Pariser DM. Red light photodynamic therapy with 10% aminolevulinic acid gel showed efficacy for treatment of superficial basal cell carcinoma in a randomized, vehicle controlled, double-blind, multicenter phase III study. *J Am Acad Dermatol* 2025; Epub ahead of print. PMID: 40846240. Full Text

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BACKGROUND: Surgical procedures remain the gold standard for treating basal cell carcinoma (BCC), although commonly associated with cosmetic defects. The demand for non-invasive alternatives remains high. OBJECTIVE: To determine efficacy and safety of red light photodynamic therapy (PDT) with 10% 5-aminolevulinic acid (ALA) gel vs. vehicle for treatment of superficial BCC (sBCC). METHODS: This randomized, double-blind, vehicle-controlled, pivotal phase III study was conducted at 21 centers in the US. Eligible participants had ≥1 naïve sBCC and received 1-2 PDT cycles (2 PDTs each cycle) followed by clinical and histological assessment 12 weeks after start of the last PDT cycle. RESULTS: Of 187 randomized participants, 145 received PDT with 10% ALA gel and 42 with vehicle. Histological clearance was 75.9% with 10% ALA gel vs 19.0% with vehicle (p<0.0001). Clinical clearance was 83.4% with 10% ALA gel vs 21.4% with vehicle (p<0.0001). 88.1% of participants treated with 10% ALA gel rated the esthetic outcome as very good or good. No previously unknown adverse events occurred. LIMITATIONS: Few participants with lesions on face/scalp; to date, a 60-month follow-up is still ongoing. CONCLUSION: 10% ALA gel showed significantly higher clearance rates than vehicle with unproblematic safety and positive esthetic outcome.

Dermatology

Stein Gold L, Gottlieb AB, Armstrong AW, Alkousakis T, Bissonnette R, Langley RG, Krueger J, Papp K, Choi O, Rowland K, Chan D, Jeyarajah J, Park-Wyllie L, Gao LL, Gordon KB, Merola JF, Lebwohl MG, and Strober B. SPECTREM Phase 3b Clinical Trial Results Through Week 16: Guselkumab Efficacy and Safety for the Treatment of Low Body Surface Area, Moderate Psoriasis With High-Impact Site Involvement. *Br J Dermatol* 2025; Epub ahead of print. PMID: 40875818. Full Text

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BACKGROUND: Patients with psoriasis affecting a low percentage of their body surface area (BSA) are underrepresented in clinical studies and may face substantial disease burden if high-impact sites are affected. OBJECTIVES: SPECTREM is a Phase 3b, randomized, placebo-controlled study evaluating guselkumab efficacy and safety in participants with low BSA (2%-15%), moderate (Investigator's Global Assessment [IGA]=3) plaque psoriasis involving ≥1 high-impact site (scalp, face, genitals, intertriginous areas). METHODS: Eligible participants were randomized 2:1 to receive guselkumab 100 mg or placebo at Week 0 and Week 4, then every 8 weeks. The primary endpoint was the proportion of participants achieving IGA 0/1 (cleared/minimal) at Week 16. Major secondary endpoints included the proportion of participants achieving ≥90% improvement in Psoriasis Area and Severity Index (PASI 90), IGA 0, and PASI 100; mean percent improvements from baseline to Week 16 in BSA and PASI; and proportions of participants achieving site-specific IGA or Physician's Global Assessment (PGA) 0/1 among those with scalp, facial, genital, or intertriginous site-specific IGA/PGA ≥3 at baseline. RESULTS: Among the 338 (guselkumab, n=225; placebo, n=113) randomized participants, mean (SD) baseline BSA was 7.6% (3.7) and PASI was 9.0 (3.8). At Week 16, all primary and major secondary endpoints were met, with guselkumab demonstrating superiority versus placebo (all p<0.001) in the proportions of participants achieving IGA 0/1 (74.2% vs 12.4%), IGA 0 (40.4% vs 3.5%), PASI 90 (52.9% vs 6.2%), and PASI 100 (32.4% vs 2.7%), and mean percent improvement from baseline in BSA (80.6% vs 6.1%) and PASI (82.6% vs 13.7%). Site-specific IGA/PGA 0/1 response rates for guselkumab versus placebo were: scalp, 75.0% (114/152) versus 14.5% (11/76); face, 87.8% (79/90) versus 28.6% (12/42); genital, 78.0% (64/82)

versus 37.5% (15/40); and intertriginous, 86.5% (96/111) versus 28.8% (15/52). In the guselkumab and placebo groups, respectively, 37.8% and 39.8% experienced ≥1 adverse event; no new safety signals were identified. CONCLUSIONS: Through Week 16, guselkumab was effective and well tolerated in participants with low BSA, moderate plaque psoriasis with involvement of high-impact sites. Statistically significant improvements across multiple clearance measures, irrespective of baseline BSA, support the effectiveness of guselkumab across a broad range of patients. CLINICALTRIALS.GOV IDENTIFIER: NCT06039189.

Dermatology
Tanghetti EA, Lebwohl MG, **Gold LS**, Green L, Draelos ZD, and Jacobson A. Resolving Hyperkeratotic Psoriasis: Mechanisms of Action and Additive Effects of Fixed-Combination Halobetasol Propionate and Tazarotene. *J Drugs Dermatol* 2025;24(8):795-801. PMID: 40773618. Full Text

BACKGROUND: Hyperkeratotic plaque psoriasis represents a distinct morphological variant that is difficult to treat with topical therapies because thick lesions may impede the penetration of active ingredients. The immunoregulatory mechanisms of topical corticosteroids (TCSs) and tazarotene (TAZ) may contribute to combating hyperkeratosis and long-term remittance of psoriasis. A fixed-combination lotion containing the potent-to-superpotent TCS halobetasol propionate (HP, 0.01%) and TAZ (0.045%), indicated for the topical treatment of plaque psoriasis in adults, was developed to harness the therapeutic benefits of each active ingredient while minimizing their safety concerns. METHODS: This review describes data supporting the efficacy of halobetasol propionate (0.01%) and tazarotene (0.045%) lotion (HP/TAZ) and remittive effect after treatment cessation in patients with hyperkeratotic plaques. RESULTS: Pivotal trials demonstrate the superior efficacy and safety of HP/TAZ over each active ingredient alone. Furthermore, we summarize a recent clinical study, which showed that HP/TAZ reduces lesional levels of tumor necrosis factor alpha and interleukin 17A, critical proinflammatory cytokines involved in keratinocyte hyperproliferation and psoriasis pathogenesis. CONCLUSION: This review suggests that HP/TAZ is a valuable option for the topical treatment of severe hyperkeratotic plaques through its additive mechanisms targeting inflammation and keratinocyte regulation.

Dermatology
Westerkam LL, van der Zee HH, Bechara FG, Goldberg S, Jemec GB, Caffrey J, Chaffin A, Chiu ES, Damitz L, Daveluy S, Garg A, George R, Guillem P, **Hamzavi IH**, Hazen PG, Horvath B, Ingram JR, Kirby JS, Matusiak L, Orenstein LAV, Orgill DP, Pena-Robichaux V, Podda M, Prens E, Resnik B, Lindhardt Saunte DM, Saylor DK, Thorlacius L, Villumsen B, Vossen A, and Sayed CJ. Establishment of standardized definitions and a core set of outcome characteristics following hidradenitis suppurativa surgery developed by an expert Delphi consensus. *J Am Acad Dermatol* 2025; Epub ahead of print. PMID: 40865729. Full Text

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BACKGROUND: Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition often requiring surgical intervention for definitive treatment. Previous studies evaluated post-surgical outcomes, but no standardization exists for collection and nomenclature for HS surgical outcomes. OBJECTIVE: To characterize and define surgical outcome terminology. METHODS: A modified Delphi protocol was used to reach consensus on data to collect and terms to describe outcomes following HS surgical procedures. A five-member steering committee created preliminary definitions and surveys which were distributed via Qualtrics to a group of international HS experts. A nine-point Likert scale was used and a score of at least 7 was needed for an item to reach agreement. RESULTS: Twenty-five dermatologists and general and plastic surgeons participated in the Delphi study. Following two rounds of surveys and feedback, the consensus terminology to describe outcomes included surgical site and regional persistence and progression. Consensus was also reached on key features to report as part of each outcome. LIMITATIONS: Limitations include narrow scope and small number of participants from limited geographical areas. CONCLUSION: Surgery persistence and progression definitions were agreed upon by a group of international HS experts. This consensus is a first step towards standardizing terminology and reporting for HS surgical outcomes.

Dermatology
Xue GR, **Clark M**, Slaven JE, and Que SKT. Rurality as a predictor of melanoma stage and treatment in Indiana: a retrospective cohort study. *Melanoma Res* 2025;35(5):366-367. PMID: 40880292. Full Text

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Dermatology
Zirwas M, Fowler JF, Jr., Tsianakas A, Devani AR, Halden P, Lai Z, Kuo Y, Nawaz H, and **Stein Gold LF**. Efficacy and Safety of Ruxolitinib Cream for the Treatment of Moderate to Severe Chronic Hand Eczema: Results From a 16-Week, Multicenter, Randomized, Double-Blind Study. *J Am Acad Dermatol* 2025; Epub ahead of print. PMID: 40889714. Full Text

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BACKGROUND: Chronic hand eczema (CHE) is a well-recognized inflammatory disorder. OBJECTIVE: To evaluate the efficacy and safety of 1.5% ruxolitinib cream in adults with moderate to severe CHE. METHODS: This phase 2 study enrolled adults with CHE from North America and Europe, an Investigator's Global Assessment (IGA)-CHE score of 3/4, ≥1 prior CHE therapy, and no current or recent history (≤5 y) of atopic dermatitis. Patients were randomized 1:1 to twice-daily 1.5% ruxolitinib cream or vehicle cream for 16 weeks. RESULTS: Among 186 randomized patients, most who applied ruxolitinib cream achieved a score of 0 (clear) or 1 (almost clear) on the IGA-CHE scale with a 2-grade improvement from baseline at Week 16 (53.2% vs 10.9% [vehicle]; P<0.0001; primary endpoint). Itch improvements (≥4-point improvement in numerical rating scale) were reported on Day 2 (9.1% vs 2.4%) and reached statistical significance on Day 7 (27.4% vs 9.0%; P=0.0024). Improvements in skin pain and quality of life were reported during the study. Ruxolitinib cream was well tolerated, with no new safety signals and few (3.2%) application site reactions. LIMITATIONS: Relatively small sample size. CONCLUSION: Ruxolitinib cream represents an effective treatment option for nonatopic CHE subtypes that are not controlled with standard therapies.

Diagnostic Radiology

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BACKGROUND AND OBJECTIVES: Temporal lobe epilepsy (TLE) is commonly associated with mesiotemporal pathology and widespread alterations of gray and white matter structures. Evidence supports a progressive condition, although the temporal evolution of TLE is poorly defined. In this ENIGMA-Epilepsy study, we aim to investigate structural alterations in gray and white matter across the adult lifespan in patients with TLE by charting both gray and white matter changes and explore the covariance of age-related alterations in both compartments. METHODS: Mega-analysis of parcellated T1-weighted and diffusion MRI data across 18 international sites for patients with TLE was compared against healthy controls. We combined median-age split groupwise comparisons with cross-sectional sliding age-window analyses to explore gray (cortical thickness, subcortical volume) and white matter microstructure (fractional anisotropy, mean diffusivity) age-related changes. Five-year range age windows were constructed from mean z scores of all patients. Covariance analyses examined the coupled correlations of gray and white matter lifespan curves for each region. RESULTS: We studied 769 patients with TLE and 885 healthy controls across an age range of 17-73 years. Robust ($p(FDR) < 0.05$) gray matter thickness/volume decline ($d < -0.20$) was seen across a broad cortico-subcortical territory, extending beyond the mesiotemporal lobe throughout the adult lifespan in patients with TLE. White matter changes were also widespread across multiple fiber tracts with peak effects in temporolimbic fibers in fractional anisotropy ($d < -0.3$, $p(FDR) < 0.05$) and mean diffusivity measures ($d > 0.3$, $p(FDR) < 0.05$). Changes spanned the adult time window and effects exceeded typical aging-related processes in patients at the level of cortical thickness, subcortical volume, and diffusion measures, particularly in patients older than 55 years. Covariance analyses revealed strong associations across multiple white matter tracts, subcortical structures, and cortical regions within and beyond the temporolimbic system. DISCUSSION: This study highlights that patients with TLE exhibit more pronounced and widespread gray and white matter atrophy across the lifespan. The cross-sectional nature of our study limits definitive conclusions on whether the atrophy shown is progressive but emphasizes the importance of prompt diagnosis and intervention in patients. Collectively, our results motivate future longitudinal studies to clarify consequences of drug-resistant epilepsy.

Diagnostic Radiology
Martinovski P, **Sly M**, **McVinnie D**, and **Massa PJ**. Use of Imaging to Prevent Unnecessary Workup and Answer a Clinical Question. *Cureus* 2025;17(7):e87158. PMID: 40755634. Full Text

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With a fair percentage of all medical care deemed unnecessary for diagnosis and treatment, it is paramount that clinicians consider the rationale for each order and whether it is truly warranted. We present the case of a 71-year-old male with a history of Roux-en-Y gastric bypass who presented with choledocholithiasis and was found to have an incidental finding of a persistently narrowed segment of the right bile duct. With the usage of multiple imaging modalities, particularly CT angiography and intravascular ultrasound via an endobiliary route during biliary drain management, it was confirmed that the narrowing of concern was caused by a benign vascular compression by the right hepatic artery as opposed to a malignancy. This case demonstrates how minimally invasive imaging can reduce further potentially unnecessary tests, and thus costs, for patients.

Diagnostic Radiology
Ngo A, Liu L, Larivière S, Kebets V, Fett S, Weber CF, Royer J, Yu E, Rodríguez-Cruces R, Zhang Z, Ooi LQR, Yeo BTT, Frauscher B, Paquola C, Caligiuri ME, Gambardella A, Concha L, Keller SS, Cendes F, Yasuda CL, Bonilha L, Gleichgerrcht E, Focke NK, Kotikalapudi R, O'Brien TJ, Sinclair B, Vivash L, Desmond PM, Lui E, Vaudano AE, Meletti S, Kälviäinen R, **Soltanian-Zadeh H**, Winston GP, Tiwari VK, Kreilkamp BAK, Lenge M, Guerrini R, Hamandi K, Rüber T, Bauer T, Devinsky O, Striano P, Kaestner E,

Hatton SN, Caciagli L, Kirschner M, Duncan JS, Thompson PM, McDonald CR, Sisodiya SM, Bernasconi N, Bernasconi A, Gan-Or Z, and Bernhardt BC. Associations between epilepsy-related polygenic risk and brain morphology in childhood. *Brain* 2025; Epub ahead of print. PMID: 40811581. Full Text

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Extensive neuroimaging research in temporal lobe epilepsy with hippocampal sclerosis (TLE-HS) has identified brain atrophy as a disease phenotype. While it is also related to a complex genetic architecture, the transition from genetic risk factors to brain vulnerabilities remains unclear. Using a population-based approach, we examined the associations between epilepsy-related polygenic risk for HS (PRS-HS) and brain structure in healthy developing children, assessed their relation to brain network architecture, and evaluated its correspondence with case-control findings in TLE-HS diagnosed patients relative to healthy individuals We used genome-wide genotyping and structural T1-weighted magnetic resonance imaging (MRI) of 3,826 neurotypical children from the Adolescent Brain Cognitive Development (ABCD) study. Surface-based linear models related PRS-HS to cortical thickness measures, and subsequently contextualized findings with structural and functional network architecture based on epicentre mapping approaches. Imaging-genetic associations were then correlated to atrophy and disease epicentres in 785 patients with TLE-HS relative to 1,512 healthy controls aggregated across multiple sites. Higher PRS-HS was associated with decreases in cortical thickness across temporo-parietal as well as fronto-central regions of neurotypical children. These imaging-genetic effects were anchored to the connectivity profiles of distinct functional and structural epicentres. Compared with disease-related alterations from a separate epilepsy cohort, regional and network correlates of PRS-HS strongly mirrored cortical atrophy and disease epicentres observed in patients with TLE-HS, and highly replicable across different studies. Findings were consistent when using statistical models controlling for spatial autocorrelations and robust to variations in analytic methods. Capitalizing on recent imaging-genetic initiatives, our study provides novel insights into the genetic underpinnings of structural alterations in TLE-HS, revealing common morphological and network pathways between genetic vulnerability and disease mechanisms. These signatures offer a foundation for early risk stratification and personalized interventions targeting genetic profiles in epilepsy.

Emergency Medicine

Amin P, Dehkan D, **Peltzer-Jones J**, Malas N, Hong V, Shobassy A, and Stowell K. Evaluation and Management of Alcohol-Intoxicated Patients with Suicide Risk in the Emergency Department: A Scoping Review. *J Acad Consult Liaison Psychiatry* 2025; Epub ahead of print. PMID: 40889686. Full Text

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BACKGROUND: The severity of suicide risk in patients who present to the emergency department (ED) with cooccurring complaints of suicidal ideation and alcohol intoxication is neither well-understood nor well-recognized by ED staff. While suicide screening has become a standard expectation in ED care, there lacks consensus on standard care practices for the evaluation and management of patients with suicidal ideation and/or attempt and alcohol intoxication. METHODS: This is a scoping review describing the evaluation and management of ED patients with suicidality and alcohol intoxication. PubMed, Ovid MEDLINE, APA PsycInfo, and CINAHL were searched using relevant terms to describe this ED population. 110 total articles were found and underwent full-text review. Twenty-nine articles met criteria for inclusion. RESULTS: Patients with suicide-related complaints while intoxicated are less likely to receive a psychiatric evaluation or to be admitted psychiatrically. This is concerning given that alcohol use is demonstrated to be both a proximal and long-term risk factor for suicide attempt(s). Existing literature includes recommendations to evaluate patients while intoxicated and to re-evaluate when sober. To create safe plans of care for these patients, clinicians need to identify the patterns of alcohol use: alcohol use to facilitate suicide, binge drinking episodes, or alcohol use disorder (AUD). ED interventions can then build from understanding of how the alcohol use and suicidality interact. Though no specific ED-based interventions were found for this patient subpopulation, interventions shown to mitigate suicide risk and/or decrease alcohol use include: brief interventions (e.g. Screening, Brief Intervention, and Referral to Treatment (SBIRT)), peer navigators, crisis safety plans, discussion about restricting access to lethal means, and/or inpatient psychiatric admission. CONCLUSION: There is a lack of published guidelines, standards of care, and best practices to help consultation-liaison, emergency psychiatrists, and ED providers in the management of this population, despite overwhelming literature linking alcohol intoxication and suicide attempt/death. Further research is needed to (1) elucidate the core elements for standardized assessments and (2) develop evidence-based interventions to improve outcomes/decrease rates of intoxicated suicide completion.

Emergency Medicine

Cai AG, **Jarou ZJ**, Janke AT, Gettel CJ, Rothenberg C, Adelman LC, Simpson M, Fisher J, and Venkatesh AK. Emergency Physician Employer Market Share and Concentration by Ownership Type. *Ann Emerg Med* 2025; Epub ahead of print. PMID: 40758080. Full Text

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STUDY OBJECTIVE: With rapid consolidation and corporatization of the emergency physician workforce over recent years, little is known about the current state of the emergency physician market. We characterized employer group market share by ownership structure and market concentration by ownership across geographies. METHODS: We selected hospitals from the Centers for Medicare and Medicaid Services (CMS) Hospital General Information Dataset (2021). Ivy Clinicians (2024) defined ownership category (majority ownership by health system, private equity, or clinician partnerships [single-site, regional, national]). National Emergency Department Inventories 2021, the most recent data set available, served as a proxy for 2024 emergency department (ED) visit volumes. The primary outcome was market share defined as the percentage of national ED annual visits staffed by employers within each ownership category. Secondary outcomes measured market concentration. RESULTS: Our sample

included 3,998 hospital-based EDs, accounting for 109.7 million ED visits in 2021. Per 2024 ownership data, health system groups staffed 33.0% of ED visits followed by private equity 24.7%, regional partnership 20.8%, national partnership 13.4%, and single-site partnership 8.1%. The top 3 private equity groups staffed 93.5% of the private equity visits. In contrast, the top 31 regional partnerships, 51 single-site partnerships, and 63 health system groups comprised 50% market share within their respective categories. Three national partnerships staff all visits in this category. Of the 306 hospital referral regions, 258 (84%) were highly concentrated. CONCLUSION: Groups with majority physician ownership staffed less than half of ED visits. The emergency medicine market is highly concentrated regionally, as well as within the private equity and national partnership ownership categories.

Emergency Medicine

Gunaga S, **Al-Hage A**, **Buchheister A**, Neelam H, **Corcoran J**, **Welchans M**, **Swan K**, Awada M, **Miller J**, and Mowbray F. Trends in hospice and palliative care consults initiated in the emergency department: An eight-year utilization analysis. *Am J Emerg Med* 2025;97:237-243. PMID: 40782511. Full Text

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BACKGROUND: Emergency departments (EDs) play a central role in end-of-life care, yet the early integration of hospice and palliative care (HPC) is often underutilized. Early access to HPC improves outcomes, aligns care with patient goals, and reduces costs. However, incorporating primary and specialized palliative care resources in the ED remains inconsistent, and utilization trends are not well understood. Our study evaluates the incidence and trends of ED-initiated HPC consults over 8 years within a large metropolitan health system. METHODS: We conducted a retrospective cohort study of electronic health records from 5 EDs between 2016 and 2023. Our cohort included all ED visits where HPC consults were ordered. We examined the annual number of HPC consults, patient demographics, and health outcomes. A subgroup analysis evaluated HPC consults per 1000 ED patients aged 60 or

older admitted for inpatient care. RESULTS: A total of 8055 HPC consults were ordered for 6370 unique patients. The average age was 78.1 years, with 56.4 % female and 75.0 % White. Of the cohort, 91.7 % were admitted, 5.3 % discharged home, and 53.2 % died in-hospital. HPC consults increased from 369 in 2016 to 1355 in 2023 (367 % increase, $p < 0.001$). The ratio of hospice to palliative care consults reversed from 1.5:1 in 2016 to 1:1.9 in 2023. Post-COVID-19, daily HPC consults rose by 173.6 % compared to pre-pandemic levels. CONCLUSIONS: ED-initiated HPC consults increased significantly over time, suggesting an evolving role for EDs in delivering primary palliative care. Further research is needed to determine national trends and identify barriers to broader implementation.

Emergency Medicine

Hill L, Goodman R, **Gray L**, Moegling M, Crady R, Saucedo J, and Hewes HA. Nurse Pediatric Competency, Certification, and Continuing Education: Impact on EDs' Pediatric Readiness. *J Emerg Nurs* 2025;51(5):904-912. PMID: 40285774. Full Text

INTRODUCTION: Children present to emergency departments regardless of their readiness to care for pediatric patients. The National Pediatric Readiness Project is an initiative to improve pediatric emergency care. Increased National Pediatric Readiness Project scores have been associated with decreased mortality. The purpose of this study is to examine the association between nurse pediatric competency, certification, and/or continuing education and weighted pediatric readiness scores. METHODS: A sub-analysis of the 2021 National Pediatric Readiness Project Assessment examining nurse pediatric competencies and overall pediatric readiness scores of emergency department of United States includes descriptive statistics, testing for the association between hospital characteristics and pediatric patient volume using Fisher's tests and Kruskal-Wallis tests, and Wilcoxon rank-sum tests of score and nurse pediatric competencies. RESULTS: The majority (89%) of emergency departments require some nurse competency evaluations. Only 20.1% of emergency departments require nurse specialty certification. Most emergency departments have a hospital-specific nurse competency evaluation policy (91.7%) and nurse continuing education policies (98.3%). Having policies for competencies is significantly associated with increased median weighted pediatric readiness scores above the national median: nursing continuing education policy weighted pediatric readiness scores 71.3 ($P = .030$), nurse specialty certification policy weighted pediatric readiness scores 83.5 ($P<.001$), and nurse hospital-specific competency evaluation policy weighted pediatric readiness scores 72.3 ($P<.001$). DISCUSSION: Most emergency departments have a requirement for nurse pediatric-specific competency evaluations, and having nursing competency requirements is associated with higher weighted pediatric readiness scores. This highlights the importance of emergency nurse pediatric competency, certification, and continuing education on pediatric readiness scores, and therefore, the potential reduction in pediatric mortality.

Emergency Medicine

Hudson CC, Rutter L, Joormann J, Passell E, McKemey RM, House SL, Beaudoin FL, An X, Stevens JS, Neylan TC, Jovanovic T, Linnstaedt SD, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Hudak LA, Pascual JL, Seamon MJ, Datner EM, Pearson C, Peak DA, Merchant RC, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Bruce SE, Harte SE, Kessler RC, Koenen KC, McLean SA, and Germine LT. Emotion identification and emotion sensitivity following interpersonal and non-interpersonal traumatic experiences: Results from the AURORA study. *Clin Psychol Sci* 2025; Epub ahead of print. PMID: 40843243. Full Text

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Social cognition is an important mechanism linking trauma to psychopathology; however, current models fail to explain individual differences in social cognition after trauma exposure. We investigated whether the interpersonal nature of trauma exposure helps to explain variability in social cognitive outcomes. Our sample was derived from the AURORA study, a national initiative involving intensive follow-up of trauma survivors for one year. We analyzed data from 2241 participants (M(age) = 35.12, 64% female, 54% Black) who experienced an assault (n = 262) or a motor vehicle collision (n = 1979). Social cognition was assessed with the Multiracial Emotion Identification Task and the Belmont Emotion Sensitivity Test. Overall emotion identification accuracy declined over time among participants who experienced interpersonal trauma (β = -.10, p = .03), but not non-interpersonal trauma (β = .00, p = .83). These results may help to enhance the prediction of psychopathological outcomes following trauma exposure.

Emergency Medicine

Huibregtse ME, Li T, Harnett NG, Yuh EL, Ely TD, Jovanovic T, Calhoun VD, Neylan TC, House SL, Clifford GD, Bucher MA, Linnstaedt SD, An X, Conti AC, Seligowski AV, Li Q, Dillon DG, Vizer LM, McKibben LA, Albertorio-Sáez LM, Beaudoin FL, Wang KKW, Matson L, Harte SE, Bruce SE, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Jones CW, Swor RA, Pearson C, Peak DA, O'Neil BJ, Kessler RC, Koenen KC, Ressler KJ, McLean SA, and Stevens JS. Association Between Acute Plasma Glial Fibrillary Acidic Protein Levels and White Matter Integrity in Recent Trauma Survivors. *J Neurotrauma* 2025; Epub ahead of print. PMID: 40763107. Full Text

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Traumatic brain injuries (TBIs) account for over 2.5 million emergency department (ED) visits each year in the United States. The bulk of TBI research in acute care settings has focused exclusively on individuals who receive computed tomography (CT) scanning. Recently, more sensitive TBI assessment tools have been identified, including blood biomarkers such as glial fibrillary acidic protein (GFAP) and magnetic resonance imaging (MRI) of white matter microstructural integrity. These methods can evaluate for evidence of TBI in CT-negative patients. However, limited prior work has investigated the relationship between blood GFAP levels and white matter microstructural integrity. The present study examined the association between acute (≤72 h) GFAP levels and white matter microstructural integrity at 2 weeks post-trauma among ED patients (n = 328) recruited after a qualifying traumatic experience. We hypothesized that acute GFAP concentrations would be associated with disrupted microstructural integrity, quantified with Tract-Based Spatial Statistics-derived diffusion tensor imaging (DTI) metrics (reduced fractional anisotropy and increased axial diffusivity [AD], radial diffusivity, and mean diffusivity), in tracts previously shown to be vulnerable to TBI. Our secondary hypothesis was that there would be a stronger association between GFAP levels and white matter integrity among female relative to male trauma survivors, in line with previous literature suggesting that females' axons are less resilient to stretch injury. To test the primary hypothesis, we fit four sets of linear regression models to assess the association between natural log-transformed acute GFAP concentration and DTI metrics for 15 white matter regions of interest (ROIs). The false discovery rate (FDR) was controlled at 0.05 for each set of models. Models were adjusted for age, sex, neuroimaging site, and a composite lifetime traumatic stress variable. To test the secondary hypotheses, we fit identical sets of linear regression models, with an additional interaction term between sex and ln(GFAP). We followed up all significant results surviving FDR correction with correlational tractography to examine the location and direction of tracts associated with the DTI metric passing through those ROIs. We observed significant and positive associations between acute GFAP and AD in the parahippocampal cingulum (B = 1.416 × 10(-5), standard error [SE] = 4.806 × 10(-6), p = 0.003, FDR-corrected p = 0.026), and the sagittal stratum (B = 1.012 × 10(-5), SE = 3.438 × 10(-6), p = 0.003, FDR-corrected p = 0.026), including fibers of the inferior longitudinal fasciculus and the inferior fronto-occipital fasciculus. Furthermore, the association between GFAP and AD of the parahippocampal cingulum was stronger in female trauma survivors compared with male trauma survivors (B = 2.898 × 10(-5), SE = 9.352 × 10(-6), p = 0.002, FDR-corrected p = 0.032). Our results

suggest that among ED patients with low rates of intracranial injuries observed on CT and MRI scans, acute peripheral levels of GFAP may be able to predict later disruption in structural connectivity.

Emergency Medicine
Pflaum-Carlson J, **Redding A**, **Murphy D**, **MacLean L**, **Hamilton J**, and **Santarossa S**. Recruitment, retention and recouperation: lessons learned from a study aimed at assessing burnout mitigation in physician learners. *BMC Res Notes* 2025;18(1):376. PMID: 40890847. Full Text

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Emergency Medicine
Thomas SJ, Patel VS, Schmitt CP, Zielinski AT, Aboukhaled MN, Steinberg CA, Moore EE, Moore HB, Thomas SG, Waxman DA, **Miller JB**, Bunch CM, Aboukhaled MW, Thomas EJ, Zackariya SK, Oryakhail H, Mehreteab A, Ludwig RE, George SM, Siddiqi AI, Zackariya BM, Qasim A, Walsh MM, and Al-Fadhl MD. The Effect of Heterogeneous Definitions of Massive Transfusion on Using Blood Component Thresholds to Predict Futility in Severely Bleeding Trauma Patients. *J Clin Med* 2025;14(15). PMID: 40807047. Full Text

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In the trauma resuscitation literature, there are inconsistent definitions of what constitutes massive transfusion and a unit of blood, complicating the use of transfusion cut-points to declare futility. This is problematic as it can lead to the inefficient use of blood products, further exacerbating current blood product shortages. Previous studies have used various transfusion cut-points per hour to define futility in retrospective analyses but have not accurately defined futility at the bedside due to patient survival even at large rates and volumes of blood transfused. In an attempt to use transfusion cut-points as a marker to help define futility, guidelines have been proposed to limit blood product waste in transfusions for severely bleeding trauma patients, such as Suspension of Transfusion and Other Procedures (STOP) for patients older than 15 and the Futility of Resuscitation Measure (FoRM), used to determine futility in patients older than 60. In an effort to construct effective bedside futile resuscitation criteria with 100% positive predictive value and specificity, this review proposes the use of specific blood component transfusion cut-points combined with parameters from both STOP and FoRM to allow for a comprehensive and accurate method of declaring futility in severely bleeding trauma patients.

Endocrinology and Metabolism
Ellis DA, Carcone AI, Buggs-Saxton C, **Bhan A**, and Dekelbab MB. Effects of individual, health system and neighborhood risks on diabetes health outcomes among emerging adults with type 1 diabetes. *Diabetes Res Clin Pract* 2025;227:112415. PMID: 40782842. Full Text

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AIMS: To test associations between individual, health system and neighborhood-level risk and protective factors, and health outcomes in a diverse sample of emerging adults (EAs) with type 1 diabetes (T1D). METHODS: Data were drawn from the baseline data collection of a clinical trial. One hundred and thirteen EAs [47.8 % White/non-Hispanic; mean age = 20.9 years; mean HbA1c = 9.5 % (IFCC = 81 mmol/mol)] completed self-report questionnaires on diabetes-self efficacy, diabetes distress, communication with diabetes health care provider, neighborhood crime and diabetes management. Structural equation modelling estimated the direct and indirect effects of individual, health care provider, and neighborhood factors on diabetes management and glycemic control. RESULTS: In the final model, self-efficacy for diabetes care was the only significant predictor of diabetes management ($\beta = 0.32$, $p < 0.001$). Neighborhood crime ($\beta = 0.17$, $p < 0.05$) and diabetes management ($\beta = -0.28$, $p < 0.05$) had significant direct effects on glycemic control, while diabetes self-efficacy had a significant indirect effect though diabetes management ($\beta = -0.090$; $p < 0.01$). CONCLUSIONS: Individual factors such as higher self-efficacy for diabetes management and neighborhood factors such as lower crime rates have protective effects on the diabetes health of EAs with T1D.

Endocrinology and Metabolism

Lal RA, Lum JW, Reed ZW, **Kruger D**, Reed JC, 3rd, Weinstock RS, Carlson AL, Kudva YC, Liljenquist D, Cobry EC, Levister CM, Aleppo G, Chen J, Ahn DT, Hirsch IB, Putman MS, Broyles F, Pinsker JE, Romey M, Lehman A, Muchmore DB, Kollman C, and Beck RW. A Multicenter Study of an Investigational Extended Wear Insulin Infusion Set in Adults with Type 1 Diabetes. *Diabetes Technol Ther* 2025; Epub ahead of print. PMID: 40780817. Full Text

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Objective: To evaluate the function and safety of the SteadiSet™ infusion set over a continuous 7-day wear period in adults with type 1 diabetes. Research Design and Methods: Participants used a SteadiSet infusion set with a t:slim X2™ insulin pump with Control-IQ™ technology, and either insulin aspart or insulin lispro, for a target of 7 days for 12 consecutive wear periods. Each set removed before 7 days was adjudicated by an independent committee to assess the cause of early removal and to determine whether criteria for primary or key secondary endpoints were met. Results: There were 260 participants who inserted 3028 infusion sets. For the primary endpoint, the Kaplan-Meier 7-day survival estimate was 95% (95% CI 94% to 96%). For the key secondary endpoint, which expanded the reasons for a failed infusion set, the Kaplan-Meier 7-day survival estimate was 84% (95% CI 82% to 86%). For both endpoints, the P value was <0.001 compared with a prespecified survival rate of 75%. Time-in-range 70-180 mg/dL (TIR) increased through day 3 of set wear and then decreased through day 7, with the average TIR being 70.6% over the entire wear period across all infusion sets, including those that failed. An increase in total daily insulin was observed from day 4 through day 7. Conclusions: The 7-day survival of the SteadiSet infusion set was very high for the primary endpoint and at an acceptable level with respect to early removal for any reason related to the device.

Gastroenterology
Govil D, **Afram R**, **Alkhafaji A**, **Woods E**, and **Affas S**. When Gains Go Wrong: A Case of Selective Androgen Receptor Modulator-Related Liver Injury. *Cureus* 2025;17(7):e87376. PMID: 40765588. Full Text

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Selective androgen receptor modulators (SARMs) causing drug-induced liver injury is a rare, albeit inadequately described, potentially serious side effect for those in the fitness industry looking to maximize muscle growth, strength gain, and fat loss as quickly as possible. We present a case of a patient with drug-induced liver injury after starting Stenabolic, a newer SARM. We report a case of a 40-year-old male who presented with vague gastrointestinal symptoms. Before the presentation, he was relatively healthy but taking multiple over-the-counter supplements. Although he had been taking most of these supplements for a long time without notable side effects, he had recently started taking Stenabolic, a performance-enhancing drug under the SARM category. Laboratory and imaging studies confirmed hepatocellular injury. After ruling out infectious and autoimmune etiology, it was thought that the likely source was Stenabolic. The patient was treated with supportive care and was advised to discontinue Stenabolic. Upon discharge, he began to show clinical improvement. Although there is limited research about Stenabolic, other agents in the SARM class have been implicated in similar patterns of liver injury. Its structural and pharmacologic similarities to anabolic steroids raise concern for hepatotoxicity through an idiosyncratic immune-mediated mechanism. This case highlights the potential hepatotoxicity of performance-enhancing supplements like Stenabolic. With the growing popularity of SARMs and limited regulation, healthcare providers should maintain a high index of suspicion for supplement-induced liver injury. Further research is needed to clarify the safety and mechanisms of these agents. Until then, their use should be discouraged.

Gastroenterology
Salam R, **Alkhafaji A**, **Govil D**, **Ahmadi F**, **Affas S**, and Hassan M. Racial Disparities in Outcomes After Liver Transplantation. *Cureus* 2025;17(7):e88693. PMID: 40861692. Full Text

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Racial disparities in liver transplant outcomes remain an area of concern despite advancements in organ allocation and post-transplant care. This retrospective cohort study analyzed adult liver transplant recipients from the United Network for Organ Sharing (UNOS) registry between 1988 and 2021 to evaluate differences in graft and patient survival between African American (AA) and Caucasian American (CA) recipients. After excluding non-Black and non-White individuals and pediatric cases, a 3:1

matched cohort was created using propensity-type matching for age, sex, body mass index, and ABO type, resulting in 50,584 patients (13,421 AA and 40,263 CA). Median graft survival was significantly lower in AAs compared to CAs (1,466 vs. 1,787 days, $p < 0.0001$), as was median patient survival (1,480 vs. 1,815 days, $p < 0.0001$). Graft failure rates at one year were 2,325/12,708 (18.3%) for AA vs. 5,884/37,762 (15.6%) for CA ($Chi^2 = 50.87$, $df = 1$, $V = 0.026$, $p < 0.0001$); at five years, 4,326/10,323 (41.9%) vs. 10,172/30,179 (33.7%), respectively ($Chi^2 = 218.35$, $V = 0.060$, $p < 0.0001$). Similarly, mortality at five years was 3,516/9,152 (38.4%) for AA vs. 8,232/26,291 (31.3%) for CA ($Chi^2 = 154.41$, $V = 0.066$, $p < 0.0001$). AAs also had higher Model for End-Stage Liver Disease (MELD) scores at listing and transplant and were more likely to be hospitalized or in the ICU at the time of transplant. Insurance coverage differed significantly, with AAs more likely to have public insurance (6,031/12,739, 47.3% vs. 13,055/36,504, 35.8%, $p < 0.0001$). These findings suggest that AA liver transplant recipients experience significantly worse outcomes, likely due to a combination of advanced disease at presentation and socioeconomic disparities.

Gastroenterology

Sbei O, Almansour Y, Sbei B, Sannah Y, Alabdelrazzak M, Alqasmi H, Abdalla O, Turfe A, and **Kutait A**. Determining the Impact of Medical Arabic Workshops on Medical Students' Preparedness and Communication Skills With Arabic-Speaking Patients. *Cureus* 2025;17(7):e87685. PMID: 40786394. Full Text

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Introduction While Wayne State University School of Medicine (WSUSOM) serves a large Arab-American patient population, medical students have limited opportunities for formal instruction in medical Arabic, which may hinder effective communication with Arabic-speaking patients. To address this gap, a series of medical Arabic workshops was implemented, focusing on medical terminology and patient interaction. This study evaluates the impact of these workshops on students' self-reported preparedness and confidence when interacting with Arabic-speaking patients. Notably, there is a lack of prior US-based studies examining the effectiveness of structured medical Arabic training for medical students, further underscoring the novelty and relevance of this research. Methods An anonymous survey was distributed to WSUSOM students who attended one or more medical Arabic workshops. The survey utilized a five-point Likert scale (1 = never, 5 = always) to assess domains such as communication confidence, comprehension preparedness, and perceived training utility. A total of 119 students completed the pre-workshop survey, and 110 completed the post-workshop survey. Unpaired t-tests were used to compare weighted averages across domains before and after the workshops, with p-values <0.05 considered significant. Results Participation in the medical Arabic workshops was associated with statistically significant improvements in students' confidence and preparedness when interacting with Arabic-speaking patients. Pre-workshop, the weighted average score for confidence in understanding Arabic in clinical settings was 2.18 (SD = 1.34), which increased to 3.14 (SD = 1.15) post-workshop ($p < 0.0001$). Similarly, students' confidence in communicating health information rose from an average of 2.10 (SD = 1.21) to 3.17 (SD = 1.09) after attending the workshops ($p < 0.0001$). Additionally, the proportion of students reporting regular use of Arabic in clinical encounters remained high, but post-workshop responses indicated a reduction in the frequency with which students needed clarification during patient interactions. Overall, the majority of participants agreed that the workshops enhanced their clinical skills and preparedness to serve Arabic-speaking patients. Conclusions Medical Arabic workshops effectively improved medical students' confidence and readiness to engage with Arabic-speaking patients. These findings suggest that targeted language and cultural competency training may enhance communication and clinical performance, and that integration of similar programs into the formal medical school curriculum could help address language barriers in patient care.

Gastroenterology

Schuman AD, McKeon M, Allen J, Altaye M, Amin MR, Bayan SL, Belafsky PC, Bock JM, DeSilva BW, Dion G, Ekbom DC, Friedman AD, Fritz M, Guardiani EA, Johnson C, Kasperbauer J, Kim B, Krekeler BN, Kuhn M, Kwak P, Ma Y, Madden LL, Matrka L, **Mayerhoff RM**, **Piraka C**, Rosen C, Tabangin M, Wilson K, Young VN, Postma G, and Howell RJ. Dysphagia Outcomes in Zenker Diverticulum: A Longitudinal POuCH Study. *Laryngoscope* 2025; Epub ahead of print. PMID: 40828004. Full Text

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OBJECTIVE: Patients with cricopharyngeus muscle dysfunction (CPMD) with and without diverticula (e.g., Zenker Diverticulum) often struggle with dysphagia for years prior to diagnosis or intervention. Surgical treatment is successful; yet, there is limited long-term data on dysphagia outcomes after surgery. METHODS: Individuals prospectively enrolled in the Prospective Outcomes of Cricopharyngeal Hypertonicity (POuCH) collaborative with and without diverticula who underwent surgery from November 2014 to August 2024 and had at least 12 months of follow-up were included. Eating Assessment Tool 10 (EAT10) was used to characterize patient-reported outcomes. Descriptive statistics were performed using means, frequencies, and spaghetti plots. RESULTS: Of 164 patients initially identified, 2 withdrew and 2 were excluded for incomplete data; 160 were included. 31% were women, with a mean (SD) age of 70.1 (11.5). Endoscopic surgery (113, 71%) was more common than open technique (47, 29%). 19.4% of patients had undergone previous surgery. Postoperatively, patients were found to have improved EAT-10 scores, with smaller changes recorded after 36 months. Median change in EAT-10 compared to preoperative score was -12 points [IQR: -18, -5] at 12 months. 39 (24%) patients were followed for > 24 months (median change -11 [IQR: -14, -7]); 26 (16%) > 36 months (-9.5 [-17, -5]), and 12 (7.5%) > 48 months (-4 [IQR: -18, 4]). Six patients died during the study period. CONCLUSION: Improved dysphagia after surgery appears stable with minimal change over time. Most patients (96.3%) survive at least 1 year. Surgical intervention for patients with CPMD with or without diverticula is an effective and reliable treatment option.

Gastroenterology

Tao MH, **Wu T**, **Gordon SC**, **Zhou Y**, **Rupp LB**, **Trudeau S**, Schmidt MA, Daida YG, and **Lu M**. Antiviral treatment Reduces Risk of Development of Lung Cancer and non-Hodgkin Lymphoma in Patients with Chronic Hepatitis C. *Cancer Epidemiol Biomarkers Prev* 2025; Epub ahead of print. PMID: 40874910. Full Text

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BACKGROUND: Antiviral treatment for hepatitis C virus (HCV) has been shown to reduce risk of liver cancer, but there are few studies on its impact on the risk of non-liver cancers. We used a large cohort of HCV patients with extensive follow-up to investigate whether receipt of antiviral therapy affects the risk of extrahepatic cancers. METHODS: 17,485 HCV patients were followed until incidence of lung cancer, non-Hodgkin lymphoma (NHL), breast or prostate cancer, death, or last follow-up. We used multivariable modeling with time-varying covariates and propensity scores to adjust for treatment selection bias; we also applied generalized estimating equations (GEE) with a multinominal link function for discrete time-to-event data. Death was considered a competing risk. RESULTS: After 15 years of follow-up, we identified 408 incident cases of cancers, including 140 lung, 72 NHL, 81 breast (female), and 115 prostate. Compared to no treatment, patients who receive either direct-acting antivirals (DAA) or interferon-based (IFN) treatment had significantly lower risk of lung cancer (hazard ratio [HR]= 0.35, 95% CI 0.24-0.52 for achieving sustained virological response [SVR]; HR= 0.34, 95% CI 0.21-0.55 for treatment failure). Risk of NHL was reduced only among patients who achieved SVR. There were no significant associations between antiviral therapy and risks of breast and prostate cancer. CONCLUSIONS: Antiviral treatment for HCV independently reduced the risk of lung cancer, while the protective association with NHL was limited to patients achieving SVRs. IMPACT: Our findings support the importance of timely initiation antiviral therapy in patients with chronic HCV.

Global Health Initiative

Kaljee LM, **Ahmedani B**, **Srinivasan S**, Wells E, Ruprecht MT, **Ahmed Y**, **Randall S**, Beckwith C, and Keuten J. Feasibility of implementation of the zero suicide model in community-based organizations serving Afghan refugees resettled in Michigan. *BMC Public Health* 2025;25(1):2769. PMID: 40814037. Full Text

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BACKGROUND: Pioneered at HFH Behavioral Health Services in 2001, the Zero Suicide (ZS) model is comprised of several evidence-based approaches including suicide screening and assessment, caring contacts, care coordination, and suicide specific psychotherapies. The ZS model has been successfully introduced in more than twenty countries; however, to date the model has been primarily introduced in higher income countries within large health systems. It is important to understand the feasibility of this approach in a range of other settings. In the current project, a feasibility study was conducted, and a pilot program is currently underway to adapt the model for use in Community-based Organizations (CBOs) serving refugee populations. METHODS: This feasibility study focused on Afghan refugees arriving in Michigan as a part of the U.S. government "Operation Allies Welcome" program. The qualitative study included interviews with social, health, and behavioral health providers and staff at CBOs serving refugee and asylum-seeking populations in Michigan and behavioral health specialists at HFH and Wayne State

University. A Stakeholders' Advisory Board was established including HFH and CBO partners. RESULTS: Afghan refugees encountered challenges on arrival and during their settlement into life in Southeastern Michigan, including linguistic, social, economic, medical, and behavioral health barriers. The data include specific recommendations made by the respondents for adaptations to the Zero Suicide model. CONCLUSION: While the need for behavioral health services for refugee communities is recognized, challenges remain in the implementation of accessible, acceptable, and adaptable programs. Within Michigan, CBOs have developed strong relationships with refugees and asylum seekers resettled into the state. The current project was designed to build on these existing infrastructures within CBOs and determine the feasibility of integrating an evidence-based suicide prevention program. Through the feasibility study, it was evident that CBOs were interested in including the Zero Suicide model as a part of their health services. However, it was clear that adaptations were needed to support the introduction of the model and that those adaptations would have to account for diverse refugee communities and varied resources and structures within each CBO.

Graduate Medical Education

Elfert K, Ismail A, **Abusuliman M**, Eldesouki M, Aloum K, Kloub M, Elghayesh M, **Passalacqua K**, Abosheaishaa H, Nassar M, Kupec J, Krafft M, and Elhanafi SE. Safety of Esophageal Dilation Procedures in Patients on Antithrombotic Therapy: A US Collaborative Network Cohort Study. *Am J Gastroenterol* 2025; Epub ahead of print. PMID: 40833435. Full Text

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BACKGROUND: Esophageal dilation procedures are frequently performed on patients who are taking antithrombotic medications. This study aimed to evaluate whether patients on antithrombotic therapies have an increased risk of bleeding from esophageal dilation. METHODS: A retrospective propensity-matched cohort study was conducted to evaluate patients in the TriNetX US Collaborative Network database who underwent esophageal dilation procedures. The primary outcome was to assess the effect of anticoagulants and dual-antiplatelet therapies (DAPT) on the rate of post-procedural gastrointestinal bleeding within 30 days. RESULTS: Patients on anticoagulants were found to be at higher risk of post-procedural gastrointestinal bleeding compared to patients not on anticoagulation (RR,1.43; 95% CI, 1.06-1.92). The anticoagulant group had higher rates of blood transfusion and ICU admission. The DAPT group had a higher rate of GI bleeding compared to no antiplatelet therapy, though this did not reach statistical significance (RR, 1.64; 95% CI, 0.97-2.75; p=0.06). When compared to aspirin monotherapy, the difference in bleeding rates was also not statistically significant (RR, 1.36; 95% CI, 0.84-2.19; p=0.2). There was no difference in the rates of blood transfusion or ICU admission when DAPT was compared separately to aspirin and to no antiplatelet groups. Additionally, early resumption of anticoagulation or antiplatelet therapy was not associated with increased post-procedural bleeding. CONCLUSION: Patients on anticoagulants at the time of esophageal dilation were at higher risk of post-procedural bleeding. DAPT was numerically associated with a higher risk of bleeding, but this did not reach statistical significance. These findings aim to inform the clinical decision-making in pre- and post-procedure management of esophageal dilation procedures.

Hematology-Oncology

Qadir H, **Palathingal Bava E**, **Gomez-Gelvez J**, **Liu W**, **Inamdar K**, **Wey E**, **Carey J**, **Shen Y**, **Kuriakose P**, and **Ghosh S**. BCL2-Rearrangment-Negative CD23+ Follicle Center Lymphoma and Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: A Rare Case of Biclonal Composite Lymphoma. *Cureus* 2025;17(7):e88727. PMID: 40861583. Full Text

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Composite lymphomas are rare and diagnostically complex, comprising two or more distinct lymphoma subtypes within the same anatomical site and often requiring a comprehensive diagnostic approach. Due to their rarity and varied presentations, further research is needed to better understand their pathogenesis, clonal relationships, and optimal management strategies. This case report highlights an unusual presentation of composite lymphoma involving the coexistence of BCL2-R-negative, CD23-positive follicle center lymphoma and chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).

Hematology-Oncology

Serres SK, Saxon-Filipe S, and **Schwartz T**. Complementary and Alternative Medicine in Breast Cancer: Considerations for the Breast Surgical Oncologist. *Ann Surg Oncol* 2025; Epub ahead of print. PMID: 40849381. Full Text

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A significant portion of cancer patients will consider or ultimately pursue complementary or alternative medicine (CAM) treatment strategies. Having a working knowledge of these topics is important for a surgical oncologist to participate in informed consent discussions when patients are considering CAM approaches. Psychological, physical, and dietary complementary approaches are discussed, as well as ethical considerations and communication strategies to approach these discussions.

Hematology-Oncology

Shambhavi S, Singh H, Ramaprasad G, Khikmatov M, Vankeshwaram V, Ashish K, Valladares C, **Bhatt T**, and Cohen SD. Efficacy of Infliximab Versus Vedolizumab in the Management of Immune Checkpoint Inhibitor-Induced Colitis: A Systematic Review and Meta-Analysis. *World J Oncol* 2025;16(4):331-341. PMID: 40810084. Full Text

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BACKGROUND: Immune checkpoint inhibitors (ICIs) can cause severe gastrointestinal immune-related adverse events (irAEs), often leading to treatment interruption and increased morbidity. Immune-mediated colitis (IMC) ranges from mild diarrhea to life-threatening colitis, sometimes requiring urgent intervention. While corticosteroids are the first-line treatment, selective immunosuppressive therapy (SIT) with either infliximab or vedolizumab is used for steroid-refractory or dependent cases. However, standardized practices are lacking, and treatment decisions are largely left to provider discretion. This study compares infliximab and vedolizumab for IMC, focusing on remission rates, recurrence, SIT dosing, and systemic steroid exposure duration. METHODS: We identified six retrospective cohort studies that

compared infliximab with vedolizumab in the treatment of IMC through a systematic search of PubMed, EMBASE, Cochrane Library, Scopus, CINAHL, Google Scholar, and Web of Science in English from inception until October 2024. From the identified literature, we extracted pertinent data such as remission and recurrence of IMC. Pooled analysis and heterogeneity analysis were performed using R Studio version 4.4.1. The risk of bias was assessed using the Newcastle-Ottawa Scale. RESULTS: A total of six studies with 645 patients were included. In ICI-associated colitis, vedolizumab was associated with lower recurrence rates (odds ratio (OR): 0.29, 95% confidence interval (CI): 0.15 - 0.54) and shorter systemic steroid exposure (mean difference (MD): -16.88 days, 95% CI: -20.47 to -13.30) compared to infliximab. While vedolizumab showed improved remission, there was no statistically significant difference in remission rates between vedolizumab and infliximab monotherapy (OR: 3.16, 95% CI: 0.29 - 34.01). Remission was achieved with fewer doses of infliximab than vedolizumab (MD: 1.16, 95% CI: 0.09 - 2.22). The mean number of vedolizumab doses was 2.57 (raw mean score (MRAW): 2.57, 95% CI: 1.43 - 2.71), while the mean number of infliximab doses was 1.36 (MRAW: 1.36, 95% CI: 0.69 - 2.02). CONCLUSIONS: Among patients with ICI-induced colitis, vedolizumab demonstrated superiority over infliximab by being associated with lower rates of colitis recurrence and decreased systemic steroid exposure, although it required a higher number of doses compared to infliximab.

Hematology-Oncology

Waliany S, Hung YP, **Rous FA**, Luo F, Capelletti M, Ressler S, Do A, Peterson J, **Meservey C**, Digumarthy SR, Ou SI, **Gadgeel SM**, Lin JJ, and Meador CB. Lung Carcinoid Tumors With Potentially Actionable Genomic Alterations and Responses to Targeted Therapies. *Clin Lung Cancer* 2025;26(5):354-363.e355. PMID: 40234130. Full Text

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BACKGROUND: Effective treatments for patients with advanced lung carcinoids remain limited. The prevalence of potentially actionable genomic alterations (AGAs) among lung carcinoids is not well-understood. MATERIALS AND METHODS: Lung carcinoids submitted for next-generation sequencing (NGS) at a Clinical Laboratory Improvement Amendments (CLIA)-certified genomics laboratory from September 2013 to March 2024 were retrospectively investigated to determine prevalence of AGAs. We evaluated outcomes with genotype-matched targeted therapies in patients with advanced lung carcinoids with AGAs identified across 3 institutions and comprehensive literature search. RESULTS: Among 321 cases of lung carcinoids profiled by NGS, 8 (2.5%) harbored potential AGAs (4 [1.2%] with commercially available targeted therapies), including KRAS mutations (n = 4, 1.2%: G12C, G12D, G12R, G12V), ALK fusions (n = 2, 0.6%), BRAF D594N (n = 1, 0.3%), and RET fusion (n = 1, 0.3%). None of the 24 typical carcinoids harbored an AGA. Collectively across these database-identified patients, our multi-institutional cohort, and literature review, we identified 36 cases of lung carcinoids with potential AGAs (24 with commercially available targeted therapies), predominantly comprising fusions of ALK (n = 14), RET (n = 5), and NTRK (n = 2). Of 27 with known disease stage, 19 had stage 4 disease, and 13 (68.4%) had outcomes reported following targeted therapies. Median treatment duration was 12.0 months (95% CI: 6.7-16.0). Median progression-free survival (PFS) was 10.6 months (95% CI: 6.7-16.0) across all targeted therapy lines and 14.0 months (95% CI: 1.3-NA) with first-line targeted therapies. Objective response rate with at least one targeted therapy was 61.5%. CONCLUSIONS: Patients with advanced lung carcinoids harboring AGAs can derive meaningful benefit from genotype-matched targeted therapies, highlighting potential role for NGS in patients with advanced carcinoids.

Hematology-Oncology

Young G, Mahlangu J, Boggio LN, Carcao M, Dargaud Y, Escobar M, Giermasz A, Hermans C, **Kuriakose P**, Miesbach W, Nance D, Rafique A, Sidonio RF, Jr., Vilchevska KV, Wang M, and Pipe SW. Treatment of severe bleeds with eptacog beta in hemophilia A or B with inhibitors: a post hoc analysis of the PERSEPT 1 and 2 trials. *Blood Vessel Thromb Hemost* 2025;2(3):100069. PMID: 40765904. Full Text

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Severe bleeding episodes (BEs) in persons with hemophilia A or B and inhibitors (PwHABIs) represent challenging clinical situations and can require treatment regimens lasting days or weeks before hemostatic control is achieved. Eptacog beta is a recombinant activated human factor VII bypassing agent approved for treating and controlling bleeding in PwHABIs aged ≥12 years. The aim of this study is to assess the efficacy and safety of eptacog beta for severe bleed treatment in PwHABIs during 2 phase 3 trials (PERSEPT 1 and PERSEPT 2). Patients could treat severe BEs with initial doses of 75 or 225 µg/kg eptacog beta at home, followed by subsequent 75 µg/kg eptacog beta infusions administered at predefined intervals in a hospital or hemophilia treatment center. Satisfactory treatment responses to eptacog beta were typically defined in this post hoc analysis by physician- and patient-reported hemostasis evaluations of "excellent" or "good." Hemostatic control of an intracranial hemorrhage (ICH) in 1 patient was assessed by computed tomography. Seven PwHABIs (aged 1-50 years) treated 8 BEs considered severe or otherwise life threatening with eptacog beta during PERSEPT 1 and PERSEPT 2. Hemostatic control of 7 of these BEs (including 3 ICH events) was achieved. Eptacog beta treatment durations ranged from 25 minutes to 96 hours. No thrombotic events were reported, and eptacog beta was well tolerated. Most severe BEs resolved with eptacog beta treatment during PERSEPT 1 and PERSEPT 2. The PERSEPT 1 and PERSEPT 2 trials were registered at www.clinicaltrials.gov as #NCT02020369 and #NCT02448680, respectively.

Hospital Medicine

Baugh AD, and **Campbell J**. Does Excluding Participants Improve Our Understanding of Lung Function? *Am J Respir Crit Care Med* 2025; Epub ahead of print. PMID: 40772957. Full Text

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Infectious Diseases

Oska N, **Peterson D**, Brothers K, **Maramraju R**, **Ayyad A**, and **Hohmann B**. Isolated Facial Vein Thrombophlebitis Caused by Fusobacterium nucleatum: A Lemierre-Variant Case. *Case Rep Infect Dis* 2025;2025:9938125. PMID: 40860904. Full Text

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Background: Lemierre's syndrome is an uncommon yet potentially fatal infection, classically secondary to bacterial pharyngeal infections. It is typically characterized by bacteremia, most frequently due to Fusobacterium necrophorum and internal jugular vein thrombophlebitis. If untreated, septic embolization may result, potentially damaging the lungs, liver, brain, or other organs. This report describes a variant of Lemierre's syndrome in a young woman with streptococcal pharyngitis, who developed Fusobacterium nucleatum bacteremia and isolated facial vein thrombophlebitis, highlighting the importance of early diagnosis and treatment. Case Presentation: A 33-year-old woman with no significant past medical history presented with sore throat, chills, and right-sided facial and neck pain. Initially diagnosed with streptococcal pharyngitis at an urgent care clinic, she presented to the emergency department soon afterwards due to the development of severe rigors and fever. Blood cultures revealed growth of Fusobacterium nucleatum, raising suspicion for Lemierre's syndrome in the setting of worsening facial and neck pain despite negative initial imaging of the soft tissue of the neck. A subsequent CT venogram confirmed isolated thrombosis of the right facial vein. The patient was treated and discharged in stable condition on a 4 week course of metronidazole and 2 weeks of ceftriaxone. Conclusion: This case emphasizes the importance of maintaining suspicion for Lemierre's syndrome in patients with bacterial pharyngitis, especially when atypical symptoms such as facial pain occur. Although the internal jugular vein is most commonly affected, facial vein thrombosis may also occur. Early antibiotic treatment is critical for preventing severe complications including septic shock and embolization.

Infectious Diseases

Prascius S, **Wells A**, **Collier AM**, **Renard A**, **Hooper D**, and **Stein T**. Reduction of Hospital-Onset Methicillin-Resistant Staphylococcus aureus (MRSA) Bacteremia with the Use of Twice Daily Alcohol-Based Nasal Antiseptic in Intensive Care Units. *Am J Infect Control* 2025; Epub ahead of print. PMID: 40840818. Full Text

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BACKGROUND: A 191-bed hospital within a Midwest healthcare system experienced an increase in hospital acquired Methicillin-resistant Staphylococcus aureus (MRSA) bacteremia. In response, the hospital sought a targeted intervention for MRSA prevention within two intensive care units using an alcohol based nasal antiseptic. METHODS: In August 2021, Infection Prevention and Control (IPC) partnered with Nursing and the alcohol-based nasal antiseptic product vendor to implement the product in the two units. Nasal antiseptic was administered twice daily. To measure process adherence, a report was created within the electronic medical record to track compliance. Patient tracking and communication of data reports to nurse leadership by IPC began shortly afterward. RESULTS: MRSA standardized infection ratios (SIR) declined with an SIR of 1.18 in 2021 to an SIR of 0.90 in 2023. The total number of MRSA cases decreased from 2021 to 2022 with four cases and one case, respectively. DISCUSSION: Barriers were identified, including personnel permitted to administer alcohol-based antiseptic, product location, and administration documentation. As these were addressed, compliance in administration began to increase. Manually tracking compliance was later replaced with an automated report for sustainability purposes. Options available to analyze the data were limited due to lack of control data.

Infectious Diseases

Surie D, Self WH, Yuengling KA, Lauring AS, Zhu Y, Safdar B, Ginde AA, Simon SJ, Peltan ID, Brown SM, Gaglani M, Ghamande S, Columbus C, Mohr NM, Gibbs KW, Hager DN, Prekker M, Gong MN, Mohamed A, Johnson NJ, Steingrub JS, Khan A, Duggal A, Gordon AJ, Qadir N, Chang SY, Mallow C, Felzer JR, Kwon JH, Exline MC, **Vaughn IA**, **Ramesh M**, Papalambros L, Mosier JM, Harris ES, Baughman A, Cornelison SA, Blair PW, Johnson CA, Lewis NM, Ellington S, Grijalva CG, Talbot HK, Casey JD, Halasa N, Chappell JD, Rutkowski RE, Ma KC, and Dawood FS. RSV Vaccine Effectiveness Against Hospitalization Among US Adults Aged 60 Years or Older During 2 Seasons. *JAMA* 2025; Epub ahead of print. PMID: 40884491. Full Text

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IMPORTANCE: Respiratory syncytial virus (RSV) vaccines for adults aged 60 years or older became available in 2023. One dose is recommended for all adults aged 75 years or older and those aged 60 to 74 years at increased risk of severe RSV; however, duration of protection is unknown. OBJECTIVE: To evaluate RSV vaccine effectiveness against RSV-associated hospitalization among adults aged 60 years or older during 2 RSV seasons. DESIGN, SETTING, AND PARTICIPANTS: A total of 6958 adults aged 60 years or older were included in this test-negative, case-control study if they were hospitalized with acute respiratory illness at any of 26 hospitals in 20 US states during the October 1, 2023, to March 31, 2024, or October 1, 2024, to April 30, 2025, RSV seasons and had respiratory virus testing within 10 days of illness onset. Case patients tested positive for RSV only; control patients tested negative for RSV, SARS-CoV-2, and influenza. Demographic and clinical data were obtained through patient interview and electronic health records. EXPOSURES: Receipt of 1 RSV vaccine dose at least 14 days before illness onset. MAIN OUTCOMES AND MEASURES: Multivariable logistic regression was used to compare the odds of RSV vaccination among hospitalized cases and controls. Models were adjusted for age, sex, race and ethnicity, geographic region, and calendar month and year. Vaccine effectiveness was estimated as (1 - adjusted odds ratio) × 100%. Analyses were stratified by timing of RSV vaccine receipt (same vs prior season) relative to illness onset. RESULTS: Of 6958 adults aged 60 years or older, 821 (11.8%) were RSV cases and 6137 (88.2%) were controls. A total of 1438 patients were Black (20.1%) and 4314 were White (62.0%); 3534 were female (50.8%). Median age was 72 years (IQR, 66-80 years) and 1829 adults (26.3%) were immunocompromised. A total of 63 cases (7.7%) and 966 controls (15.7%) were vaccinated. Estimated vaccine effectiveness against RSV-associated hospitalization was 58% (95% CI, 45%-68%) during 2 seasons and 69% (95% CI, 52%-81%) for same-season vaccination vs 48% (95% CI, 27%-63%; P = .06) for prior-season vaccination. Estimated vaccine effectiveness during 2 seasons was significantly lower among immunocompromised adults (30%; 95% CI, -9% to 55%) than immunocompetent adults (67%; 95% CI, 53%-77%; P = .02) and among those with cardiovascular disease (56%; 95% CI, 32%-72%) vs without (80%; 95% CI, 62%-90%; P = .03). CONCLUSIONS AND RELEVANCE: Respiratory syncytial virus vaccines prevented RSV-associated hospitalization during 2 seasons, although effectiveness was lower in patients with immunocompromise and cardiovascular disease than in those without these conditions. Ongoing monitoring is needed to determine the optimal RSV revaccination interval.

Infectious Diseases

Turner NA, Hamasaki T, Doernberg SB, Lodise TP, King HA, Ghazaryan V, Cosgrove SE, Jenkins TC, Liu C, Sharma S, Zaharoff S, Wahid L, Renard VJ, Cook P, Raad I, Hachem R, Chaftari AM, Sims M, DeMarco C, Miller LG, McCarthy MW, Morse CG, Lucasti C, Forrest GN, Cherabuddi K, Polk C, Fazili T, Rupp ME, Thompson GR, 3rd, Kim K, Strnad L, Schnee AE, McKinnell JA, **Ramesh M**, Silveira FP, McCarty TP, Lee TC, McDonald EG, Paolino K, Wiegand K, Wall A, Riccobene T, Patel R, Rappo U, Evans S, Chambers HF, Fowler VG, Jr., and Holland TL. Dalbavancin for Treatment of Staphylococcus aureus Bacteremia: The DOTS Randomized Clinical Trial. *JAMA* 2025;334(10):866-877. PMID: 40802264. Full Text

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IMPORTANCE: Dalbavancin is a long-acting intravenous lipoglycopeptide that may be effective for treatment of complicated Staphylococcus aureus bacteremia without requiring long-term intravenous access. OBJECTIVE: To evaluate the efficacy and safety of dalbavancin vs standard therapy for completion of treatment of complicated S aureus bacteremia. DESIGN, SETTING, AND PARTICIPANTS: Open-label, assessor-masked, randomized clinical trial conducted from April 2021 to December 2023 at 23 medical centers in the US (n = 22) and Canada (n = 1). Participant follow-up lasted 70 days (180 days for participants with osteomyelitis); date of final follow-up was December 1, 2023. Hospitalized adults with complicated S aureus bacteremia who achieved blood culture clearance following at least 72 hours but no more than 10 days of initial antibacterial therapy were included. Participants were excluded if they had central nervous system infection, retained infected prosthetic material, left-sided endocarditis, or severe immune compromise. INTERVENTIONS: Participants were randomly assigned to receive either 2 doses of intravenous dalbavancin (n = 100; 1500 mg on days 1 and 8) or 4 to 8 total weeks of standard intravenous therapy (n = 100; cefazolin or antistaphylococcal penicillin if methicillin susceptible;

vancomycin or daptomycin if methicillin resistant). MAIN OUTCOMES AND MEASURES: The primary outcome was the desirability of outcome ranking (DOOR) at day 70, which involved 5 components (clinical success, infectious complications, safety complications, mortality, and health-related quality of life) and was assessed for superiority (achieved if the 95% CI for the probability of dalbavancin having a superior DOOR was >50%). Secondary outcomes included clinical efficacy at day 70 (prespecified noninferiority margin of 20%) and safety. RESULTS: Of 200 participants randomized (mean [SD] age, 56 [16.2] years; 62 females [31%]), 167 (84%) survived to day 70 and had an efficacy assessment. Participants without a day 70 efficacy assessment were treated as clinical failures in the analyses. The probability of a more desirable day 70 outcome with dalbavancin vs standard therapy was 47.7% (95% CI, 39.8% to 55.7%). Regarding secondary outcomes, clinical efficacy was documented in 73 of 100 for dalbavancin and 72 of 100 for standard therapy (difference, 1.0% [95% CI, -11.5% to 13.5%]), meeting the noninferiority criterion. Serious adverse events were reported in 40 of 100 participants who received dalbavancin and 34 of 100 participants who received standard therapy; treatment-related adverse events were uncommon in both groups. CONCLUSIONS AND RELEVANCE: Among adult participants with complicated S aureus bacteremia who achieved blood culture clearance, dalbavancin was not superior to standard therapy by desirability of outcome ranking. When considered with other efficacy and safety outcomes these findings may help inform use of dalbavancin in clinical practice. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT04775953.

Internal Medicine

Abosheaishaa H, Elsayed H, Abdelhalim O, Haddad IME, Harfoush MK, Abdallfatah A, Sethi A, **Abusuliman M**, Karna R, and Bilal M. Vonoprazan and amoxicillin dual therapy versus bismuth-based therapy for Helicobacter pylori eradication: a systematic review and meta-analysis of randomized controlled trials. *Proc (Bayl Univ Med Cent)* 2025;38(5):716-721. PMID: 40821497. Full Text

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INTRODUCTION: Helicobacter pylori infection can cause peptic ulcer disease, chronic gastritis, primary gastric lymphoma, and gastric cancer. Treatment with bismuth-based quadruple therapy is typically the first line of treatment but can be challenging due to increased pill burden and adverse effects, leading to nonadherence to therapy. Recent studies have shown that vonoprazan can be used in combination with amoxicillin as a potential treatment option. We conducted a systematic review and meta-analysis to assess the efficacy and tolerability of vonoprazan-based dual therapy as compared to bismuth-based therapy (BBT). METHODOLOGY: We conducted a comprehensive search of multiple electronic databases including PubMed, Embase, and Cochrane Library to identify randomized controlled studies assessing vonoprazan and amoxicillin (VA) in comparison to BBT for H. pylori treatment in adults >18 years of age. Studies with pediatric populations, written in languages other than English, or without control groups were excluded. RESULTS: Out of the 1968 citations, 9 studies including 2039 patients were included in the final analysis. There were 463 and 481 men in the VA and the BBT groups, respectively. The mean age ranged from 38.1 to 48.7 years in the VA group and from 38.6 to 46.1 in the BBT group. The VA group had an eradication rate similar to that of the BBT group (odds ratio [OR]: 0.32, 95% confidence interval [CI]: 0.26-0.40; P = 0.08). The VA group had a lower incidence of total adverse events than the BBT group (OR: 0.32, 95% CI: 0.26-0.40; P = 0.0001), including a reduced occurrence of nausea and vomiting (OR: 0.42, 95% CI: 0.28-0.65; P = 0.0001). There was no difference in compliance between the VA and BBT groups (OR: 1.16, 95% CI: 0.76-1.76; P = 0.50). CONCLUSION: Our study showed a similar eradication rate of H. pylori but a significantly lower incidence of adverse events in the VA group compared with the BBT group. Our analysis suggests that a VA-based regimen is an acceptable treatment option for H. pylori patients who cannot tolerate BBT.

Internal Medicine

Aburumman R, Abdul Razzak F, Kerbage A, Brunaldi V, Mrad R, Al Annan K, and Abu Dayyeh B. Endoscopic management of esophageal perforations: a multi-center study. *Surg Endosc* 2025; Epub ahead of print. PMID: 40854992. Full Text

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BACKGROUND: Esophageal perforation (EP) is a rare but life-threatening condition with an incidence of approximately 3.1 per million annually. While iatrogenic injury during endoscopy is the leading cause, other etiologies include spontaneous rupture, trauma, and malignancy. EP can present with nonspecific symptoms, most commonly chest pain or dysphagia, and diagnostic delays are associated with worse outcomes. Multiple non-operative strategies exist, including primary closure, stenting (bypass), combination therapy, and conservative management. However, data guiding the optimal approach remain limited. The aim of this study was to evaluate outcomes of different non-operative management strategies for EP and identify predictors of successful repair. METHODS: We retrospectively analyzed adult patients with EP across three Mayo Clinic sites between 2007 and 2023. Patients were categorized into four groups based on treatment modality. Demographics, clinical features, imaging, endoscopic intervention, and outcomes were recorded. The primary outcome was clinical success, defined as avoidance of surgical intervention. Logistic regression was used to identify predictors of success. RESULTS: A total of 72 patients were included (mean age 63.7 years, 65.3% male). The most common cause was iatrogenic injury (58.3%), and the distal esophagus was the most frequent site (67.6%). Non-operative success was 100% in the primary closure and combination groups, and 42.9% in the conservative group ($p < 0.001$). On multivariate analysis, non-conservative therapy significantly predicted success (aOR 22.4, 95% CI [1.2-407.4], $p = 0.036$). CONCLUSION: Primary closure and combination endoscopic approaches offer superior outcomes in managing EP. Early intervention with appropriate modality selection is critical to avoid surgical escalation and improve prognosis.

Internal Medicine

Arham M, Dad A, Bin Abdul Malik MH, Sajjad T, Bin MA, Haider F, Khan M, Hamza A, Arif MH, **Qureshi MA**, Abdul Jabbar AB, Javed MA, and Bakht K. Diagnostic accuracy of discovery NM 530c CZT SPECT for myocardial perfusion imaging in coronary artery disease: a systematic review and meta-analysis. *Int J Cardiovasc Imaging* 2025; Epub ahead of print. PMID: 40773029. Full Text

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Coronary artery disease (CAD) is the leading cause of cardiovascular mortality (CVD), accounting for 1 in 5 CVD-related deaths. The advent of non-invasive imaging modalities has driven the use of myocardial perfusion imaging (MPI) to enhance diagnostic accuracy and improve clinical outcomes in CAD. Building on the role of myocardial perfusion imaging (MPI), this meta-analysis assesses the diagnostic accuracy of the Discovery NM 530c CZT SPECT for CAD compared with invasive coronary angiography (ICA ± FFR)

and noninvasive modalities, including PET, MRI, and coronary CT angiography. A systematic search of six databases was conducted to identify studies evaluating the diagnostic accuracy of the NM 530c CZT-SPECT for detecting CAD. Comparator modalities included ICA ± FFR, PET, MRI, or coronary CTA performed within 90 days. Diagnostic performance was assessed using pooled sensitivity, specificity, summary receiver operating characteristic (SROC) curves, and diagnostic odds ratio (DOR), using R (v2024.12.0 + 467) with the "meta" and "mada" packages. A bivariate meta-analysis of 11 studies showed a pooled sensitivity of 83.5% (95% CI: 77.3-88.3%) and specificity of 75.8% (95% CI: 67.8-82.3%), with an AUC of 0.858 and diagnostic odds ratio (DOR) of 15.9. Likelihood ratios were 3.45 (positive) and 0.22 (negative). The SSS ≥ 4 subgroup showed the highest sensitivity (0.881) and DOR (19.21). The univariate random-effects model yielded a pooled sensitivity of 83% and specificity of 77%. Heterogeneity was moderate, and Deeks' test showed no publication bias (p = 0.83). This meta-analysis establishes the Discovery NM 530c CZT SPECT as a reliable and clinically effective non-invasive modality for detecting coronary artery disease (CAD), with a pooled sensitivity of 0.835, specificity of 0.758, and AUC of 0.858, supporting its diagnostic utility across diverse clinical settings.

Internal Medicine

Elfert K, Ismail A, **Abusuliman M**, Eldesouki M, Aloum K, Kloub M, Elghayesh M, **Passalacqua K**, Abosheaishaa H, Nassar M, Kupec J, Krafft M, and Elhanafi SE. Safety of Esophageal Dilation Procedures in Patients on Antithrombotic Therapy: A US Collaborative Network Cohort Study. *Am J Gastroenterol* 2025; Epub ahead of print. PMID: 40833435. Full Text

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BACKGROUND: Esophageal dilation procedures are frequently performed on patients who are taking antithrombotic medications. This study aimed to evaluate whether patients on antithrombotic therapies have an increased risk of bleeding from esophageal dilation. METHODS: A retrospective propensity-matched cohort study was conducted to evaluate patients in the TriNetX US Collaborative Network database who underwent esophageal dilation procedures. The primary outcome was to assess the effect of anticoagulants and dual-antiplatelet therapies (DAPT) on the rate of post-procedural gastrointestinal bleeding within 30 days. RESULTS: Patients on anticoagulants were found to be at higher risk of post-procedural gastrointestinal bleeding compared to patients not on anticoagulation (RR,1.43; 95% CI, 1.06-1.92). The anticoagulant group had higher rates of blood transfusion and ICU admission. The DAPT group had a higher rate of GI bleeding compared to no antiplatelet therapy, though this did not reach statistical significance (RR, 1.64; 95% CI, 0.97-2.75; p=0.06). When compared to aspirin monotherapy, the difference in bleeding rates was also not statistically significant (RR, 1.36; 95% CI, 0.84-2.19; p=0.2). There was no difference in the rates of blood transfusion or ICU admission when DAPT was compared separately to aspirin and to no antiplatelet groups. Additionally, early resumption of anticoagulation or antiplatelet therapy was not associated with increased post-procedural bleeding. CONCLUSION: Patients on anticoagulants at the time of esophageal dilation were at higher risk of post-procedural bleeding. DAPT was numerically associated with a higher risk of bleeding, but this did not reach statistical significance. These findings aim to inform the clinical decision-making in pre- and post-procedure management of esophageal dilation procedures.

Internal Medicine
Govil D, **Afram R**, **Alkhafaji A**, **Woods E**, and **Affas S**. When Gains Go Wrong: A Case of Selective Androgen Receptor Modulator-Related Liver Injury. *Cureus* 2025;17(7):e87376. PMID: 40765588. Full Text

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Selective androgen receptor modulators (SARMs) causing drug-induced liver injury is a rare, albeit inadequately described, potentially serious side effect for those in the fitness industry looking to maximize muscle growth, strength gain, and fat loss as quickly as possible. We present a case of a patient with drug-induced liver injury after starting Stenabolic, a newer SARM. We report a case of a 40-year-old male who presented with vague gastrointestinal symptoms. Before the presentation, he was relatively healthy but taking multiple over-the-counter supplements. Although he had been taking most of these supplements for a long time without notable side effects, he had recently started taking Stenabolic, a performance-enhancing drug under the SARM category. Laboratory and imaging studies confirmed hepatocellular injury. After ruling out infectious and autoimmune etiology, it was thought that the likely source was Stenabolic. The patient was treated with supportive care and was advised to discontinue Stenabolic. Upon discharge, he began to show clinical improvement. Although there is limited research about Stenabolic, other agents in the SARM class have been implicated in similar patterns of liver injury. Its structural and pharmacologic similarities to anabolic steroids raise concern for hepatotoxicity through an idiosyncratic immune-mediated mechanism. This case highlights the potential hepatotoxicity of performance-enhancing supplements like Stenabolic. With the growing popularity of SARMs and limited regulation, healthcare providers should maintain a high index of suspicion for supplement-induced liver injury. Further research is needed to clarify the safety and mechanisms of these agents. Until then, their use should be discouraged.

Internal Medicine
Jamal L, Syeda R, **Jamal F**, **Kasmikha Z**, and **Crawford J**. The atrial mass without an auscultatory "plop": renal cell carcinoma presenting with cardiac syncope-a case report. *AME Case Rep* 2025;9:95. PMID: 40761210. Full Text

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BACKGROUND: Renal cell carcinoma (RCC) presenting with extension of tumor thrombus into the inferior vena cava (IVC) and right atrium is a rare, life-threatening condition that requires surgical treatment with the simultaneous involvement of multiple surgical subspecialties. CASE DESCRIPTION: We present a case of a 65-year-old male who presented to the hospital with syncope, and was subsequently diagnosed with a level four cavoatrial sinus tumor thrombus extending from a primary renal mass. The patient had no concerning physical exam and electrocardiogram (EKG) findings, however, transthoracic and transesophageal echocardiography revealed severely reduced systolic function with a hyperechoic, vascular, and cystic mass extending from the IVC into the right atrial cavity that originated from a renal mass that involved the right renal vein and IVC. CONCLUSIONS: The purpose of this case is to highlight the critical importance of early recognition and timely intervention in patients who present with nonspecific symptoms, such as syncope, which may signal underlying fatal conditions. This case illustrates RCC with tumor thrombus extending into the IVC and right atrium. This rare but serious manifestation highlights the need for a high index of suspicion and comprehensive evaluation when faced with vague clinical presentations. Early recognition not only facilitates appropriate management but can also alter the patient's prognosis and survival outcomes.

Internal Medicine
LeRoy DI, **Ognjanovski E**, **Desai A**, **Cook AV**, and **Barretto R**. A Case of Sickle Cell Beta Thalassemia and Recurrent Septicemia. *Cureus* 2025;17(7):e87521. PMID: 40777684. Full Text

Internal Medicine, Henry Ford Health System - Warren, Warren, USA.

Sickle cell anemia and beta-thalassemia are among the most common hemoglobin disorders. They are characterized by abnormal hemoglobin production, leading to ineffective erythropoiesis and severe anemia. Compound forms, such as sickle cell beta-thalassemia (HbS/β-thalassemia), may experience a wide range of complications, including impaired splenic function and increased susceptibility to infections. In this case report, we describe the case of a 57-year-old female patient with sickle cell/beta0-thalassemia (Sß0) with frequent and prolonged hospital admissions for sepsis complicated by recurrent liver abscess requiring multiple procedures for intrahepatic drainage. This patient was found to have an abscess with cholelithiasis, with a multiseptated hypodense collection within the liver. Recurrent liver abscesses are rare and underreported in this population. This case highlights the need for further research to clarify pathophysiology and ultimately improve management.

Internal Medicine
Multani NS, **Affas ZR**, and **Alexander PB**. LIMA-LAD Steal Syndrome as a Cause of Post-CABG Angina. *JACC Case Rep* 2025;30(25):104828. PMID: 40883084. Full Text

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BACKGROUND: Coronary steal from unligated side branches of the left internal mammary artery (LIMA) after coronary artery bypass grafting may lead to recurrent angina. CASE SUMMARY: A 64-year-old man presented with recurrent angina 2 years after coronary artery bypass grafting. Imaging showed perfusion defects in the territory of the left anterior descending artery (LAD). Coronary angiography revealed a large patent LIMA side branch. A percutaneous vascular plug successfully occluded the side branch, with symptom resolution. DISCUSSION: There is conflicting evidence regarding the diagnosis and treatment of coronary steal syndrome from LIMA graft. Despite the lack of formal guidelines, reversible anterior wall defects on stress testing may help identify patients with clinically significant symptoms. TAKE-HOME MESSAGES: The side branches of the LIMA when unligated represent a relatively common anatomical variation that could have clinical implications. Large, unligated side branches when accompanied by anterior wall ischemia may indicate a diagnosis of LIMA-LAD steal amenable to percutaneous intervention.

Internal Medicine
O'Neill B, **Halboni A**, Giustino G, **Engel P**, **Fram G**, **Frisoli T**, Fang JX, **O'Neill W**, **Villablanca P**, and Wang DD. Treatment Patterns of Patients With Mitral Valve Disease and Critical Neo-LVOT Obstruction. *Catheter Cardiovasc Interv* 2025; Epub ahead of print. PMID: 40793929. Full Text

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BACKGROUND AND AIMS: Among patients with severe mitral valve (MV) disease and predicted high-risk of left ventricular outflow track obstruction (LVOTO), the patterns of treatment and clinical outcomes have not previously described. The aim of this study was to explore outcomes of this patient population. METHODS: We conducted a single-center study including all consecutive patients with severe MV disease who were evaluated by a multidisciplinary structural heart disease team for MV therapies between 2018 and 2023. All patients underwent pre-procedural contrast cardiac computed tomography (CT). We defined high risk for LVOTO as a post-transcatheter mitral valve replacement (TMVR) predicted neo-LVOT < 150 mm(2). RESULTS: A total of 157 patients with a median Neo-LVOT of 0 (IQR 0-80.4) were included. Median age was 79 (72-83), and most were females (89.2%). A total of 59 patients (37.6%) had severe mitral stenosis, 48 (30.6%) had severe mitral regurgitation, and 98 (58%) had both. The median STS score was 22.6 (17-29.6). Most patients were in NYHA class III or IV (77.1%), and the

median KCCQ-12 was 48.9 (IQR: 29-68.7). Overall, the majority of patients were assigned to medical therapy (54.1%). There were a total of 41 deaths (26.1%) at a median follow-up time of 247 days (IQR: 70-568). When separated into non-severe MAC and severe MAC, patients with severe MAC had higher rates of all-cause mortality at 1 year (unadjusted HR: 2.44; 95% CI: 1.13-5.24; p = 0.02). Severe MAC patients were more likely to be assigned to medical therapy. Treatment allocation was not independently associated with a higher or lower risk of death. CONCLUSIONS: Patients with severe MV disease at high-risk for LVOTO (LVOT < 150 mm(2)) after TMVR were overwhelmingly female and were most frequently assigned to medical therapy. Patients with severe MAC had higher rates of death. Treatment allocation was not independently associated with mortality. Novel transcatheter therapies are needed to definitively treat this high-risk population.

Internal Medicine

Ogunniyi K, Aghasili CC, Akinmoju O, Olaiya VO, Abib O, Odueke AY, **Popoola HA**, Onyenokwe V, Onaolapo D, Usman AM, Friedman A, Awoyemi T, Nfonoyim J, and Rotatori F. Advances in Non-statin Lipid Therapies: A Narrative Review of Evolving Strategies for Cardiovascular Risk Reduction. *Am J Cardiovasc Drugs* 2025; Epub ahead of print. PMID: 40884609. Full Text

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Despite the well-established benefits of statin therapy in reducing atherosclerotic cardiovascular disease (ASCVD) risk, many patients fail to achieve recommended low-density lipoprotein cholesterol (LDL-C) targets or experience statin intolerance, necessitating alternative approaches. This review examines advances in non-statin lipid-lowering therapies, focusing on proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors (monoclonal antibodies and inclisiran), bempedoic acid, and other non-statin lipid medications. We evaluate their mechanisms of action, clinical efficacy, and safety profiles on the basis of landmark trials. A conceptual framework for personalized lipid management is proposed, addressing residual cardiovascular risk, statin intolerance, and complex patient profiles. Clinical decision pathways are presented for high-risk patients, statin-intolerant individuals, and those with adherence challenges. We explore emerging therapies targeting novel pathways, including lipoprotein(a), apolipoprotein C-III inhibitors, angiopoietin-like protein 3 (ANGPTL3) inhibitors, cholesteryl ester transfer protein (CETP) inhibitors, and gene-editing technologies. Implementation barriers, including cost considerations, insurance challenges, and global access disparities, are discussed alongside solutions.

Internal Medicine

Oska N, **Peterson D**, Brothers K, **Maramraju R**, **Ayyad A**, and **Hohmann B**. Isolated Facial Vein Thrombophlebitis Caused by Fusobacterium nucleatum: A Lemierre-Variant Case. *Case Rep Infect Dis* 2025;9938125. PMID: 40860904. Full Text

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Background: Lemierre's syndrome is an uncommon yet potentially fatal infection, classically secondary to bacterial pharyngeal infections. It is typically characterized by bacteremia, most frequently due to

Fusobacterium necrophorum and internal jugular vein thrombophlebitis. If untreated, septic embolization may result, potentially damaging the lungs, liver, brain, or other organs. This report describes a variant of Lemierre's syndrome in a young woman with streptococcal pharyngitis, who developed Fusobacterium nucleatum bacteremia and isolated facial vein thrombophlebitis, highlighting the importance of early diagnosis and treatment. Case Presentation: A 33-year-old woman with no significant past medical history presented with sore throat, chills, and right-sided facial and neck pain. Initially diagnosed with streptococcal pharyngitis at an urgent care clinic, she presented to the emergency department soon afterwards due to the development of severe rigors and fever. Blood cultures revealed growth of Fusobacterium nucleatum, raising suspicion for Lemierre's syndrome in the setting of worsening facial and neck pain despite negative initial imaging of the soft tissue of the neck. A subsequent CT venogram confirmed isolated thrombosis of the right facial vein. The patient was treated and discharged in stable condition on a 4 week course of metronidazole and 2 weeks of ceftriaxone. Conclusion: This case emphasizes the importance of maintaining suspicion for Lemierre's syndrome in patients with bacterial pharyngitis, especially when atypical symptoms such as facial pain occur. Although the internal jugular vein is most commonly affected, facial vein thrombosis may also occur. Early antibiotic treatment is critical for preventing severe complications including septic shock and embolization.

Internal Medicine

Patel T, Farhan M, Al Shabout GHF, Mohammed MA, Abuelata Z, Shalaby AS, Alkassar A, Khadra AB, Kuznetsova MM, Misra G, Goyal A, and **Rashi F**. Gastric electrical stimulation versus standard medical therapies for long-term symptom control and improved quality of life in drug-refractory gastroparesis patients. *Ann Med Surg (Lond)* 2025;87(6):3794-3799. PMID: 40486634. Full Text

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OBJECTIVES: This systematic review and meta-analysis evaluated the effectiveness of gastric electrical stimulation (GES) in alleviating symptoms of gastroparesis (GP) compared to alternative medical therapies. METHODS: We conducted a comprehensive search of PubMed, Cochrane Library, and Embase from January 2004 to October 2024 using MeSH terms and keywords related to GP and GES. The search included randomized controlled trials (RCTs) and observational studies published in English. Data extraction followed PRISMA and AMSTAR guidelines. The primary outcome was symptom control, measured using the weighted mean difference and a 95% confidence interval (CI). Statistical analysis was performed using RevMan software, and the certainty of evidence was assessed using the GRADE tool. RESULTS: A total of 1918 articles were screened, with 4 studies included in the final analysis. The mean difference in symptom control was -0.16 (95% CI: -0.57, 0.26). Heterogeneity was assessed using the chi-square Test, and inconsistency was quantified using the I(2) index. CONCLUSIONS: GES provides some symptomatic relief in GP, particularly for nausea and vomiting, though the improvements were not statistically significant. Future research should focus on non-crossover RCTs to minimize bias and further explore GES efficacy in idiopathic and postsurgical gastroparesis cases.

Internal Medicine

Rangavajla G, **Patel R**, **Nguyen F**, **Vickers B**, **Abdelhai O**, **La Starza B**, **Ilg K**, **Maskoun W**, **Ebinger M**, **Lahiri M**, **Khan A**, **Greenberg J**, **Fram G**, **Alrayes H**, **Lok Lai LK**, **Wyman J**, **Parikh S**, **Zweig B**, **Dawdy J**, **Bowerman N**, **Engel Gonzalez P**, **O'Neill W**, **Villablanca P**, **Lee J**, **O'Neill BP**, **Raad M**, and **Frisoli TM**. Atrioventricular Block After EVOQUE Transcatheter Tricuspid Valve Replacement. *Struct Heart* 2025;9(9):100701. PMID: 40822378. Full Text

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•Based on a real-world study of 106 Evoque transcatheter tricuspid valve replacement (TTVR) recipients, a total of 14 (25%) cases of new atrioventricular (AV) block occurred after Evoque implantation in the 55 patients without prior pacemakers who met study inclusion criteria. This incidence is similar to that reported in the TRISCEND II clinical trial.•New AV block occurred in a median of 26 hours after Evoque TTVR (interquartile range: 5-60 hours), but there were cases of new AV block that occurred as late as 7 days after the procedure.•Of the 14 new cases of AV block, 12 were treated successfully with implantation of a leadless pacemaker (Micra) under fluoroscopic guidance without procedural complications or compromising the valve implantation.•The institutional strategy of 48-hour post-Evoque inpatient monitoring for all patients followed by mobile cardiac outpatient telemetry identified 11 of 14 cases of new AV block as before discharge from the hospital and 1 case as an outpatient before symptom onset.

Internal Medicine
Salam R, **Alkhafaji A**, **Govil D**, **Ahmadi F**, **Affas S**, and Hassan M. Racial Disparities in Outcomes After Liver Transplantation. *Cureus* 2025;17(7):e88693. PMID: 40861692. Full Text

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Racial disparities in liver transplant outcomes remain an area of concern despite advancements in organ allocation and post-transplant care. This retrospective cohort study analyzed adult liver transplant recipients from the United Network for Organ Sharing (UNOS) registry between 1988 and 2021 to evaluate differences in graft and patient survival between African American (AA) and Caucasian American (CA) recipients. After excluding non-Black and non-White individuals and pediatric cases, a 3:1 matched cohort was created using propensity-type matching for age, sex, body mass index, and ABO type, resulting in 50,584 patients (13,421 AA and 40,263 CA). Median graft survival was significantly lower in AAs compared to CAs (1,466 vs. 1,787 days, $p < 0.0001$), as was median patient survival (1,480 vs. 1,815 days, $p < 0.0001$). Graft failure rates at one year were 2,325/12,708 (18.3%) for AA vs. 5,884/37,762 (15.6%) for CA ($Chi^2 = 50.87$, $df = 1$, $V = 0.026$, $p < 0.0001$); at five years, 4,326/10,323 (41.9%) vs. 10,172/30,179 (33.7%), respectively ($Chi^2 = 218.35$, $V = 0.060$, $p < 0.0001$). Similarly, mortality at five years was 3,516/9,152 (38.4%) for AA vs. 8,232/26,291 (31.3%) for CA ($Chi^2 = 154.41$, $V = 0.066$, $p < 0.0001$). AAs also had higher Model for End-Stage Liver Disease (MELD) scores at listing and transplant and were more likely to be hospitalized or in the ICU at the time of transplant. Insurance coverage differed significantly, with AAs more likely to have public insurance (6,031/12,739, 47.3% vs. 13,055/36,504, 35.8%, $p < 0.0001$). These findings suggest that AA liver transplant recipients experience significantly worse outcomes, likely due to a combination of advanced disease at presentation and socioeconomic disparities.

Internal Medicine
Waseem MH, Abideen ZU, Khan M, Sajid B, Ramzan NUH, Farid R, Iqbal J, Ahmed J, Kabir A, Shahzad M, Asif J, Osama M, Aimen S, **Chaudhary AJ**, and Cheema AH. Efficacy and Safety of Anticoagulants in Patients With Cirrhosis and Portal Vein Thrombosis: A Systematic Review and Meta-Analysis of Randomized and Non-Randomized Studies. *JGH Open* 2025;9(8):e70194. PMID: 40786130. Full Text

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BACKGROUND: Portal vein thrombosis (PVT) contributes substantially to morbidity and mortality in cirrhotic patients. A clear insight into the anticoagulation therapy benefits in these patients could improve clinical decision-making. This meta-analysis aimed to assess the efficacy and safety of Anticoagulants in cirrhotic patients with PVT. METHODS: PubMed, Cochrane Library, and ScienceDirect were searched from inception to September 2024. The Risk Ratios (RR) with 95% Confidence Interval (CI) were pooled for dichotomous outcomes under the random effects model using Review Manager 5.4.1. The primary endpoint of interest is PVT recanalization. Quality assessment was done through the Newcastle Ottawa Scale and the Cochrane RoB2.0 tool. Leave-one-out sensitivity analysis was done to investigate the cause of heterogeneity. Publication bias was assessed through funnel plots. RESULTS: Twenty-three studies (including 19 cohorts and 4 Randomized trials), pooling 81,599 patients, were included in the analysis. Anticoagulants significantly increased the PVT recanalization (RR = 2.00; 95% CI: [1.59, 2.52]; p < 0.00001; I (2) = 13%), PVT improvement (RR = 1.98; 95% CI: [1.70, 2.29], p < 0.00001; I (2) = 0%) while decreasing the PVT stability (RR = 0.78; 95% CI: [0.62,0.99], p = 0.04; I (2) = 19%) and PVT progression (RR = 0.42; 95% CI: [0.29, 0.60], p < 0.00001; I (2) = 27%). Other outcomes including mortality (RR = 0.53; 95% CI: [0.27, 1.03]; p = 0.06; I (2) = 94%), total bleeding (RR = 1.02; 95% CI: [0.76, 1.37], p = 0.89; I (2) = 31%), esophageal variceal bleeding (RR = 0.74; 95% CI: [0.54, 1.01], p = 0.06; I (2) = 56%), Gastrointestinal bleeding (RR = 1.07; 95% CI: [0.78, 1.48]; p = 0.66, I (2) = 13%) and Intracranial hemorrhage (RR = 1.19; 95% CI: [0.89, 1.58], p = 0.24, I (2) = 0%) were comparable between the 2 arms. CONCLUSION: Anticoagulants significantly increased PVT recanalization and PVT improvement while decreasing PVT stability and PVT progression in cirrhotic patients. Other outcomes were comparable between the two groups.

Nephrology

Alshwayyat S, Almasri N, Alshwaiyat Y, Alshwayyat TA, AlAwwa R, Alshwayyat M, Jamaan MH, Alhamadi MA, **Mahfouz R**, Alshwayat A, and Al-Kurdi MA. Personalized survival predictions in chromophobe renal cell carcinoma: development of a machine learning-based web tool. *Int Urol Nephrol* 2025; Epub ahead of print. PMID: 40824376. Full Text

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PURPOSE: Chromophobe renal cell carcinoma (ChRCC) is a rare subtype of renal cancer, characterized by distinct clinical and genetic features. Existing studies on ChRCC are limited, and there is a critical need to explore the prognostic factors and treatment outcomes in this patient population. We used machine learning (ML) to build prognostic models and developed the first predictive web-based tool for survival. METHODS: The SEER database (2000-2020) was used for this study's analysis. To identify the prognostic variables, we conducted Cox regression analysis and constructed prognostic models using five ML algorithms to predict the 5-year survival. A validation method incorporating the area under the curve (AUC) of the receiver operating characteristic (ROC) curve was used to validate the accuracy and reliability of ML models. We also performed Kaplan-Meier survival analysis. RESULTS: Our study analyzed 10,700 patients with ChRCC and identified metastasis and tumor size as significant predictors

of survival. Subtotal nephrectomy was associated with the highest survival rates. Chemotherapy and radiotherapy were infrequently used but were associated with worse survival outcomes, particularly in patients with metastasis. The developed ML models demonstrated high accuracy in predicting survival, and a web-based tool offered real-time survival predictions based on patient-specific data. CONCLUSION: Our study identified key prognostic factors and developed a machine learning-based web tool for personalized survival predictions. Metastasis and tumor size are critical in determining patient outcomes, with subtotal nephrectomy showing the highest survival rate.

Nephrology

Hidalgo LG, Madill-Thomsen KS, Reeve J, Mackova M, Gauthier P, Demko Z, Prewett A, Lee M, Alhamad T, Anand S, Arnol M, Baliga R, Banasik M, Blosser CD, Bobba S, Brennan D, Bromberg J, Budde K, Chamienia A, Chow K, Ciszek M, Costa N, Dęborska-Materkowska D, Debska-Ślizień A, Domański L, Fatica R, **Francis I**, Fryc J, Gill J, Gill J, Glyda M, Gourishankar S, Gryczman M, Gupta G, Hruba P, Hughes P, Jittirat A, Jurekovic Z, Kamal L, Kamel M, Kant S, Kojc N, Konopa J, Kumar D, Lan J, Lowe D, Mazurkiewicz J, Miglinas M, Moinuddin I, Mueller T, Myślak M, Naumnik B, Pączek L, **Patel A**, Perkowska-Ptasińska A, Piecha G, Poggio E, Bloudíčkova SR, Regele H, Schachtner T, Shojai S, Sikosana MLN, Slatinská J, Smykal-Jankowiak K, Haler Ž V, Viklicky O, Vucur K, Weir MR, Wiecek A, Zaky Z, and Halloran PF. Improving the histologic detection of DSA-negative antibody-mediated rejection in kidney transplants. *Am J Transplant* 2025; Epub ahead of print. PMID: 40854490. Full Text

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Emerging treatments for antibody-mediated rejection (ABMR, NEJM391(2):122-132) have increased the importance of ABMR detection when donor-specific antibody (DSA) is negative. We addressed this issue in the Trifecta-Kidney study (ClinicalTrials.gov #NCT04239703) using three centralized tests in 690 kidney transplant biopsies: DSA (One Lambda Inc.), blood donor-derived cell-free DNA (dd-cfDNA, Prospera™ test, Natera, Inc.), and molecular biopsy assessment (MMDx). We used an "AutoBanff 2022" algorithm to model the impact of alternative DSA interpretations on the histologic diagnosis of "DSA-negative" ABMR following Banff guidelines, including agreement with dd-cfDNA and molecular ABMR. Lowering MFI cutoffs for DSA-positivity did not improve detection of DSA-negative ABMR. However, simply calling all DSA positive allowed Banff 2022 guidelines to identify 46% more ABMR cases with no measurable DSA, and per Net Reclassification Improvement increased agreement between histologic diagnoses and both dd-cfDNA (P=7.72E-7) and molecular ABMR (P=7.69E-7). New ABMR cases were as strongly positive for dd-cfDNA and molecular ABMR as those found using the conventional DSA interpretation. A validation set analysis using INTERCOMEX study data (ClinicalTrials.gov NCT#01299168) confirmed these findings, and found that the new DSA-negative ABMR cases identified by calling all DSA positive had the same risk for graft loss as those found with conventional DSA interpretation. Trifecta-Kidney Study ClinicalTrials.gov #NCT04239703.

Neurology
Brown N, Patel S, Khan MF, Gensler RT, Khan HI, Munjal V, Gendreau JL, and **Reardon T**. Utilization of Adipose-Derived Stem Cells in Cranial Nerve Regeneration: A Comprehensive Review. *Cureus* 2025;17(7):e88706. PMID: 40761970. Full Text

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Large peripheral nerve injuries may require surgical reconnection. Cell-based therapies have also been investigated for nerve regeneration. Within the context of this modern treatment paradigm for peripheral nerve injuries, we investigated the role of adipose-derived stem cells (ADSCs) in the regeneration of cranial nerves. PubMed and Embase databases were used to search for primary studies reporting the use of ADSCs in the regeneration of cranial nerves. A total of 12 studies were included, all of which presented data on specific neural injury, therapy, and functional outcomes. Eight studies focused on the facial nerve (66.7%), two on the optic nerve (16.7%), one on the olfactory nerve (8.3%), and one on the hypoglossal nerve (8.3%). One study applied ADSCs to human cranial nerve injuries, while the remainder studied animal models. In these studies, ADSC groups had higher numbers of myelinated fibers, increased myelin thickness, and diameter of muscle fibers, as well as greater magnitude of compound muscle action potentials (CMAP) when compared to controls. In studies focused on optic nerve regeneration, significant improvements across visual tests were observed. ADSCs demonstrate potential utility in regard to their ability to facilitate functional recovery of cranial nerves in humans and animal models. As such, this therapy merits further investigation so that its true clinical applications can be determined.

Neurology
Chen J, Ngo A, Rodriguez-Cruces R, Royer J, Caligiuri ME, Gambardella A, Concha L, Keller SS, Cendes F, Yasuda CL, Alvim MKM, Bonilha L, Gleichgerrcht E, Focke NK, Kreilkamp BAK, Domin M, Von Podewils F, Langner S, Rummel C, Wiest R, Martin P, Kotikalapudi R, Bender B, O'Brien TJ, Sinclair B, Vivash L, Kwan P, Desmond P, Lui E, Duma GM, Bonanni P, Ballerini A, Vaudano AE, Meletti S, Tondelli M, Alhusaini S, Doherty CP, Cavalleri G, Delanty N, Kalviainen R, Jackson GD, Kowalczyk M, Mascalchi M, Semmelroch M, Thomas RH, **Soltanian-Zadeh H**, **Davoodi-Bojd E**, Zhang J, Lenge M, Guerrini R, Bartolini E, Hamandi K, Foley S, Rüber T, Bauer T, Weber B, Caldairou B, Depondt C, Absil J, Carr SJA, Abela E, Richardson MP, Devinsky O, Pardoe HR, Severino M, Striano P, Tortora D, Kaestner E, Hatton SN, Arienzo D, Vos SB, Ryten M, Taylor PN, Duncan JS, Whelan CD, Galovic M, Winston GP,

Thomopoulos SI, Thompson PM, Sisodiya SM, Labate A, McDonald C, Caciagli L, Bernasconi N, Bernasconi A, Lariviere S, Schrader DV, and Bernhardt BC. Changes in Gray Matter Morphology and White Matter Microstructure Across the Adult Lifespan in People With Temporal Lobe Epilepsy. *Neurology* 2025;105(6):e213688. PMID: 40845263. Full Text

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BACKGROUND AND OBJECTIVES: Temporal lobe epilepsy (TLE) is commonly associated with mesiotemporal pathology and widespread alterations of gray and white matter structures. Evidence supports a progressive condition, although the temporal evolution of TLE is poorly defined. In this ENIGMA-Epilepsy study, we aim to investigate structural alterations in gray and white matter across the adult lifespan in patients with TLE by charting both gray and white matter changes and explore the covariance of age-related alterations in both compartments. METHODS: Mega-analysis of parcellated T1-weighted and diffusion MRI data across 18 international sites for patients with TLE was compared against healthy controls. We combined median-age split groupwise comparisons with cross-sectional sliding age-window analyses to explore gray (cortical thickness, subcortical volume) and white matter microstructure (fractional anisotropy, mean diffusivity) age-related changes. Five-year range age windows were constructed from mean z scores of all patients. Covariance analyses examined the coupled correlations of gray and white matter lifespan curves for each region. RESULTS: We studied 769 patients with TLE and 885 healthy controls across an age range of 17-73 years. Robust (p(FDR) < 0.05) gray matter thickness/volume decline (d < -0.20) was seen across a broad cortico-subcortical territory, extending beyond the mesiotemporal lobe throughout the adult lifespan in patients with TLE. White matter changes were also widespread across multiple fiber tracts with peak effects in temporolimbic fibers in fractional anisotropy (d < -0.3, p(FDR) < 0.05) and mean diffusivity measures (d > 0.3, p(FDR) < 0.05). Changes spanned the adult time window and effects exceeded typical aging-related processes in patients at the level of cortical thickness, subcortical volume, and diffusion measures, particularly in patients older than 55 years. Covariance analyses revealed strong associations across multiple white matter tracts,

subcortical structures, and cortical regions within and beyond the temporolimbic system. DISCUSSION: This study highlights that patients with TLE exhibit more pronounced and widespread gray and white matter atrophy across the lifespan. The cross-sectional nature of our study limits definitive conclusions on whether the atrophy shown is progressive but emphasizes the importance of prompt diagnosis and intervention in patients. Collectively, our results motivate future longitudinal studies to clarify consequences of drug-resistant epilepsy.

Neurology
Ji K, and **Schwenkel GJ**. Fibroblasts Attenuate Anti-Tumor Drug Efficacy in Tumor Cells via Paracrine Interactions with Tumor Cells in 3D Plexiform Neurofibroma Cultures. *Cells* 2025;14(16). PMID: 40862755. Full Text

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Plexiform neurofibromas (hereafter called pNF1) are often diagnosed in early childhood and occur in about 30% of neurofibromatosis type 1 (NF1) patients. pNF1 exhibits aggressive growth along a nerve in the body and has substantial potential for progression to malignant peripheral nerve sheath tumors that are rarely curable. There are two recently FDA-approved drugs, selumetinib and mirdametinib, for pNF1 patients who have symptomatic and inoperable plexiform neurofibromas; however, these treatments achieve only approximately 30% tumor shrinkage. Fibroblasts, the most abundant cell types within the pNF1 tumor microenvironment, are implicated in pNF1 growth and invasion; however, how fibroblasts affect a drug response of pNF1 remains poorly understood. In the present study, we focused on contributions of fibroblasts to the drug resistance in pNF1 via their secretome. We employed our established three-dimensional (3D) culture system incorporating human pNF1 tumor cells (Nf1(-/-)) and primary fibroblasts (Nf1(+/-)) grown in our patented microfluidic culture chips for monocultures and parallel cocultures in which 3D pNF1 structures and fibroblasts share their secretome without direct cell-to-cell contact. Three-dimensional pNF1 structures in 3D parallel cocultures with fibroblasts exhibited greater drug resistance than ones in monocultures. We found that pNF1 tumor cells showed increased P-glycoprotein expression when incubated with fibroblast-derived conditioned media or parallel cocultured with fibroblasts, compared to control conditions. Pharmacological inhibition of P-glycoprotein partially restored drug sensitivity. Additionally, fibroblasts showed higher resistance to selumetinib and mirdametinib than pNF1 tumor structures, likely due to elevated P-glycoprotein levels. This study is the first to define precise roles of fibroblasts in pNF1 drug resistance, emphasizing the potential of fibroblast-targeted therapies as a promising approach to improve pNF1 treatment outcomes.

Neurology
Nematullah M, **Fatma M**, Zhou G, Prajapati B, **Rashid F**, **Ayasolla K**, **Ahmed ME**, **She R**, **Mir S**, **Zahoor I**, **Hoda N**, **Rattan R**, and **Giri S**. Immune-responsive gene 1: The mitochondrial key to Th17 cell pathogenicity in CNS autoimmunity. *Proc Natl Acad Sci U S A* 2025;122(32):e2427052122. PMID: 40758870. Full Text

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Pathogenic Th17 cells play crucial roles in CNS autoimmune diseases such as multiple sclerosis (MS), but their regulation by endogenous mechanisms remains unknown. Through RNA-seq analysis of primary brain glial cells, we identified immune-responsive gene 1 (Irg1) as one of the highly upregulated genes under inflammatory conditions. Validation in the spinal cords of animals with experimental autoimmune encephalomyelitis (EAE), a preclinical MS model, confirmed elevated Irg1 levels in myeloid, CD4, and B cells in the EAE group, raising concerns as to whether Irg1 is detrimental or protective. Irg1 knockout

(KO) mice exhibited severe EAE disease, increased mononuclear cell infiltration, and increased levels of triple-positive CD4+ T cells expressing IL17a, GM-CSF, and IFNγ. Adoptive transfer in Rag-1 KO and single-cell RNA sequencing highlighted the crucial role of Irg1 in shaping pathogenic Th17 cells. A lack of Irg1 in macrophages elevates Class II expression, promoting the polarization of myelin-primed CD4+ T cells into pathogenic Th17 cells via the NLRP3/IL-1β axis. Moreover, bone marrow chimeras revealed that immune cells lacking Irg1 maintained pathogenic and inflammatory phenotypes, suggesting its protective role in autoimmune diseases, including MS.

Neurology

Patel T, **Hanani C**, Noor A, Cheema S, Farhan M, Sohail R, Goyal A, David John J, Omole AE, and Millis RM. Adaptive deep brain stimulation targeting the subthalamic nucleus in a patient with Parkinson's disease: A CARE compliant case report. *Medicine (Baltimore)* 2025;104(34):e44130. PMID: 40859483. Full Text

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RATIONALE: Adaptive deep brain stimulation (aDBS) represents a notable advancement in treating Parkinson's disease (PD), as it offers enhanced therapeutic outcomes and personalized management by adjusting stimulation parameters in real-time according to individual neural signals. This approach minimizes adverse effects commonly associated with standard continuous deep brain stimulation (cDBS). This case report describes the progress of a 62-year-old man with severe PD who demonstrated notable enhancement in motor symptoms and quality of life throughout a 3-month trial period using aDBS. PATIENT CONCERNS: A 62-year-old man who has been suffering from Parkinson's disease. DIAGNOSES: The patient had been diagnosed with PD for 10 years. The patient's motor symptoms, including dyskinesia during the on-state and akinesia during the off-state, progressively worsened over time. INTERVENTIONS: The patient underwent bilateral subthalamic nuclei DBS surgery with cDBS. Following progressive worsening of motor symptoms, he was transitioned to aDBS. OUTCOMES: The aDBS system adaptively modified stimulation parameters by utilizing real-time neural feedback from beta band activity detected in the subthalamic nucleus, resulting in decreased dyskinesia and reduced reliance on medication. The customized strategy led to a significant improvement in motor symptoms, a reduction in dyskinesia, and an overall enhancement in quality of life during the 3-month trial period. LESSONS: Existing evidence highlights the ability of aDBS to improve motor control and reduce problems associated with DBS, such as speech and gait abnormalities. Research findings have demonstrated significant improvements in motor scores and a reduction in stimulation time, highlighting the effectiveness of aDBS and its ability to prolong the lifespan of devices.

Neurology

Patel T, Henna F, Yousuf Ibrahim H, Maloth AK, Rehman AU, Zehra Kazmi SR, Hussain A, and **Hanani C**. Evolving treatment strategies in meningioma: from traditional approaches to emerging therapies. *Ann Med Surg (Lond)* 2025;87(8):5087-5097. PMID: 40787520. Full Text

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BACKGROUND: Meningiomas are the second most prevalent adult central nervous system neoplasm, developing from arachnoid cap cells. While most are benign (WHO Grade I), atypical (Grade II), and anaplastic (Grade III), meningiomas portray aggressive behavior, higher relapse rates, and resistance to standard treatments. OBJECTIVE: To study the progression of treatment strategies for meningiomas, underscoring emerging treatments and challenges, especially in recurrent and high-grade subtypes. METHODS: A narrative review was conducted, identifying studies from the PubMed, Scopus, and Google Scholar databases (2000-2025). Keywords included "meningioma," "surgery," "radiotherapy," "targeted therapy," "immunotherapy," and "PRRT." Included studies addressed conventional or novel treatments for meningiomas. RESULTS: Surgical resection continues as the gold standard, with the extent of removal impacting recurrence. Radiotherapy, comprising fractionated and stereotactic techniques, plays a vital role when surgery is incomplete or not possible. Chemotherapy demonstrates limited benefit. Advances in molecular profiling have shown genetic drivers (e.g., NF2, TRAF7, AKT1) and hormonal receptors as clinical targets. Emerging options include mTOR inhibitors (everolimus), anti-angiogenic agents (bevacizumab), PD-1/PD-L1 inhibitors (pembrolizumab), and peptide receptor radionuclide therapy (PRRT). Drug delivery treatments like convection-improved delivery show promise in improving CNS penetration. Nonetheless, resistance mechanisms, the absence of validated biomarkers, and insufficient trial data pose significant challenges. CONCLUSION: Management of severe aggressive meningiomas is evolving with novel molecular and immunotherapeutic strategies. A multidisciplinary treatment strategy combining surgery, radiation, and targeted therapies, facilitated by further clinical trials and biomarker research, is necessary to enhance patient outcomes.

Neurology

Ranxhi B, Bangash ZR, Chbihi ZM, Qadri Z, Islam NN, Todi SV, **LeWitt PA**, and Tsou WL. Regulation of polyamine interconversion enzymes affects α-Synuclein levels and toxicity in a Drosophila model of Parkinson's Disease. *NPJ Parkinsons Dis* 2025;11(1):231. PMID: 40770267. Full Text

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Parkinson's Disease (PD) is a neurodegenerative disorder characterized by α-synuclein accumulation and aggregation, leading to disrupted cellular homeostasis, impaired mitochondrial function, and neuroinflammation, ultimately causing neuronal death. Recent biomarker studies reveal elevated serum levels of L-ornithine-derived polyamines correlating with PD progression and clinical subtypes, though their precise role in PD pathology remains unclear. We investigated the impact of polyamine-interconversion enzymes (PAIEs) on α-synucleinopathy in a Drosophila melanogaster model of PD, evaluating key degenerative features such as lifespan, locomotor function, tissue integrity, and α-synuclein accumulation. Knockdown of ornithine decarboxylase 1 (ODC1), spermidine synthase (SRM), and spermine oxidase (SMOX) reduced α-synuclein toxicity, while suppression of spermidine/spermine N1-acetyltransferase 1 (SAT1) and spermine synthase (SMS) exacerbated it. Conversely, overexpressing SAT1 or SMOX significantly reduced α-synuclein toxicity, highlighting their potential role in PD. These findings underscore the critical role of polyamine pathways in modulating α-synuclein toxicity, offering novel therapeutic targets for PD.

Neurology

Sternberg MB, **Air E**, **Schwalb J**, **Barkley GL**, **Constantinou JEC**, **Smith BJ**, and **Wasade VS**. Seizure and psychosocial outcomes in patients with DBS for intractable epilepsy. *Clin Neurol Neurosurg* 2025;257:109096. PMID: 40782607. Full Text

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OBJECTIVES: This study evaluates seizure outcomes in patients with intractable epilepsy treated with Deep Brain Stimulation (DBS) and explores correlations with demographic and psychosocial factors. METHODS: We analyzed data from patients who underwent Medtronic-DBS implantation between 2018 and 2023 at our institution. Collected variables included sex, age, epilepsy type, prior epilepsy surgeries, age at diagnosis and DBS implantation, DBS lead location, seizure outcomes, anti-seizure medication (ASM) use, employment, Patient Reported Outcomes Measurement Information System (PROMIS) Depression T-scores pre- and post-DBS, antidepressant use, and driving status. Patients were classified as Total Responders (TR) if they achieved ≥ 50 % seizure reduction. Associations between responder status and assessed factors were analyzed using chi-square and Mann-Whitney U tests. RESULTS: Seventeen patients (five males, twelve females; mean age 37.1 years, SD=10.7) were included, with an average epilepsy duration of 24.3 years (SD=13.1) before DBS. Leads were placed in the anterior thalamus (88 %) and centro-median nuclei (12 %). Fourteen patients (82 %) had multifocal epilepsy, while three (18 %) had symptomatic generalized epilepsy. TR status was achieved in 59 % of patients at a mean follow up of 32 months. Responder status correlated with higher ASM burden but not with other psychosocial factors. CONCLUSION: DBS therapy resulted in > 50 % seizure reduction in 59 % of patients with intractable epilepsy, with responders exhibiting a higher median ASM burden. While psychosocial factors were not significantly linked to seizure outcomes, TR patients demonstrated a relative worsening of Depression T-scores compared to non-responders, warranting further investigation.

Neurology

Tripathi A, Dasgupta D, Dahabieh MS, Griffard-Smith R, Pant A, Bugbee A, Yellapu NK, Burt E, Choi BHY, Ellis AE, Sheldon RD, **Giri S**, Koestler D, Jones RG, Yadav VN, and Pyaram K. Nrf2 drives activation-driven expansion of CD4(+)T cells by modulating glucose and glutamine metabolism. *Cell Rep* 2025;44(9):116177. PMID: 40857154. Full Text

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Upon antigenic stimulation, CD4(+)T cells undergo clonal expansion elevating their bioenergetic demands and utilization of nutrients like glucose and glutamine. The nuclear factor erythroid-2-related factor 2 (Nrf2) is a well-known regulator of oxidative stress, but its involvement in modulating the metabolism of CD4(+)T cells remains unexplored. We report that Nrf2 protein levels are temporally regulated in activated CD4(+)T cells, with elevated expression during early activation followed by a decline. T cell-specific constitutive activation of Nrf2, by deletion of its negative regulator Keap1, enhances early activation and interleukin-2 (IL-2) expression, upregulates T cell receptor (TCR) signaling, and increases activation-driven expansion of CD4(+)T cells. Mechanistically, elevated Nrf2 activity in activated CD4(+)T cells increases chromatin accessibility and proliferation-associated gene expression. Metabolically, high Nrf2 alters glucose metabolism and promotes glutamine metabolism via glutaminolysis to support CD4(+)T cell hyperproliferation. In summary, we elucidate the role of Nrf2 beyond traditional antioxidation in modulating the activation-driven expansion of CD4(+)T cells by influencing their nutrient metabolism and gene expression.

Neurosurgery

Bettegowda C, **Noushmehr H**, Affinito A, Ahluwalia MS, Ansorge O, Ayasoufi K, Bagley S, Barnholtz-Sloan J, Best M, Brandsma D, Brodie C, Brüning-Richardson A, **Castro AV**, Chang SM, Condorelli G, Daher A, Datta V, de Groot J, French P, Galanis E, Golebiewska A, Hamerlik P, Hanemann CO, Holdhoff M, Huse J, Khasraw M, LeBlang S, Melin B, Mouliere F, O'Leary C, Rak J, Ray A, Robinson S, Rominiyi O, Roncaroli F, Rudà R, Seoane J, Sol N, van den Bent MJ, Vogelbaum MA, Walbert T, Watts C, Weiss T, Weller M, Wen PY, Wykes V, Yip S, Short SC, and Soffietti R. Preanalytical variables and analytes in liquid biopsy approach for brain tumors: A comprehensive review and recommendations from the RANO Group and the Brain Liquid Biopsy Consortium. *Neuro Oncol* 2025; Epub ahead of print. PMID: 40884415. Full Text

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This review explores the pivotal role of preanalytical variables in bringing liquid biopsy approaches into the clinic for brain tumors. Preanalytical variables encompass a range of critical issues, from blood sample collection and handling to the impact of tumor heterogeneity and patient-specific factors. These variables introduce challenges such as false positives, false negatives, and variability in the analysis of tumor signals, which can hinder the diagnostic and prognostic utility of liquid biopsies. Understanding the nuances of preanalytical variables is essential for the successful implementation of liquid biopsy in clinical settings. This paper delves into strategies aimed at mitigating the influence of preanalytical variables by emphasizing the importance of standardized sample collection protocols, optimized sample processing and storage, quality control measures, and the integration of multiple liquid biopsy modalities.

Neurosurgery

Bhatti G, Sufriyana H, Romero R, Patel T, Tekola-Ayele F, Alsaggaf I, Gomez-Lopez N, Su ECY, **Done B**, Hoffmann S, van Bömmel A, Wan C, Albrecht J, Novak C, Chaiworapongsa T, Sirota M, Aghaeepour N, Stolovitzky G, Bryant DR, and Tarca AL. Placental epigenetic clocks derived from crowdsourcing: Implications for the study of accelerated aging in obstetrics. *iScience* 2025;28(8):113181. PMID: 40822353. Full Text

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Epigenetic gestational age acceleration has been implicated in obstetric syndromes including preeclampsia, yet robust conclusions require accurate and unbiased epigenetic age models. Herein, we curated 1,842 public placental methylomes and organized a DREAM challenge to develop models of gestational age. Participants were blinded to the test data that we generated from 384 placentas encompassing normal and complicated pregnancies. Models developed during and post-challenge compared favorably to existing models in terms of accuracy, yet they were better calibrated throughout gestation and indicated that reports of accelerated epigenetic aging in preterm preeclampsia were likely due to modeling artifacts. The models show that accelerated aging is associated with a decrease in birthweight percentiles in male neonates delivered at term. By contrast, preterm accelerated aging was protective against delivery of a small-for-gestational-age neonate regardless of fetal sex. This work informs our understanding of the fetal sex-dimorphic role of the placenta epigenome in obstetrics.

Neurosurgery

Crowell C, Zhu Z, Li Y, Varela ML, Ostrom Q, Cimino PJ, Patel SH, Baker SJ, Bettegowda C, **Noushmehr H**, Kleinman CL, Canty L, Cruzeiro GAV, Nellan A, Becher O, Davidson TB, Hambardzumyan D, Green A, Thorne R, Wilson K, Theeler B, Gregory J, Mathen P, Biassou N, McThenia S, Erker C, Galvin R, Soldatos A, Lowenstein PR, Castro MG, and Jackson S. A review of diffuse hemispheric glioma, H3 G34-mutant disease development, DNA repair, microenvironment, and treatments on the horizon. *NPJ Precis Oncol* 2025;9(1):283. PMID: 40813437. Full Text

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Diffuse hemispheric glioma H3 G34-mutant is primarily diagnosed in adolescents/young adults. While molecular diagnostics have improved, cellular mechanisms that drive tumor progression and therapy resistance are poorly understood. Combining previous published studies with findings from the 2024 NIH G34-mutant symposium aid in summarizing translational and clinical updates on disease development, cellular repair processes, and the immune microenvironment. This collective work is meant to outline opportunities for treatment and prolonged survival.

Neurosurgery
Shaftel KA, and **Chang V**. Commentary: How Do Robotics and Navigation Facilitate Minimally Invasive Spine Surgery? A Case Series and Narrative Review. *Neurosurgery* 2025; Epub ahead of print. PMID: 40767492. Full Text

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Neurosurgery
Sternberg MB, **Air E**, **Schwalb J**, **Barkley GL**, **Constantinou JEC**, **Smith BJ**, and **Wasade VS**. Seizure and psychosocial outcomes in patients with DBS for intractable epilepsy. *Clin Neurol Neurosurg* 2025;257:109096. PMID: 40782607. Full Text

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OBJECTIVES: This study evaluates seizure outcomes in patients with intractable epilepsy treated with Deep Brain Stimulation (DBS) and explores correlations with demographic and psychosocial factors. METHODS: We analyzed data from patients who underwent Medtronic-DBS implantation between 2018 and 2023 at our institution. Collected variables included sex, age, epilepsy type, prior epilepsy surgeries, age at diagnosis and DBS implantation, DBS lead location, seizure outcomes, anti-seizure medication (ASM) use, employment, Patient Reported Outcomes Measurement Information System (PROMIS) Depression T-scores pre- and post-DBS, antidepressant use, and driving status. Patients were classified as Total Responders (TR) if they achieved ≥ 50 % seizure reduction. Associations between responder status and assessed factors were analyzed using chi-square and Mann-Whitney U tests. RESULTS: Seventeen patients (five males, twelve females; mean age 37.1 years, SD=10.7) were included, with an average epilepsy duration of 24.3 years (SD=13.1) before DBS. Leads were placed in the anterior thalamus (88 %) and centro-median nuclei (12 %). Fourteen patients (82 %) had multifocal epilepsy, while three (18 %) had symptomatic generalized epilepsy. TR status was achieved in 59 % of patients at a mean follow up of 32 months. Responder status correlated with higher ASM burden but not with other psychosocial factors. CONCLUSION: DBS therapy resulted in > 50 % seizure reduction in 59 % of patients with intractable epilepsy, with responders exhibiting a higher median ASM burden. While psychosocial factors were not significantly linked to seizure outcomes, TR patients demonstrated a relative worsening of Depression T-scores compared to non-responders, warranting further investigation.

Neurosurgery

Xing L, Cai Y, Zhang Y, Mozel K, Tang Z, Tang T, Mottini V, Nigam S, Smith BR, **Lee IY**, **Nagaraja TN**, Wang P, Li X, Gao T, and Li J. TriMag Microrobots: 3D-Printed Microrobots for Magnetic Actuation, Imaging, and Hyperthermia. *Adv Mater* 2025;e19708. Epub ahead of print. PMID: 40787971. Full Text

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Microrobots hold immense potential in biomedical applications, including drug delivery, disease diagnostics, and minimally invasive surgeries. However, two key challenges hinder their clinical translation: achieving scalable and precision fabrication, and enabling non-invasive imaging and tracking within deep biological tissues. Magnetic particle imaging (MPI), a cutting-edge imaging modality, addresses these challenges by detecting the magnetization of nanoparticles and visualizing superparamagnetic nanoparticles (SPIONs) with sub-millimeter resolution, free from interference by biological tissues. This capability makes MPI an ideal tool for tracking magnetic microrobots in deep tissue environments. In this study, "TriMag" microrobots are introduced: 3D-printed microrobots with three integrated magnetic functionalities-magnetic actuation, magnetic particle imaging, and magnetic hyperthermia. The TriMag microrobots are fabricated using an innovative method that combines two-photon lithography for 3D printing biocompatible hydrogel structures with in situ chemical reactions to embed the hydrogel scaffold with Fe(3)O(4) nanoparticles for good MPI contrast and CoFe(2)O(4) nanoparticles for efficient magnetothermal heating. This approach enables scalable, precise fabrication of helical magnetic hydrogel microrobots. The resulting TriMag microrobots, with the synergistic effects of Fe(3)O(4) and CoFe(2)O(4) nanoparticles, demonstrate efficient magnetic actuation for controlled movement, precise imaging via MPI for imaging and tracking in biological fluid and organs, including porcine eye and mouse stomach, and magnetothermal heating for tumor ablation in a mouse model. By

combining these capabilities, the fabrication and imaging approach provides a robust platform for non-invasive monitoring and manipulation of microrobots for transformative applications in medical treatment and biological research.

Nursing

Hill L, Goodman R, **Gray L**, Moegling M, Crady R, Saucedo J, and Hewes HA. Nurse Pediatric Competency, Certification, and Continuing Education: Impact on EDs' Pediatric Readiness. *J Emerg Nurs* 2025;51(5):904-912. PMID: 40285774. Full Text

INTRODUCTION: Children present to emergency departments regardless of their readiness to care for pediatric patients. The National Pediatric Readiness Project is an initiative to improve pediatric emergency care. Increased National Pediatric Readiness Project scores have been associated with decreased mortality. The purpose of this study is to examine the association between nurse pediatric competency, certification, and/or continuing education and weighted pediatric readiness scores. METHODS: A sub-analysis of the 2021 National Pediatric Readiness Project Assessment examining nurse pediatric competencies and overall pediatric readiness scores of emergency department of United States includes descriptive statistics, testing for the association between hospital characteristics and pediatric patient volume using Fisher's tests and Kruskal-Wallis tests, and Wilcoxon rank-sum tests of score and nurse pediatric competencies. RESULTS: The majority (89%) of emergency departments require some nurse competency evaluations. Only 20.1% of emergency departments require nurse specialty certification. Most emergency departments have a hospital-specific nurse competency evaluation policy (91.7%) and nurse continuing education policies (98.3%). Having policies for competencies is significantly associated with increased median weighted pediatric readiness scores above the national median: nursing continuing education policy weighted pediatric readiness scores 71.3 ($P = .030$), nurse specialty certification policy weighted pediatric readiness scores 83.5 ($P<.001$), and nurse hospital-specific competency evaluation policy weighted pediatric readiness scores 72.3 ($P<.001$). DISCUSSION: Most emergency departments have a requirement for nurse pediatric-specific competency evaluations, and having nursing competency requirements is associated with higher weighted pediatric readiness scores. This highlights the importance of emergency nurse pediatric competency, certification, and continuing education on pediatric readiness scores, and therefore, the potential reduction in pediatric mortality.

Nursing

Shamoun CJ, Baby P, Bautista C, Carlisle B, Guanci MM, Gunna S, **Distefano S**, Joseph S, Kruger L, Li Y, Martinez RCK, Da Silvan AR, Okubo N, Siaron KB, Sila F, Wilson S, Yousef KM, and Olson DM. Neuromonitoring in Neuroscience Nursing: Collaboration From the 2025 International Neuroscience Nursing Symposium. *J Neurosci Nurs* 2025;57(4):152-157. PMID: 40498645. Full Text

INTRODUCTION: Neuromonitoring enhances patient assessment in neuroscience nursing, yet its integration varies globally. At the 2025 International Neuroscience Nursing Research Symposium, nurses from 16 countries discussed the adoption of neuromonitoring devices. This proceedings article explores international perspectives on neuromonitoring use, barriers, and facilitators. METHODS: Participants summarized their country's neuromonitoring technology level, key facilitators and barriers to adoption, and devices with the greatest potential impact. RESULTS: Significant disparities exist in neuromonitoring accessibility. Developed countries frequently use continuous electroencephalography, intracranial pressure monitoring, and pupillometry, whereas lower-resource settings face financial and training limitations. Key facilitators include policy support, funding, and interdisciplinary training, whereas barriers include cost, limited resources, and competency gaps. CONCLUSION: Nurses worldwide recognize how neuromonitoring may improve outcomes. International collaboration, standardization of training, and technological advancements could help bridge disparities in access and implementation. Addressing systemic barriers and investing in education and policy support will enhance equitable neuromonitoring integration, ultimately improving neurological patient care across diverse healthcare settings.

Obstetrics, Gynecology and Women's Health Services

Ayyash MK, Al-Kouatly HB, **Shaman M**, and McLaren RA, Jr. Preterm birth trends in the United States post aspirin recommendation guidelines. *J Natl Med Assoc* 2025; Epub ahead of print. PMID: 40849217. Full Text

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OBJECTIVES: To evaluate changes in preterm birth (PTB) rates in the U.S. following the United States Preventive Services Task Force (USPSTF) aspirin recommendation guidelines. METHODS: A retrospective cohort study was conducted using the US Natality database. The pre-aspirin (pre-ASA) group included births from 2010-2014, while the post-aspirin (post-ASA) group included births from 2016-2021. Births from 2015, the guideline publication year, were excluded. Outcomes were overall PTB rates (<37 weeks) and early PTB rates (<34 weeks). Univariable and multivariable analyses were performed. Projected trends based on 2010-2014 data were compared to observed trends post-guideline implementation to assess differences. RESULTS: The pre-ASA group included 12.1 million births, and the post-ASA group included 17.6 million. Adjusted analyses showed lower PTB rates in the post-ASA group: <37 weeks (8.4 % vs 8.8 %; aOR 0.940 [0.937-0.944]) and <34 weeks (2.3 % vs 2.4 %; aOR 0.92 [0.910-0.923]). However, observed post-ASA trends closely followed projected trends until 2021, when PTB rates exceeded projections. CONCLUSION: Although adjusted analyses suggest modest reductions in PTB following USPSTF aspirin guidelines, observed trends did not show a clear reduction following aspirin implementation.

Obstetrics, Gynecology and Women's Health Services

Bossick AS, **Su WK**, **Abood J**, **Arruga Novoa YNV**, **Chamseddine P**, **Vilkins A**, and **Wegienka GR**. Trajectories and risk factors of depressive symptomatology following hysterectomy. *Menopause* 2025; Epub ahead of print. PMID: 40794489. Full Text

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OBJECTIVES: Hysterectomy is the second most common gynecological surgery performed on reproductive aged women in the United States. It is not known if some groups of women are more susceptible to depression after hysterectomy. METHODS: Participants were scheduled for hysterectomy for benign causes and not undergoing a concomitant urogynecological procedure. Patient Health Questionnaire-9 (PHQ-9) was collected 2 weeks before, and 1, 4, and 6 weeks, and 3, 6, and 12 months post-hysterectomy to understand depressive symptoms associated with surgery. PHQ-9 patterns were identified with latent class analyses. Multivariable multinomial logistic regression was used to estimate relative risk ratios (RRR) and 95% CIs of associations between baseline sociodemographic, clinical, and operative-related characteristics and PHQ-9 class. RESULTS: Three latent classes (C) were identified from their PHQ-9 score patterns among 455 participants: high and increasing (C1, 15.6%), high and decreasing (C2, 27.7%), and persistently low PHQ-9 trajectory (C3, 56.7%). Insurance type, financial toxicity, pain level, and surgical decision satisfaction before surgery were statistically significantly associated with class membership. At surgery, C1 members were more likely to have public insurance (RRR=2.04, CI: 1.02-4.08), worse finances (0.92, 0.89-0.96), and higher pain (1.22, 1.10-1.35) than members of C3. C2 members were more likely to have worse finances (0.94, 0.91-0.96) than C3 members. C1 members tended to have higher pain (1.14, 1.02-1.26) than C2 members. CONCLUSIONS: Depression symptomology after hysterectomy may be associated with presurgical insurance type, financial toxicity, current pain level, and satisfaction. More research is needed to investigate whether

these factors can be incorporated into preoperative counseling and screening tools to guide shared decision-making regarding depression and surgery.

Obstetrics, Gynecology and Women's Health Services
Nematullah M, **Fatma M**, Zhou G, Prajapati B, **Rashid F**, **Ayasolla K**, **Ahmed ME**, **She R**, **Mir S**, **Zahoor I**, **Hoda N**, **Rattan R**, and **Giri S**. Immune-responsive gene 1: The mitochondrial key to Th17 cell pathogenicity in CNS autoimmunity. *Proc Natl Acad Sci U S A* 2025;122(32):e2427052122. PMID: 40758870. Full Text

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Pathogenic Th17 cells play crucial roles in CNS autoimmune diseases such as multiple sclerosis (MS), but their regulation by endogenous mechanisms remains unknown. Through RNA-seq analysis of primary brain glial cells, we identified immune-responsive gene 1 (Irg1) as one of the highly upregulated genes under inflammatory conditions. Validation in the spinal cords of animals with experimental autoimmune encephalomyelitis (EAE), a preclinical MS model, confirmed elevated Irg1 levels in myeloid, CD4, and B cells in the EAE group, raising concerns as to whether Irg1 is detrimental or protective. Irg1 knockout (KO) mice exhibited severe EAE disease, increased mononuclear cell infiltration, and increased levels of triple-positive CD4+ T cells expressing IL17a, GM-CSF, and IFNγ. Adoptive transfer in Rag-1 KO and single-cell RNA sequencing highlighted the crucial role of Irg1 in shaping pathogenic Th17 cells. A lack of Irg1 in macrophages elevates Class II expression, promoting the polarization of myelin-primed CD4+ T cells into pathogenic Th17 cells via the NLRP3/IL-1β axis. Moreover, bone marrow chimeras revealed that immune cells lacking Irg1 maintained pathogenic and inflammatory phenotypes, suggesting its protective role in autoimmune diseases, including MS.

Obstetrics, Gynecology and Women's Health Services
Ponton-Almodovar A, **Udumula MP**, Khullar V, **Rashid F**, **Rattan R**, **Bernard JJ**, and **Horibata S**. GPT2 mediates glutamine metabolism-driven metabolic alterations in platinum-resistant ovarian cancer cells. *Sci Rep* 2025;15(1):30528. PMID: 40835655. Full Text

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Metabolic reprogramming is recognized as a hallmark of cancer frequently associated with drug resistance in ovarian cancer. This is problematic as ovarian cancer is one of the deadliest gynecologic cancers with platinum resistance contributing to poor survival. However, the mechanism by which ovarian cancer cell metabolism contributes to platinum resistance is not well understood. Herein, metabolic signatures were determined in platinum-resistant ovarian cancer cell lines compared to the more platinum-sensitive parental lines. Chemoresistant ovarian cancer cells showed increased oxidative phosphorylation (OXPHOS) compared to chemosensitive cells. This was associated with elevated levels of glutaminolysis and tricarboxylic acid (TCA)-related metabolites supporting their dependence on OXPHOS. Key enzymes involved in glutaminolysis, specifically, glutamic-pyruvic transaminase 2 (GPT2), were upregulated in chemoresistant compared to chemosensitive cells. Interestingly, high GPT2 gene expression is associated with worse prognosis in ovarian cancer patients, adding translational relevance to the pre-clinical findings. GPT2 knockout in chemoresistant cells restored the metabolic phenotype to that of the sensitive cells and reversed drug resistance. These data suggest that GPT2 is a critical link between glutaminolysis, the TCA cycle, and OXPHOS and is a potential target to attenuate the increased metabolic activity associated with a chemoresistant phenotype.

Ophthalmology and Eye Care Services

Khanam L, Mukherjee U, **Srivastava SB**, and Singh SP. Zinc oxide and PEIE as electron transport layers: an in-depth investigation of optoelectronic behaviour in inverted organic solar cells. *Physica Scripta* 2025;100(8):16. PMID: Not assigned. Full Text

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Understanding the device physics of organic solar cells (OSCs) involves the investigation of various optoelectronic mechanisms, like photogeneration, rsssecombination, transport of charge carriers, and interfacial stability. The PCE and stability of OSC devices (processed in ambient conditions) are significantly influenced by the transport layer materials and their optical, electrical, and structural properties. Analyzing the electrical and optical behavior of charge transport layers is crucial for optimizing device performance. For the inverted-OSC devices, Zinc oxide (ZnO), a widely used ETL, typically requires high-temperature annealing (>= 150 degrees C) to achieve sufficient crystallinity and electrical performance. However, this processing temperature poses challenges for flexible substrates and can impact device scalability. Moreover, ZnO exhibits limitations, including a relatively high work function for electron extraction, increasing interfacial resistances, and inferior charge extraction capability. In this study, we report an in-depth comparative investigation of the optoelectronic behavior of inorganic (ZnO) and organic (PEIE) ETLs in inverted-OSC architecture having PTB7-Th: PC71BM as an active layer. PEIE, a solution-processable polymer that requires low-temperature processing (100 degrees C), offers multiple advantages, including smoother surface morphology, reduced electrical resistances (R-s and R-t), and a lower work function, all of which contribute to enhanced charge extraction and overall device performance. A wide range of characterization techniques, such as atomic force microscopy (AFM), UV-Vis spectroscopy, Ellipsometry, and Scanning Kelvin Probe Microscopy (SKPM), were employed to gain insights into the nanostructural morphology of the thin films, optical characteristics, and the alignment of energy levels at the ITO/ETLs/BHJ active layer interface. In addition to the current (J)-voltage (V) characteristics, the impedance spectroscopic (IS) analysis is conducted for a comparative investigation of the electrical behavior of ZnO (prepared with Zinc acetate dihydrate and Zinc acetate precursors) and PEIE ETLs-based OSCs. The encapsulated devices were recurrently characterized for up to 60 days in

ambient conditions to analyze the impact of ETLs on the stability of OSCs. Impedance spectroscopy measurements and Mott-Schottky analysis reveal that the charge carrier dynamics and various electrical parameters exhibit improvements with PEIE ETL compared to ZnO ETLs. The device incorporating PEIE ETL demonstrated notable improvements in key photovoltaic parameters, including a higher J(sc) (13.7 mA cm(-2)), enhanced FF (64.5%), and reduced R-s (6.2 Omegacm(2)) compared to ZnO(2) based (J(sc) = 13.1 mA cm(-2), FF = 62.2%, R-s = 9.1 Omegacm(2)) and ZnO(1) based (J(sc) = 12.7 mA cm(-2), FF = 53.1%, R-s = 10 Omegacm(2)) devices. The outcome represents a substantial enhancement, surpassing the efficiencies obtained with ZnO ETLs prepared using anhydrous zinc acetate and zinc acetate dihydrate by 16% and 4%, respectively.

Ophthalmology and Eye Care Services
Patel N, **Robbins CC**, Gelman E, and **Desai UR**. Bilateral Endogenous Nocardia Endophthalmitis: A Case Report. *Ophthalmic Surg Lasers Imaging Retina* 2025;1-4. Epub ahead of print. PMID: 40833366. Full Text

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This report describes a case of presumed bilateral endogenous Nocardia endophthalmitis in order to guide clinicians in recognizing and treating this atypical etiology of ocular infection. A 56-year-old woman with a history of renal transplant presented with bilateral subretinal abscesses in the setting of a subcarinal infection with cultures positive for Nocardia. She was treated with serial intravitreal injections of amikacin for presumed bilateral endogenous Nocardia endophthalmitis with clinical improvement. Visual acuities were 20/200 in the right eye and 20/30 in the left eye approximately 6 months after initial presentation. Amikacin appears to be the drug of choice for treatment of Nocardia ocular infections. Endogenous Nocardia endophthalmitis tends to present differently than its exogenous counterpart, with the former subtype tending to present in a more indolent manner with choroidal abscesses. Providers should maintain a high suspicion for Nocardia as a potential etiology of ocular infection in immunocompromised patients.

Orthopedics/Bone and Joint Center
Afsari A, **Best B**, and Khan U. Letter to the Editor on "Elevated Risk of Infection and Reoperation in Low-Energy Gunshot Tibial Fractures: A Comparative Analysis". *J Orthop Trauma* 2025; Epub ahead of print. PMID: 40839891. Full Text

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Central Michigan University College of Medicine, Mt Pleasant, MI.

Orthopedics/Bone and Joint Center
Archutowski J, **Juma S**, **Searls WC**, **Roderique T**, and **Pampati V**. Suture Button with Tension Band Fixation for Patella fractures: A Retrospective Case Series. *Spartan Med Res J* 2025;10(1):30-36. PMID: 40785985. Full Text

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INTRODUCTION: There is a high rate of surgical complications and removal of symptomatic hardware for patients who have undergone open reduction internal fixation (ORIF) for transverse patella fractures. In recent years there has been increased interest in more low profile ORIF techniques to combat these issues. The aim of this study was to evaluate if a reduced hardware burden would correlate with fewer complications and equal rates of fracture union when compared to traditional techniques for treating transverse patella fractures. METHODS: Nine patient charts were retrospectively reviewed dating between June 2015 and March 2023. All patients sustained a transverse patella fracture and underwent ORIF with a suture button and suture tension band construct by a single surgeon. The primary outcome

measure was rate of radiographic fracture union at final follow up. Secondary outcome measures included any need for removal of hardware or other revision procedure, surgical and medical complications, postoperative pain score and the ability to perform a straight leg raise. RESULTS: Eight of nine patients demonstrated radiographic evidence of fracture consolidation with an average follow-up time of 17.9 months (range 12-26 months). One patient required an additional operation for revision ORIF before going on to successful union. No patients underwent a procedure for removal of hardware before final follow up. All patients were able to hold a straight leg raise at final follow up. CONCLUSIONS: Suture button with suture tension band construct is a reasonable treatment option for treating transverse patella fractures. Surgeons may employ this technique for older patients or those with some fracture comminution, although there should be some caution and close follow up for displacement.

Orthopedics/Bone and Joint Center

Bandovic I, **Olson A**, Smith A, **Centanni R**, **Khan U**, **Leadbetter V**, **Afsari A**, and **Best B**. Residual radiographic fracture displacement in healed tibial plateau fractures: comparison after treatment with suprapatellar nailing versus lateral plating. *OTA Int* 2025;8(3):e418. PMID: 40842942. Full Text

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OBJECTIVES: Compare maintenance of articular reduction and alignment in bicondylar tibial plateau fractures (OTA/AO 41-C2/C3) treated with suprapatellar intramedullary nailing (IMN) versus dual-plate open reduction and internal fixation (ORIF). DESIGN: Retrospective Cohort Study. SETTING: Single Level I academic trauma center. PATIENTS/PARTICIPANTS: Fifty-eight adults treated between July 2012 and July 2022 (28 IMN, 30 ORIF); groups were matched for age, body mass index, and fracture pattern. INTERVENTION: Semiextended suprapatellar IMN with ≥1 independent lag screw compared with dual-plate ORIF performed through standard open approaches. MAIN OUTCOME MEASUREMENTS: Joint-line depression, condylar widening, medial proximal tibial angle (MPTA), and posterior proximal tibial angle (PPTA) at union (12 months). RESULTS: Initial displacement was greater in the ORIF cohort (joint-line 8.2 mm vs. 5.6 mm, P = 0.014; widening 7.2 mm vs. 5.8 mm, P = 0.150). At 12 months, healed widening (0.6 mm IMN vs. 1.0 mm ORIF, P = 0.856), healed depression (2.0 mm vs. 1.1 mm, P = 0.991), MPTA (89.9° vs. 89.6°, P = 0.699), and PPTA (11.3° vs. 9.8°, P = 0.078) did not differ. No secondary loss of reduction requiring revision occurred. CONCLUSION: Suprapatellar IMN maintained healed joint line displacement, condylar widening, MPTA, and PPTA in OTA/AO C1, C2, and certain C3 fractures. The MPTA and PPTA were surgically restored and maintained. This technique may be useful in certain circumstances where ORIF of the tibial plateau fractures places the soft tissue envelope at risk or where an intramedullary implant is otherwise preferred. LEVEL OF EVIDENCE: Level III.

Orthopedics/Bone and Joint Center

Banfield NF, Kleinsmith RM, Hadro A, Huyke-Hernandez FA, Doxey SA, Schweitzer A, Ristow J, **Braman JP**, and Cunningham BP. Effect of postoperative NSAID use on opioid consumption after rotator cuff repair. *J Orthop* 2025;66:173-178. PMID: 40510511. Full Text

Department of Orthopaedic Surgery, University of Minnesota, Minneapolis, MN, USA.
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BACKGROUND: Opioid consumption following rotator cuff repair (RCR) remains a significant concern in post-surgical pain management. The use of nonsteroidal anti-inflammatory drugs (NSAIDs) has been proposed as a multimodal analgesic approach to reduce opioid use and improve recovery. However, the impact of NSAIDs on opioid consumption and clinical outcomes following RCR remains unclear, with conflicting findings from previous studies. The purpose of this study is to compare opioid consumption in patients prescribed a short course of NSAIDs after RCR versus those who were not prescribed NSAIDs.

METHODS: A retrospective cohort study was conducted including 125 patients who underwent primary arthroscopic RCR between 2012 and 2022. Patients were categorized into two groups based on the surgeon's practice change in May 2017: those who were not prescribed NSAIDs post-surgery and those who were prescribed NSAIDs for six weeks post-surgery. Data on opioid prescription, the need for opioid and NSAID refills, postoperative complications, and patient-reported outcomes (PROs) were collected and analyzed. RESULTS: No significant differences were observed between the two groups regarding demographic characteristics or preoperative MRI findings. The NSAID group demonstrated a significant reduction in opioid prescription compared to the non-NSAID group, receiving less morphine milligram equivalents (MME) on the day of surgery (306.7 ± 30.2 vs. 1007.4 ± 302.1, $p < 0.001$). Furthermore, patients in the NSAID group required fewer opioid refills (21.6 % vs. 37.5 %), though this difference did not reach statistical significance ($p = 0.085$). Both groups showed similar functional outcomes, with no significant differences in postoperative complications or clinical rotator cuff healing failures. CONCLUSION: This study demonstrates that a short course of NSAIDs following rotator cuff repair reduces opioid consumption without negatively affecting functional outcomes or tendon healing. These findings support the potential role of NSAIDs in reducing opioid reliance post-surgery and advocate for their inclusion in multimodal pain management protocols for RCR.

Orthopedics/Bone and Joint Center
Chen Z, **Gudi M**, **Lindahl A**, and **Day CS**. Calculating Value in Hand and Wrist Care: A Systematic Review on the Current Literature. *J Hand Surg Glob Online* 2025;7(5). PMID: Not assigned. Full Text

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Purpose: Global health care systems are shifting toward value-based care models, with the hand and wrist field presenting a notable opportunity to enhance quality and efficiency because of large patient volumes, a variety of pathologies, and diversity in treatment options. This systematic review aimed to investigate the literature on calculations of value between different treatment options in hand and wrist care. Methods: Adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines, two reviewers searched three databases to identify, screen, and evaluate research articles within hand and wrist care comparing the value between treatment groups based on real-world clinical data. Results: Nineteen of 181 hand and wrist articles screened met our predetermined inclusion criteria. Studies primarily employed the EuroQol 5-Dimension survey for quality metrics with the payer or societal cost perspective. The incremental cost-effectiveness ratio formula was the most used value calculation. The majority of included studies originate from Europe. Studies assessing distal radius fracture care highlighted reduced imaging strategies as more cost effective than traditional methods and bandaging as more cost effective than rigid immobilization. Studies assessing scaphoid fractures identified immediate magnetic resonance imaging intervention to outperform standard care and cast treatment combined with early fixation to be superior to standalone surgery or no treatment. Conclusions: Global literature on value-based comparative studies in hand and wrist care demonstrates variability in methodology, limiting direct comparisons. Most real-world studies were conducted within single-payer systems, highlighting the potential for further investments in value analysis protocols in multipayer systems. Clinical relevance: Establishing a standardized methodology for value assessment, will enable better comparisons and improvements in hand and wrist care. As global health care costs continue to rise, conducting research that identifies high-value care across diverse health care systems is essential to ensure sustainable, effective, and patient-centered care for all stakeholders.

Orthopedics/Bone and Joint Center
Cominos ND, **Juma SL**, Haddad J, **Pantuso A**, and **Khalil LS**. Iliac Epiphyseal Avulsion Repair Using a Suture Bridge and Lag Screw Construct. *Arthrosc Tech* 2025. PMID: Not assigned. Full Text

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Apophyseal avulsion fractures in adolescents are not uncommon, particularly among young athletes participating in explosive sports. Typically, avulsion fractures around the pelvis occur associated with a forceful eccentric contraction, in which a tendon avulses its osseous origin from the underlying apophysis.

An atypical or less commonly encountered avulsion fracture pattern involves the apophysis from the iliac wing extending distally to include the anterior superior iliac spine. This fracture pattern is subject to deforming forces from varying directions, which must be considered during fixation, as these are the attachment sites for both abdominal muscles and the origin of the sartorius. This Technical Note details a reduction and fixation technique for the treatment of an iliac apophyseal avulsion fracture. This approach leverages double-loaded anchors in the ilium in a suture-bridge construct, combined with lag screw boney compression and fixation. This hybrid approach addresses deforming forces from the abdominal musculature and sartorius while respecting soft tissue attachments and anatomic fracture fixation principles.

Orthopedics/Bone and Joint Center

Cornish ER, Zheng H, **Markel DC**, Hallstrom BR, and Hughes RE. Variation in KOOS JR improvement across total knee implant designs: a cohort study from Michigan Arthroplasty Registry Collaborative Quality Initiative. *Acta Orthop* 2025;96:587-594. PMID: 40762095. Full Text

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BACKGROUND AND PURPOSE: Arthroplasty registries report revision risk, but patient-reported outcomes may also measure implant performance. We aimed to evaluate (i) change in patient-reported outcome measures (PROMs) across multiple total knee arthroplasty (TKA) designs in a regional registry, (ii) the association of patellar resurfacing on the change in PROMs, and (iii) the variation in PROMs change within implants with or without patellar resurfacing. METHODS: This is a cohort of primary TKAs from Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI) performed between January 1, 2017 and September 30, 2021. The dependent measure was change in KOOS JR. Independent variables were implant name and patellar resurfacing. Multivariate modeling adjusted for patient-level factors. A previous report suggests a change of 23 points in KOOS JR as clinically relevant in achieving acceptable pain/function levels. A clinically relevance ratio (CRR) of those achieving the threshold of 23 points to the overall group was calculated for each implant. RESULTS: 18 implant designs met the inclusion criteria. There were 51,606 cases with complete preoperative and postoperative KOOS JR matched pairs. There was variation in improvement from preoperative to postoperative unadjusted KOOS JR scores across implant designs ($P < 0.001$), ranging from 18.7 (95% confidence interval [CI] 16.8-20.6) to 27.0 (CI 24.9-29.2). Patellar resurfacing resulted in greater KOOS JR improvement 1.0 (CI 0.5-1.5, $P < 0.001$). Of the cases with resurfaced patellae, the CRR was 50.2% (CI 49.7-50.7). For cases without resurfaced patellae, the CRR was 47.2% (CI 45.9-48.5). The association of implant design persisted whether the patella was resurfaced or not, evident in the adjusted mean change in KOOS JR ($P < 0.001$), ranging from 20.1 (CI 17.6-22.6) to 25.5 (CI 24.3-26.7) for resurfaced and from 17.0 (CI 13.9-20.1) to 23.3 (CI 20.3-26.2) for not resurfaced, and the CRR difference ($P < 0.001$), ranging from 45.8% (CI 42.5-48.6) to 55.8% (CI 50.4-60.8) for resurfaced and from 37.9% (CI 27.4-44.7) to 51.4% (CI 43.9-56.6) for not resurfaced. CONCLUSION: Implant design and patellar resurfacing both show an association with KOOS JR improvement. Variations in implant design persist whether the patella is resurfaced or not. Implant selection and patellar resurfacing may be associated with patient outcomes.

Orthopedics/Bone and Joint Center

Doka R, Mijic D, Badman BL, **Juma SL**, **Geers B**, and **Bishai SK**. Rotator Cuff Repair Augmented With a Reinforced Bioabsorbable Autobiologic Matrix. *Arthrosc Tech* 2025. PMID: Not assigned. Full Text

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Rotator cuff tears are one of the most common shoulder pathologies in the adult population, present in approximately 25% of individuals in their 60s and 50% in individuals in their 80s. With several techniques and technological advances in repairing symptomatic rotator cuff tears, the rate of retear rates remains elevated. Synthetic grafts have been developed to aid with rotator cuff repair by providing biomechanical

advantage, improved healing at bone tendon interface, while also remaining a cost-effective option when compared with costly revision rates. BioCharge Autobiologic Matrix is a synthetic scaffold approved by the Food and Drug Administration and developed to augment rotator cuff repairs by improving the ultimate load to failure rate while also providing improved enthesis architecture at the tendon-bone interface when observed at a microscopic level. The goal of this Technical Note is to describe the technique of rotator cuff repair with BioCharge augmentation.

Orthopedics/Bone and Joint Center
Foreman M, Amador I, Tabarestani A, **Hao KA**, Benjamin J, Casauay J, Dada O, Desai P, Jennings A, Orriols A, Popp R, Saengchote SA, **Khlopas A**, Hones K, Hutchison R, Kim J, Wright TW, and Chughtai M. Wound Irrigation Prior to Closure During Routine Upper-Extremity Surgery: Is There a Difference in Wound Complications? *Hand (N Y)* 2025; Epub ahead of print. PMID: 40831404. Full Text

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BACKGROUND: Presently, there is no consensus within the field of orthopedics on whether irrigation prior to wound closure in routine upper-extremity surgery reduces wound complications. Therefore, preclosure wound irrigation could provide time and cost savings. The aim of this study was to evaluate the effectiveness of wound irrigation in routine upper-extremity procedures. METHODS: We conducted a retrospective review of adult patients undergoing routine upper-extremity surgery at a single institution from 2013 to 2022. Patients were included if they underwent soft tissue upper extremity surgery. Patients were excluded for having concomitant lacerations, penetrating injuries, open fractures, or unknown irrigation technique. Our primary outcome was comparison of the rate of wound complications based on whether irrigation was used. Multivariable logistic regression was additionally used to determine whether irrigation prior to closure was associated with a lower incidence of postoperative wound complications independent of potential confounders. RESULTS: We included 1425 patients. The mean age was 55.2 ± 16 years and 65% were female. The incision was irrigated prior to closure in 65% of surgeries. Wound complications occurred in 2.9% of patients (n = 41). On bivariable analysis, irrigation prior to closure was not associated with a decreased incidence of wound complications (3.5% vs 1.8%, P = .070). When adjusting for age, sex, BMI, operative time, history of prior surgery, diabetes, tobacco use, corticosteroid use, and immunosuppressant use, the employment of irrigation prior to wound closure was not associated with lower odds of wound complications in either bivariable (OR: 1.99, 95% CI 0.94-4.19, P = .07) or multivariable (OR: 1.88, 95% CI 0.88-4.04, P = .08) analysis. CONCLUSION: Use of irrigation prior to wound closure was not associated with a difference in the odds of postoperative wound complications. Surgeons should consider forgoing irrigation prior to closure to increase operating room efficiency and provide cost savings to the patients and payers.

Orthopedics/Bone and Joint Center
Gandhi S, Lai CS, Newton M, Hartner S, Fleischer M, Salisbury M, Gellci K, Park DK, **Baker EA**, and **Baker KC**. Local RANTES/CCL5 Delivery and Peripheral Blood Mobilization of Endogenous Marrow-Derived Mesenchymal Stem Cells to Mitigate Lumbar Intervertebral Disc Degeneration. *Global Spine J* 2025; Epub ahead of print. PMID: 40876831. Full Text

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Study DesignTranslational rodent study.ObjectivesTo investigate (1) chemokine-mediated mesenchymal stem cell mobilization and homing to the intervertebral disc and (2) using this technique to mitigate intervertebral disc degeneration in a rat model.Methods(1) Recruitment of mesenchymal stem cells (MSCs) to intervertebral discs (IVD) was investigated using intradiscal chemokines. Hydrogel containing SDF-1, RANTES, MCP-1, or empty control was injected intradiscally, followed by near-infrared (NIR)

imaging to observe MSC localization. (2) A rat IVD degeneration model was induced by annular puncture. Intradiscal RANTES injection and/or systemic AMD3100 injection was performed. Longitudinal imaging and histological analyses including Rutges Score (histologic degeneration) assessed IVD degeneration mitigation post-treatment up to 12-weeks. Statistical analyses included ANOVA and mixed-effects models to evaluate recruitment, retention, and regenerative potential of MSCs.Results(1) 24 rats were included in the investigation of MSC recruitment. In vivo NIR signal on 1-day post-intervention was highest with RANTES ($P < .05$). Ex vivo NIR signal at 14-days post-intervention was highest with RANTES ($P < .05$). (2) 36 IVD degeneration model rats underwent intradiscal RANTES and/or AMD3100 injection. AMD3100-treated groups showed larger nucleus pulposus (NP) volumes and reduced histologic damage, with lower Total Rutges scores ($P = .004$). RANTES treatment alone reduced Total Rutges scores ($P = .009$) and protected against IVD height loss at 6 weeks.ConclusionsIntradiscal delivery of RANTES/CCL5 promotes a sustained and targeted recruitment of MSCs to the IVD. In a rat model of IVD degeneration, administration of systemic AMD3100 and intradiscal RANTES mitigates IVD degeneration.

Orthopedics/Bone and Joint Center
Khalil LS, **Cominos ND**, Terrian L, **Driessche AM**, **Pantuso A**, and Farrow LD. Surgical Techniques to Address Patellofemoral Instability: An Individualized Approach. *Arthrosc Tech* 2025. PMID: Not assigned. Full Text

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Patellar instability involves complex decision making and an individualized approach. Often, patients with high-risk pathoanatomic features present after a single or recurrent dislocation events. Consideration of the patient's osseous anatomy, age, dynamic examination findings, evaluation of soft-tissue tension, dislocation history, and goals are all integral to the treatment plan. With regards to surgical intervention, medial patellofemoral ligament reconstruction is the most commonly performed procedure to provide static stability to the patella. Concomitant proximal and distal realignment procedures can be performed, but consensus is lacking for whom these may be necessary. This Technique Note describes the order of operations and the author's preferred technique for performing a medial patellofemoral ligament reconstruction using hamstring autograft concurrently with lateral retinacular lengthening, vastus medialis oblique advancement, native medial patellofemoral ligament imbrication, and tibial tubercle osteotomy or patellar tendon shortening through 2 main incisions, for a patient with high-risk pathoanatomic features and examination.

Orthopedics/Bone and Joint Center
Lindahl A, **Hill T**, **Mazier E**, **Patel M**, **Kahn G**, **Zhou Y**, and **Day CS**. "Patient-Specific" Cost and Quality Value Comparison of Endoscopic Carpal Tunnel Release in Two Surgical Settings. *J Hand Surg Glob Online* 2025;7(5):100802. PMID: 40837494. Full Text

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PURPOSE: Prior studies have demonstrated that transitioning surgeries from a hospital outpatient department (HOPD) to an ambulatory surgical center (ASC) lowers costs. With 500,000 carpal tunnel release (CTR) surgeries annually, CTR offers an opportunity to determine the value of one of the most performed upper-extremity surgeries. We aim to quantify the value of an endoscopic CTR in a HOPD compared to an ASC by analyzing differences in costs and patient outcomes. We hypothesize the ASC will provide greater value by lowering costs while maintaining patient outcomes. METHODS: Total costs were comprised of time-driven activity-based labor costs (TDABC), activity-based supply costs, and claims-based facility costs. Differences in preoperative Patient-Reported Outcome Measure (PROM) Information System Upper Extremity (UE) and Pain Interference (PI) scores and 3-month postoperative PROM Information System UE and PI scores were calculated to determine PROM Information System Quality-Adjusted Life Years (QALY(UE/PI)). Total costs were divided by QALYs for each PROM to

calculate the Value(UE/PI) of each cohort. The magnitude of the difference in value between cohorts was elucidated by calculating incremental cost-effectiveness ratios. RESULTS: A total of 25 patients comprised each cohort. The ASC generated 28% lower costs compared to the HOPD ($3,370.73 ± $128.80 vs $4,654.75 ± $140.19). Average QALY(UE) and QALY(PI) gain was not significantly greater for patients at the ASC compared to the HOPD (QALY(UE) 1.06 vs 0.89; QALY(PI) 1.22 vs 0.92). The ASC demonstrated 40% to 45% greater value, represented by a lower cost/QALYs, compared to the HOPD (Value(UE) $3,168.81/QALY vs $5,242.78/QALY, Value(PI) $2,759.90/QALY vs $5,038.04/QALY). CONCLUSIONS: We observed between 40% to 45% greater value by performing CTRs in the ASC. Although ASCs lowered costs by 28%, costs alone do not fully explain the value differential. Patient-reported outcomes serve a valuable role in providing a holistic picture of the value being delivered to patients. Providers can use this information to guide patient decision-making regarding operative treatment options for carpal tunnel syndrome. TYPE OF STUDY/LEVEL OF EVIDENCE: Economic/Decision Analysis II.

Orthopedics/Bone and Joint Center

Lizzio VA, **James CL**, **Kasto JK**, **Sanii RY**, and **Muh SJ**. Fulfillment of Patients' Expectations for Reverse Total Shoulder Arthroplasty for the Treatment of Rotator Cuff Tear Arthropathy Utilizing the Exactech Equinoxe Platform. *J Shoulder Elbow Surg* 2025; Epub ahead of print. PMID: 40835106. Full Text

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BACKGROUND: Despite the increasing utilization of reverse total shoulder arthroplasty (rTSA), there remains limited data regarding perioperative expectations and fulfillment of expectations for patients undergoing rTSA for rotator cuff tear arthropathy (CTA). Thus, the purpose of this study was to determine the proportion of expectations that are fulfilled following rTSA, and to determine which patient characteristics are associated with fulfilment of expectations at two-year follow-up. METHODS: Preoperatively, patients completed the Hospital for Special Surgery's Shoulder Surgery Expectation Survey, American Shoulder and Elbow Surgeons Score (ASES), visual analogue score (VAS) for pain, and a Single Assessment Numeric Evaluation (SANE) score for the affected shoulder. At two-year follow-up, patients were asked to what extent each of their corresponding preoperative expectations which they had previous cited as "very important" were now fulfilled, and again completed the patient-reported outcomes. Demographic and range of motion data were also collected. RESULTS: Seventy-seven patients met all inclusion criteria and were included in this study. The expectations most frequently cited as being "very fulfilled" postoperatively were improvement in self-care (75%), improvement in ability to drive/put on seatbelt (77%), and relief of daytime pain (73%). Eighty-one percent of patients cited improvement in shoulder ROM as an important expectation preoperatively but only 53% reported that this expectation was "very fulfilled" postoperatively. Patients with better postoperative ASES scores ($p<0.001$), better VAS scores ($p<0.001$), and better SANE scores ($p<0.001$) compared to the average patient had a greater proportion of expectations fulfilled. CONCLUSIONS: Patients undergoing rTSA for CTA had greatest fulfillment of expectations for improvement in self-care, ability to drive, and relief of daytime pain at two-year follow-up. Relatively few patients reported fulfillment of expectations for shoulder ROM. Better postoperative ASES, VAS, and SANE scores correlated with greater fulfillment of expectations. It is important to understand traditional objective metrics considered for success to surgeons may not be the same as a patient's perspective. Using this information, surgeons can better tailor their preoperative discussions with patients to appropriately manage expectations.

Orthopedics/Bone and Joint Center

Wilson TG, **Baghel M**, and **Ali SA**. Osteoarthritis year in review 2025: Genetics, genomics, and epigenetics. *Osteoarthritis Cartilage* 2025; Epub ahead of print. PMID: 40848985. Full Text

Bone and Joint Center, Henry Ford Health, Detroit, MI, USA; Henry Ford Health + Michigan State University Health Sciences, Detroit, MI, USA.

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OBJECTIVE: This review provides an overview of the work performed in the realms of genetics, genomics and epigenetics in osteoarthritis (OA) research over the past year. METHOD: A search was performed in the EMBASE database for original research articles and reviews published between March 2, 2024 and April 24, 2025. The search strategy consisted of the term "osteoarthritis" paired with keywords related to genetics, genomics and epigenetics. Articles were curated using Covidence software according to their relevance. For discussion in this review, priority was given to publications in top quartile rheumatology journals. RESULTS: Our initial search identified 2240 unique articles, of which 42 are highlighted within this review. This year included the publication of the largest OA genetics study to date by the Genetics of Osteoarthritis Consortium. Higher impact OA genomics studies often involved the integration of multiple methodologies including chromatin accessibility mapping, single-cell RNA-sequencing and spatial transcriptomics analyses. Epigenetics studies included the characterization of non-coding RNAs, with an emphasis on microRNAs, in OA. CONCLUSION: Over the past year, we saw significant advancements in the comprehensive molecular mapping of OA joint tissues. Further strides were made in the characterization of key OA-associated pathways, gene families and microRNAs that could be exploitable therapeutic targets.

Orthopedics/Bone and Joint Center

Ziedas A, **Dube M**, **Elagamy N**, **Nasir M**, **Doerr M**, and **Frush T**. Athletic Performance at the National Football League Scouting Combine After Arthroscopic Meniscal Surgery. *Orthop J Sports Med* 2025;13(7):23259671251360405. PMID: 40756373. Full Text

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BACKGROUND: Meniscal surgery is common and debilitating in National Football League (NFL)-bound athletes. Although statistical performance has been demonstrated after surgery, functional performance as measured at the NFL Combine is not well-defined. PURPOSE/HYPOTHESIS: The purpose of this study was to determine the functional performance, production scores, athleticism scores, overall scores, and draft position of NFL Combine participants after meniscal surgery compared with a matched control group. It was hypothesized that there would be no difference in functional performance or graded scores between athletes with meniscal surgery compared with controls. STUDY DESIGN: Cohort Study; Level of evidence, 3. METHODS: NFL-caliber athletes who had previous arthroscopic meniscal repair or meniscectomy and participated in the NFL Scouting Combine between 2014 and 2024 were compared with a control group. Data included the 40-yard dash, 10-second split, vertical, broad jump, shuttle, 3-cone drill, production, athleticism, and overall scores, prospect grades, and draft position. RESULTS: A total of 48 athletes were included in the repair group; 43 athletes were included in the meniscectomy group, with the same number of controls after matching. Compared with controls, players in the meniscal repair group had significantly slower 3-cone drill (7.40 +/- 0.43 vs 7.20 +/- 0.38 seconds; P = .018), shuttle drill (4.51 +/- 0.26 vs 4.38 +/- 0.26 seconds; P = .016), lower athleticism (69.74 +/- 12.95 vs 76.13 +/- 11.28; P = .012), and overall scores (70.95 +/- 14.22 vs 77.47 +/- 8.30; P = .007). There was no significant difference in the 40-yard dash (P = .439) or vertical tests (P = .559). Players in the meniscectomy group had a significantly slower shuttle compared with controls (4.45 +/- 0.31 vs 4.34 +/- 0.18 seconds; P = .047), lower athleticism (69.62 +/- 12.53 vs 76.67 +/- 10.84; P = .007), and overall scores (70.59 +/- 10.56 vs 75.24 +/- 9.52; P = .035). There was no significant difference in the 40-yard dash (P = .164) or vertical tests (P = .108). There was no significant correlation between the NFL Combine performance and time from surgery. CONCLUSION: While overall athletic performance remained largely unaffected by arthroscopic meniscal repair or meniscectomy, specific drills, such as the 3-cone and shuttle drills, demonstrated significant declines, suggesting a negative effect on agility and quickness. Metrics used to score NFL prospects were also inferior in the meniscal repair and meniscectomy groups. These findings highlight the potential effects of meniscal surgery on athletic performance, underscoring the need for surgeon guidance on expectant postsurgical functional deficits for NFL-caliber athletes.

Otolaryngology – Head and Neck Surgery
Cecola C, Patel K, **Jones LR**, **Oghenefefiro O**, and Hetzler LT. Surgical Management of Unilateral Cleft Lip. *Facial Plast Surg Clin North Am* 2025. PMID: Not assigned. Full Text

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Otolaryngology – Head and Neck Surgery
Schuman AD, McKeon M, Allen J, Altaye M, Amin MR, Bayan SL, Belafsky PC, Bock JM, DeSilva BW, Dion G, Ekbom DC, Friedman AD, Fritz M, Guardiani EA, Johnson C, Kasperbauer J, Kim B, Krekeler BN, Kuhn M, Kwak P, Ma Y, Madden LL, Matrka L, **Mayerhoff RM**, **Piraka C**, Rosen C, Tabangin M, Wilson K, Young VN, Postma G, and Howell RJ. Dysphagia Outcomes in Zenker Diverticulum: A Longitudinal POuCH Study. *Laryngoscope* 2025; Epub ahead of print. PMID: 40828004. Full Text

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OBJECTIVE: Patients with cricopharyngeus muscle dysfunction (CPMD) with and without diverticula (e.g., Zenker Diverticulum) often struggle with dysphagia for years prior to diagnosis or intervention. Surgical treatment is successful; yet, there is limited long-term data on dysphagia outcomes after surgery. METHODS: Individuals prospectively enrolled in the Prospective Outcomes of Cricopharyngeal Hypertonicity (POuCH) collaborative with and without diverticula who underwent surgery from November 2014 to August 2024 and had at least 12 months of follow-up were included. Eating Assessment Tool 10 (EAT10) was used to characterize patient-reported outcomes. Descriptive statistics were performed using means, frequencies, and spaghetti plots. RESULTS: Of 164 patients initially identified, 2 withdrew and 2 were excluded for incomplete data; 160 were included. 31% were women, with a mean (SD) age of 70.1 (11.5). Endoscopic surgery (113, 71%) was more common than open technique (47, 29%). 19.4% of patients had undergone previous surgery. Postoperatively, patients were found to have improved EAT-10 scores, with smaller changes recorded after 36 months. Median change in EAT-10 compared to preoperative score was -12 points [IQR: -18, -5] at 12 months. 39 (24%) patients were followed for

> 24 months (median change -11 [IQR: -14, -7]); 26 (16%) > 36 months (-9.5 [-17, -5]), and 12 (7.5%) > 48 months (-4 [IQR: -18, 4]). Six patients died during the study period. CONCLUSION: Improved dysphagia after surgery appears stable with minimal change over time. Most patients (96.3%) survive at least 1 year. Surgical intervention for patients with CPMD with or without diverticula is an effective and reliable treatment option.

Otolaryngology – Head and Neck Surgery
Shukla ME, Misono S, Amini A, Sieracki R, Takiar V, Ward MC, Bakst R, Chandra RA, **Chang SS**, Choi K, Galloway T, Hu KS, Robbins JR, **Siddiqui F**, Walker G, Witek ME, and Margalit DN. Executive Summary of the American Radium Society Appropriate Use Criteria for Management of Early Glottic Cancer: A Review. *JAMA Otolaryngol Head Neck Surg* 2025; Epub ahead of print. PMID: 40875219. Full Text

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IMPORTANCE: Stage I squamous cell carcinoma (SCC) of the glottic larynx carries a favorable prognosis after treatment with endoscopic surgery or radiation therapy (RT). In addition to tumor control, goals of therapy include preservation of voice quality, swallow function, and breathing. Multidisciplinary consensus guidelines are needed to assist clinicians in treatment selection and the appropriate use of both surgical and radiation-based techniques. OBSERVATIONS: Treatment of clinical T1N0 glottic SCC has evolved over time, with advances in both transoral laser microsurgery and RT designed to become more targeted and reduce the overall treatment burden for patients. When selecting a treatment option, consideration should be given to patient-specific factors, including tumor position/extent, age, and medical and psychosocial factors. This 16-member multidisciplinary American Radium Society (ARS) Head and Neck Cancer Appropriate Use Criteria (AUC) expert panel performed a review of the English-language medical literature from 2000 to 2022 to inform consensus guidelines. Clinical case variants were developed to represent commonly encountered clinical scenarios, and the RAND/UCLA appropriateness method was used to rate the appropriate use of various treatments. The modified Delphi method was used to reach consensus recommendations, which were approved by the ARS Executive Committee and subject to public comment per established ARS procedures. CONCLUSIONS AND RELEVANCE: Given the range of treatment options available, early glottic SCC management should be done in a multidisciplinary fashion including otolaryngologists and radiation oncologists. The ARS Head and Neck AUC expert panel created an appropriate-use consensus document by performing a literature review of the current treatment strategies for stage I glottic SCC, providing recommendations regarding the appropriateness of surgery or RT for various clinical scenarios and highlighting areas of controversy and uncertainty.

van der Poel N, Shah G, Wolter N, Georgalas C, Vroegop A, Couloigner V, Simon F, Stapleton AL, Crosby D, Ramaswamy U, Walz P, Al-Barazi R, Wormald PJ, Ortiz E, Villamor P, Min JY, Pacheco A, Langdon C, Naik P, Peer S, Mehanna R, **Craig JR**, and Saibene AM. Management of pott's puffy tumor: a Delphi-method international clinical consensus statement. *Eur Arch Otorhinolaryngol* 2025; Epub ahead of print. PMID: 40782155. Full Text

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PURPOSE: Pott's puffy tumor (PPT) is a rare and complex condition that requires a comprehensive diagnostic approach and multi-faceted treatment strategy. It is associated with a significant risk of intracranial complications. The purpose of this clinical consensus statement (CCS) is to systematically assess diagnostic and therapeutic approaches of patients with PPT, using the best available evidence and expertise of the panel. The results and recommendations are intended to support clinicians in making informed decisions when managing patients with PPT and to standardize diagnostic, antibiotic, and surgical management across institutions. This consensus also aimed to provide a basis for a subsequent international prospective registry to inform data-driven care. METHODS: A literature review was performed via PubMed, and an international panel of 23 experts judged 33 statements in two rounds using a modified Delphi method survey to establish expert recommendations on the diagnostic considerations, medical and surgical management, and postoperative considerations. Strong consensus was defined by a mean score of ≥ 8.00 with no outliers, and consensus by a mean score of ≥ 7.00 with no more than 1 outlier. RESULTS: A strong consensus was reached on important aspects of the diagnosis and treatment of patients with PPT. Most pivotal are the importance of urgent imaging, imaging of the brain with a preference of MRI, the importance of broad spectrum intravenous antibiotic treatment, and the goal of surgery - resolution of the periosteal abscess and clearance of the frontal sinus drainage

pathway - which can be established in various ways and is case and surgeon dependent. CONCLUSION: In patients with PPT, a high index of suspicion of intracranial complications is important to prevent any delay in treatment initiation. The recommendations formulated in this international consensus statement aim to improve the diagnosis and care for patients with PPT and to address gaps and uncertainties in current guidelines. Items that did not reach consensus may serve as areas for further research.

Otolaryngology – Head and Neck Surgery
Yaremchuk K, and Merati AL. Wellness and Otolaryngology-Head and Neck Surgery: Reflections and Realities. *Otolaryngol Clin North Am* 2025; Epub ahead of print. PMID: 40849267. Full Text

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Pathology and Laboratory Medicine
Jacquot C, Di Mola M, Jacob R, Mathur G, Pacheco C, Vivero A, Corey Z, **Lopez-Plaza I**, and Annen K. Developing a Protocol for Therapeutic Plasma Exchange in Tandem With Continuous Renal Replacement Therapy (CRRT) and ExtraCorporeal Membrane Oxygenation (ECMO) in Pediatric Patients. *J Clin Apher* 2025;40(4):e70051. PMID: 40848240. Full Text

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Therapeutic plasma exchange (TPE) in pediatric patients presents many challenges, including management of a large extracorporeal volume (ECV) and calcium replacement for patients who may not be able to express signs of hypocalcemia or other associated adverse events with a large ECV. Pediatric patients who are critically ill on continuous renal replacement therapy (CRRT) and/or extracorporeal membrane oxygenation (ECMO) may have indications for TPE, such as sepsis or liver failure anticipating transplant. It may be difficult or clinically detrimental to take the patient off the CRRT or ECMO circuit to perform TPE. Connecting the TPE device into the preexisting circuit is feasible with the understanding of the principles of the circuit flow set up and monitoring to mitigate adverse events. Effective communication among clinical teams managing distinct extracorporeal circuits is critical to ensuring coordinated patient care.

Pathology and Laboratory Medicine
Rizkalla CN, Tretiakova M, Williamson SR, Akgul M, **Al-Obaidy KI**, Acosta AM, Idrees MT, Chan E, and Sangoi AR. Overlapping Morphologic and Immunophenotypic Features of Plasmacytoid Urothelial Carcinoma and Urothelial Carcinoma With Osteoclast-Like Giant Cells. *Int J Surg Pathol* 2025; Epub ahead of print. PMID: 40827073. Full Text

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Osteoclast-rich undifferentiated carcinoma of the urinary tract, herein referred to as urothelial carcinoma with osteoclast-like giant cells (UCOGC), is an uncommon tumor currently classified under "poorly differentiated" urothelial carcinoma subtype composed of osteoclast-like giant cells intermixed with abundant mononuclear cells. Not infrequently, the mononuclear component exhibits eccentric nuclear localization reminiscent of plasmacytoid urothelial carcinoma. Given an index tumor where the mononuclear component of UCOGC showed prominent plasmacytoid histology and concomitant plasmacytoid urothelial carcinoma immunophenotype (aberrant loss of membranous E-cadherin with cytoplasmic p120 expression), herein we explore E-cadherin/p120 immunoreactivity in 14 UCOGC with sequencing performed on 4 tumors. Plasmacytoid histology in the mononuclear was identified in all 14 (100%) UCOGC, extent ranging from 20% to 70% (mean = 40%). In 13 of 14 UCOGCs, the mononuclear component showed loss of membranous E-cadherin while strong cytoplasmic p120 staining was present in all 14 tumors. Four UCOGCs also contained separate elements of plasmacytoid subtype urothelial carcinoma, all exhibiting aberrant loss of membranous E-cadherin with cytoplasmic p120 expression. NGS testing showed no evidence of E-cadherin mutations in 4 tested UCOGCs. Although both plasmacytoid UC and UCOGC are associated with poor outcomes, given the established clinicopathologic and molecular features of plasmacytoid urothelial carcinoma, it is prudent to avoid misclassifying UCOGC as plasmacytoid urothelial carcinoma based on the shared aberrant immunoprofile of the mononuclear (loss of membranous E-cadherin with cytoplasmic p120 expression). Recognition of the intimately admixed osteoclast-like giant cells characteristic of UCOGC (often overlooked when sparse and/or in a small biopsy setting) is key for accurate diagnosis.

Pathology and Laboratory Medicine

Sekela ME, Snyder EL, Welsby IJ, Toyoda Y, Alsammak M, Sodha NR, Beaver TM, Pelletier JPR, Gorham JD, McNeil JS, Sniecinski RM, Pearl RG, Nuttall GA, Sarode R, Reece TB, Benjamin RJ, Kaplan A, Davenport RD, Ipe TS, Benharash P, **Lopez-Plaza I**, Sadler P, Reik R, Gammon RR, Pitman JP, Liu K, Bentow S, Corash L, Mufti N, and Varrone J. Transfusion of Amustaline/Glutathione Pathogen-Reduced Red Blood Cells in Cardiac Surgery - A Randomized Phase III Clinical Trial. *Anesthesiology* 2025. PMID: Not assigned. Full Text

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Background: Transfusion has a persistent low risk of transfusion-transmitted infection and transfusion-associated graft-versus-host disease that may be addressed using pathogen-reduction. The Red Cell Pathogen Inactivation (ReCePI) trial tested whether amustaline/glutathione pathogen-reduced Red Cells are non-inferior to conventional transfusions for support of acute surgical blood loss. Methods: A Phase III, double-blinded, non-inferiority trial randomized cardiac or thoracic-aorta surgery patients with increased risk of Red Cell transfusion to receive pathogen-reduced or conventional Red Cells during and for seven days post-surgery. The primary endpoint was the proportion of patients with acute kidney injury (AKI) defined as an increase from baseline of ≥0.3 mg/dL serum creatinine within 48 hours of surgery. Non-inferiority was claimed if the upper bound 95%C.I. of the treatment difference was less than half (50%) of the observed conventional arm incidence. Adverse events and treatment-emergent Red Cell antibodies were assessed for 28 and 75-days, respectively. Results: Five hundred eighty-one subjects were randomized and 321 (55%) transfused with study Red Cells. Transfused subjects in both arms had similar baseline demographics, medical histories, hemoglobin levels and surgical procedures. Hemoglobin Day 3 nadir levels (8.6g/dL [7.8-9.2] pathogen-reduced; 8.4g/dL [7.8-9.3] conventional arm, P=0.52) were comparable. Incidence of AKI by 48 hours was 46/157 (29.3%) in the pathogen-reduced, and 45/161 (28.0%) in the conventional arm (treatment difference 0.7%, 95%C.I. -8.9, 10.4%, non-inferiority margin 14.0%, P=0.001 for non-inferiority). AKI within 7 days by KDIGO staging criteria was not

different (59/159 [37.1%] pathogen-reduced; 55/162 [34.0%] conventional arm; p=0.53) but stage III was more common in the pathogen-reduced arm (pathogen-reduced 15/159 [9.4%]; conventional arm 7/162 [4.3%], p=0.075). Five of 159 (3.1%) pathogen-reduced Red Cell recipients developed specific, low-titer antibodies without evidence of hemolysis. Conclusions: The incidence of AKI in recipients of pathogen-reduced Red Cells was non-inferior to conventional Red Cell transfusion. Treatment-emergent antibodies were uncommon and not clinically significant.

Pharmacy

Ammar A, **Sorochak N**, **Paxton R**, **Lipari M**, and **Giuliano C**. Association Between the Use of Long-Acting Insulin and Hypoglycemia in Critically Ill Patients with Diabetes. *J Intensive Care Med* 2025; Epub ahead of print. PMID: 40888642. Full Text

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Introduction: Hypoglycemia in critically ill patients increases morbidity and mortality. Subcutaneous long-acting insulin (LAI) in patients without diabetes is associated with hypoglycemia in the SICU. However, limited evidence exists in patients with diabetes. Methods: This was a single-center, retrospective cohort study evaluating patients with T2DM who were admitted to the SICU for 24 h and received LAI in combination with sliding scale insulin (LAI + SSI) or sliding scale insulin (SSI) alone. The primary outcome was the incidence of hypoglycemia (BG < 70 mg/dL) in patients who received LAI + SSI or SSI. Secondary outcomes evaluated the number of glucose values across defined categories: hypoglycemia (54-70 mg/dL), severe hypoglycemia (<54 mg/dL), euglycemia (70-180 mg/dL), hyperglycemia (>180 mg/dL) and glycemic variability. Results: A total of 228 patients were included in the final analysis. The incidence of hypoglycemia occurred in 17.5% of patients in the LAI + SSI cohort and 18.4% in the SSI cohort (p = .86). After controlling for confounders, no differences were observed with LAI + SSI versus SSI for hypoglycemia (OR 1.09, 95% CI 0.46-2.6, p = .85). Secondary outcomes demonstrated no difference in total hypoglycemia (37 vs 31, p = .80), severe hypoglycemia (15 vs 34, p = .17) and euglycemia (1622 vs 1780, p = .22) in the LAI + SSI cohort compared to SSI alone. Hyperglycemia occurred more frequently with LAI + SSI. However, after adjusting for confounders there was no difference in hyperglycemia (OR 1.8, 95% CI 0.7-4.6, p = .22). No difference was observed in glycemic variability between LAI + SSI and SSI (26.5 vs 24.5, p = .21). Conclusion and Relevance: The addition of LAI to SSI in SICU patients with T2DM was not associated with an increased risk of hypoglycemia.

Pharmacy

Dobry P, Lane R, **Whittaker P**, Gwaltney A, Smith S, Hudson B, Carabetta S, **Brual R**, Sawyer L, Perez M, Truong M, DeVier M, Dalton K, **Edwin SB**, **Giuliano C**, **Haan BJ**, and Daley M. Two paths to paralysis: A multicenter comparison of cisatracurium to atracurium in the management of acute respiratory distress syndrome. *J Crit Care* 2025;91:155227. PMID: 40848334. Full Text

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PURPOSE: Neuromuscular blocking agents (NMBAs) such as cisatracurium and atracurium are used to facilitate lung-protective ventilation in moderate-to-severe acute respiratory distress syndrome (ARDS).

Although cisatracurium has been more extensively studied, data comparing these agents directly are limited. This study compares clinical outcomes between atracurium and cisatracurium in patients with moderate-to-severe ARDS. MATERIALS AND METHODS: This multicenter, retrospective cohort study was conducted between January 2017 and December 2023 across 11 Ascension Health hospitals. Mechanically ventilated adults with a PaO(2)/FiO(2) ratio < 150 who received a continuous infusion of atracurium or cisatracurium for at least 12 h within 48 h of ARDS diagnosis were included. The primary endpoint was ventilator-free days at day 28. RESULTS: A total of 384 patients were included, with 192 in each group. Median 28-day ventilator-free days did not differ between groups in the unmatched (0 [IQR 0-16.7] vs. 0 [IQR 0-16.4], p = 0.72) or matched (0 [IQR 0-18.3] vs. 0 [IQR 0-14.4], p = 0.09) cohorts. These findings were further confirmed by multivariable analysis. After matching, there were no significant differences in 90-day inpatient mortality, length of stay, or duration of mechanical ventilation. While patients receiving cisatracurium showed greater improvements in PaO(2)/FiO(2) ratio at 72 h (p < 0.01), resolution of ARDS was similar between groups. Safety outcomes were comparable between agents. CONCLUSIONS: Atracurium and cisatracurium demonstrated similar safety and effectiveness in patients with moderate-to-severe ARDS. These results suggest that atracurium is a viable alternative to cisatracurium for the treatment of ARDS.

Pharmacy

Kunz Coyne AJ, Alosaimy S, Lucas K, Morrisette T, Molina KC, DeKerlegand A, Schrack MR, Kang-Birken SL, Hobbs ALV, Agee J, Perkins NB, 3rd, Biagi M, Pierce M, Truong J, Andrade J, Bouchard J, Gore T, King MA, Pullinger BM, Claeys KC, **Herbin S**, Cosimi R, Tart S, Veve MP, Jones BM, Rojas LM, Feehan AK, Zhao JJ, Witucki P, and Rybak MJ. Eravacycline use in immunocompromised patients: multicenter evaluation of timely versus late initiation on clinical outcomes. *Microbiol Spectr* 2025;e0056525. Epub ahead of print. PMID: 40856499. Full Text

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Infections from multidrug-resistant (MDR) bacteria lead to worse outcomes in immunocompromised patients. Eravacycline (ERV) is effective against MDR gram-negative and gram-positive bacteria, but its effects in immunocompromised populations remain unstudied. We aimed to evaluate clinical end points of immunocompromised patients receiving timely versus late ERV therapy. This multicenter, retrospective, observational study (October 2018 to September 2022) included adult immunocompromised patients hospitalized and treated with ERV for ≥72 h. The primary outcome was a composite of all-cause 30-day mortality, failure to improve clinically while on ERV, and/or microbial recurrence within 30 days of ERV initiation. Inverse probability of treatment weighting (IPTW) and Kaplan-Meier analyzes were used. Eighty-two patients from 17 US centers were included (median age 62 years; 59% male; intensive care unit admissions 57%). In the unadjusted cohort, timely ERV significantly reduced odds of clinical treatment failure (odds ratio [OR]: 0.321, 95% confidence interval [CI]: 0.129-0.800, P = 0.012) and microbial recurrence (OR: 0.545, 95% CI: 0.326-0.913, P = 0.034) compared to late ERV; in the IPTW-adjusted cohort, these associations remained significant with ORs of 0.675 (95% CI: 0.465-0.979, P = 0.029) for treatment failure and 0.384 (95% CI: 0.142-0.943, P = 0.041) for recurrence. Kaplan-Meier analysis showed a higher cumulative proportion of clinical treatment failure in the late ERV group (57%) compared to the timely ERV group (30%, P = 0.013), with a significantly longer time to clinical treatment failure in the timely ERV group (log-rank P = 0.034). Timely initiation of ERV in immunocompromised patients may improve clinical outcomes by reducing treatment failure and microbial recurrence compared to later initiation.IMPORTANCEThis multicenter, retrospective study evaluates the impact of timely versus late initiation of eravacycline (ERV) in immunocompromised patients with multidrug-resistant (MDR) bacterial infections. Immunocompromised patients face heightened risks of severe infections due to weakened immune defenses and limited treatment options, yet data on ERV use in this population are scarce. Our findings demonstrate that timely ERV initiation ≤72 h from index culture collection) significantly reduces clinical treatment failure and microbial recurrence compared to late initiation, with inverse probability of treatment weighting-adjusted odds ratios of 0.675 (P = 0.029) for treatment failure and 0.384 (P = 0.041) for recurrence. Kaplan-Meier analysis further confirms that delayed ERV therapy is associated with a higher cumulative incidence of clinical failure (57% vs 30%, P = 0.013). These results highlight the importance of early ERV initiation in optimizing outcomes for immunocompromised patients and addressing the growing challenge of MDR infections, emphasizing the need for further prospective studies to confirm these findings.

Pharmacy

Mulugeta SG, **Kantharia S**, **Veve MP**, **Vincent S**, **Beaulac A**, and **Patel N**. Impact of Methicillin-Resistant Staphylococcus aureus Nasal PCR Versus Culture on Vancomycin Utilization in Pneumonia Management. *J Pharm Technol* 2025; Epub ahead of print. PMID: 40786007. Full Text

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Introduction: Methicillin-resistant Staphylococcus aureus pneumonia (PNA) can be ruled out via methicillin-resistant Staphylococcus aureus (MRSA) culture and polymerase chain reaction (PCR) nasal screening, facilitating the de-escalation of empiric anti-MRSA agents like intravenous vancomycin. This study evaluated the impact of transitioning from culture to PCR-based MRSA nasal screening in patients with PNA. Methods: This Institutional Review Board (IRB)-approved retrospective quasi-experimental study was conducted at a 5-hospital system and included adult, nonpregnant hospitalized patients from September to December 2021 ("culture group") and September to December 2022 ("PCR group") and diagnosed with PNA. Exclusion criteria were ventilator-acquired PNA or positive MRSA respiratory culture. The primary endpoint was the number of vancomycin levels obtained. Secondary endpoints were vancomycin duration as well as acute kidney injury (AKI) and all-cause 30-day readmission rates. Results: Two-hundred patients were included: 100 in each group. Baseline characteristics were similar. There were 117 vancomycin levels obtained: 67 (67) and 50 (50) in the culture and PCR group, respectively (P = .021). Median vancomycin duration was 50% shorter in the PCR group: 2 days (1-3) versus 3 days (2-4), P < .001. After adjusting for confounders, the culture group was more likely to have vancomycin levels obtained compared to the PCR group: adjusted odd ratio (aOR) (95% confidence interval [CI])] = 1.833 (1.016-3.309). Long-term obstructive pulmonary disease was associated with reduced risk of ordering vancomycin levels: aOR [95% CI] = 0.426 (0.218-0.831). Readmission and AKI rates were comparable. Conclusion: Transitioning from culture to PCR-based MRSA nasal screening significantly reduced vancomycin levels obtained from patients and shortened vancomycin duration without negatively impacting patient outcome.

Public Health Sciences

Bertini A, **Stephens A**, Finocchiaro A, Viganò S, **Dinesh A**, **Guivatchian E**, Perri A, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Briganti A, Salonia A, Montorsi F, Sood A, Menon M, **Rogers C**, and **Abdollah F**. Long-term Cancer Control Outcomes After Robot-assisted Radical Prostatectomy in Pathologically Non-organ-confined High-risk Prostate Cancer: 20-year Report from a Single Tertiary Referral Center. *Eur Urol Focus* 2025; Epub ahead of print. PMID: 40774843. Full Text

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BACKGROUND AND OBJECTIVE: Exhaustive evidence on the long-term efficacy of robot-assisted laparoscopic prostatectomy (RALP) in non-organ-confined high-risk prostate cancer (PC) is still lacking. Our aim was to evaluate long-term oncological outcomes in this subset of patients treated with RALP at a single referral center. METHODS: We included 803 patients with pathologically non-organ-confined high-risk PC (≥pT3a and/or pN1) at RALP between 2001 and 2022 at Henry Ford Hospital (Detroit, MI, USA).

All patient underwent RALP using the Vattikuti Institute technique, with or without extended pelvic lymph node dissection (external iliac, obturator, and internal iliac nodes). The Kaplan-Meier method was used to estimate overall survival (OS) and additional treatment-free survival. The probability of PC-specific survival (PCSS) was estimated via the competing-risks method. Competing-risk and Cox regression analyses were used to identify potential predictors of PC-specific mortality (PCSM), any-cause mortality (ACM), and additional treatment. KEY FINDINGS AND LIMITATIONS: We included 803 patients, of whom 415 (51.5%) had pT3a, 385 (47.9%) had ≥pT3b, 323 (40%) had pN1, and 670 (84%) had grade group 4-5 PC. Of the 635 patients with status information regarding additional treatment, 416 received further therapy after surgery. Specifically, 46, 110, and 260 underwent RT only, HT only, or RT + HT, respectively. Median follow-up was 72 mo (interquartile range 28-120). The 20-yr survival rates were 72.7% (95% confidence interval [CI] 56.8-86,5%) for PCSS and 45.2% (95% CI 29.1-60.1%) for OS. The rates of survival free from additional treatment were 31.3% (95% CI 26.1-36.5%) at 10 yr and 20.3% (95% CI 14.9-26.4%) at 15 yr. Multivariable regression revealed pT3b-4 stage as an independent predictor of PCSM (hazard ratio [HR] 2.50; p = 0.008), ACM (HR 1.84; p = 0.006), and additional treatment (HR 1.69; p < 0.001). CONCLUSIONS AND CLINICAL IMPLICATIONS: For patients with non-organ-confined high-risk PC, RALP achieves long-term oncological control. This study provides the longest follow-up after RALP as the primary local treatment for patients with truly aggressive PC forms and offers valuable insights for patient counseling on long-term outcomes.

Public Health Sciences

Bertini A, **Stephens A**, Finocchiaro A, Viganò S, Perri A, Lughezzani G, Buffi N, Sorce G, Ficarra V, Briganti A, Salonia A, Montorsi F, Sood A, Menon M, **Rogers C**, and **Abdollah F**. Mortality and Additional Treatment Rates in Pathologically High-Risk Prostate Cancer With Prostate-Specific Antigen Persistence at Robot-Assisted Radical Prostatectomy: Long-Term Report From Single Tertiary Referral Center. *Prostate* 2025; Epub ahead of print. PMID: 40785187. Full Text

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BACKGROUND: Long-term cancer control efficacy of robotic-assisted laparoscopic prostatectomy (RALP) in men with pathologically high-risk prostate cancer and prostate-specific antigen (PSA) persistence remains poorly addressed in the literature. Our aim was to evaluate long-term survival and additional treatment (AT) rates in these individuals. METHODS: We included 803 patients who underwent RALP for pathologically high-risk PCa (pT ≥ 3a, pN0-1 or GG ≥ 4) between 2001 and 2022 at a single tertiary referral center (Henry Ford Hospital, Detroit). Patients without adequate information about PSA persistence were excluded from the analysis (n = 128). Kaplan-Meier curves estimated AT free-survival (ATFS) and all-cause mortality (ACM) free-survival, whereas the competing risk method was used to estimate cancer-specific mortality (CSM) free-survival, after stratification according to PSA persistence. Competing risk and Cox regression models tested the impact of PSA persistence on three endpoints: AT rates, CSM, and ACM. RESULTS: Our final cohort consisted of 675 who underwent RALP for pathologically high-risk PCa, 187 (27.7%) of whom had PSA persistence. The median age at surgery was 64 years (IQR 59-68), and the median follow-up duration was 75 months (IQR 33-125). Patients with PSA persistence were more likely to have higher PSA values at surgery (8 vs. 7 ng/mL, p < 0.001), pT3b-4 PCa (62.5% vs. 39.9%, p < 0.001), pN1 PCa (55.6% vs. 35.7%, p < 0.001), and positive surgical margins (PSMs) (65.2% vs. 43.4%, p < 0.001). Moreover, patients in the PSA persistence group had higher proportion undergoing only hormone therapy (HT) (24.1% vs. 11.9%, p < 0.001) and radiotherapy (RT) plus HT (50.8% vs. 31.1%, p < 0.001), reporting higher median PSA values at RT (0.6 vs. 0.2 ng/mL, p < 0.001), compared to patients with undetectable PSA. At 10 years after RALP, CSM-FS and ACM-FS

were 79.7% versus 90.3% (Gray-test p-value = 0.001) and 72.1% versus 79.6% (log-rank p-value = 0.013), for persistent versus undetectable PSA, respectively. The 10-year rates of ATFS were 6.6% versus 33.2% (log-rank p-value < 0.0001), for persistent versus undetectable PSA, respectively. At MVA, persistent PSA was associated with AT (HR: 3.05, p < 0.001), but not with CSM (HR: 1.49, p = 0.2) or ACM (HR: 1.09, p = 0.9). CONCLUSION: Patients with pathologically high-risk PCa and PSA persistence after RALP, despite being at greater hazard of AT (HT and/or RT), did not have less favorable cancer control outcomes at 10 years than their counterparts with undetectable PSA levels. Our report provides the longest follow-up after RALP for this subset of patients, making it a valuable resource for counseling patients on the long-term oncologic outcomes of this procedure and postoperative adjuvant/salvage therapies.

Public Health Sciences

Bossick AS, **Su WK**, **Abood J**, **Arruga Novoa YNV**, **Chamseddine P**, **Vilkins A**, and **Wegienka GR**. Trajectories and risk factors of depressive symptomatology following hysterectomy. *Menopause* 2025; Epub ahead of print. PMID: 40794489. Full Text

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OBJECTIVES: Hysterectomy is the second most common gynecological surgery performed on reproductive aged women in the United States. It is not known if some groups of women are more susceptible to depression after hysterectomy. METHODS: Participants were scheduled for hysterectomy for benign causes and not undergoing a concomitant urogynecological procedure. Patient Health Questionnaire-9 (PHQ-9) was collected 2 weeks before, and 1, 4, and 6 weeks, and 3, 6, and 12 months post-hysterectomy to understand depressive symptoms associated with surgery. PHQ-9 patterns were identified with latent class analyses. Multivariable multinomial logistic regression was used to estimate relative risk ratios (RRR) and 95% CIs of associations between baseline sociodemographic, clinical, and operative-related characteristics and PHQ-9 class. RESULTS: Three latent classes (C) were identified from their PHQ-9 score patterns among 455 participants: high and increasing (C1, 15.6%), high and decreasing (C2, 27.7%), and persistently low PHQ-9 trajectory (C3, 56.7%). Insurance type, financial toxicity, pain level, and surgical decision satisfaction before surgery were statistically significantly associated with class membership. At surgery, C1 members were more likely to have public insurance (RRR=2.04, CI: 1.02-4.08), worse finances (0.92, 0.89-0.96), and higher pain (1.22, 1.10-1.35) than members of C3. C2 members were more likely to have worse finances (0.94, 0.91-0.96) than C3 members. C1 members tended to have higher pain (1.14, 1.02-1.26) than C2 members. CONCLUSIONS: Depression symptomology after hysterectomy may be associated with presurgical insurance type, financial toxicity, current pain level, and satisfaction. More research is needed to investigate whether these factors can be incorporated into preoperative counseling and screening tools to guide shared decision-making regarding depression and surgery.

Public Health Sciences

Lindahl A, **Hill T**, **Mazier E**, **Patel M**, **Kahn G**, **Zhou Y**, and **Day CS**. "Patient-Specific" Cost and Quality Value Comparison of Endoscopic Carpal Tunnel Release in Two Surgical Settings. *J Hand Surg Glob Online* 2025;7(5):100802. PMID: 40837494. Full Text

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PURPOSE: Prior studies have demonstrated that transitioning surgeries from a hospital outpatient department (HOPD) to an ambulatory surgical center (ASC) lowers costs. With 500,000 carpal tunnel release (CTR) surgeries annually, CTR offers an opportunity to determine the value of one of the most

performed upper-extremity surgeries. We aim to quantify the value of an endoscopic CTR in a HOPD compared to an ASC by analyzing differences in costs and patient outcomes. We hypothesize the ASC will provide greater value by lowering costs while maintaining patient outcomes. METHODS: Total costs were comprised of time-driven activity-based labor costs (TDABC), activity-based supply costs, and claims-based facility costs. Differences in preoperative Patient-Reported Outcome Measure (PROM) Information System Upper Extremity (UE) and Pain Interference (PI) scores and 3-month postoperative PROM Information System UE and PI scores were calculated to determine PROM Information System Quality-Adjusted Life Years (QALY(UE/PI)). Total costs were divided by QALYs for each PROM to calculate the Value(UE/PI) of each cohort. The magnitude of the difference in value between cohorts was elucidated by calculating incremental cost-effectiveness ratios. RESULTS: A total of 25 patients comprised each cohort. The ASC generated 28% lower costs compared to the HOPD ($3,370.73 ± $128.80 vs $4,654.75 ± $140.19). Average QALY(UE) and QALY(PI) gain was not significantly greater for patients at the ASC compared to the HOPD (QALY(UE) 1.06 vs 0.89; QALY(PI) 1.22 vs 0.92). The ASC demonstrated 40% to 45% greater value, represented by a lower cost/QALYs, compared to the HOPD (Value(UE) $3,168.81/QALY vs $5,242.78/QALY, Value(PI) $2,759.90/QALY vs $5,038.04/QALY). CONCLUSIONS: We observed between 40% to 45% greater value by performing CTRs in the ASC. Although ASCs lowered costs by 28%, costs alone do not fully explain the value differential. Patient-reported outcomes serve a valuable role in providing a holistic picture of the value being delivered to patients. Providers can use this information to guide patient decision-making regarding operative treatment options for carpal tunnel syndrome. TYPE OF STUDY/LEVEL OF EVIDENCE: Economic/Decision Analysis II.

Public Health Sciences

Moore CM, Secor EA, Everman JL, Fairbanks-Mahnke A, Jackson N, Pruesse E, Diener K, Morin A, Arbes SJ, Bacharier LB, Bendixsen CG, Calatroni A, Dupont WD, Furuta GT, Gebretsadik T, Gruchalla RS, Gupta RS, Khurana Hershey GK, Kattan M, Liu AH, Lussier SJ, Murrison LB, Numata M, O'Connor GT, River-Spoljaric K, Phipatanakul W, Rothenberg ME, Seroogy CM, **Zoratti EM**, Castina S, Jackson DJ, Camargo CA, Jr., **Johnson CC**, Ethridge R, Ramratnam S, Stelzig L, Teach SJ, Togias AG, Fulkerson PC, Hartert TV, and Seibold MA. The common cold is associated with protection from SARS-CoV-2 Infections. *J Infect Dis* 2025; Epub ahead of print. PMID: 40795882. Full Text

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BACKGROUND: Adults and children often respond differently to SARS-CoV-2 infection, with adults facing a higher risk of symptomatic and severe illness. We hypothesize that children's protection from symptomatic SARS-CoV-2 may be due to more frequent respiratory viral infections, which prime their airway antiviral defenses. METHODS: Using case-cohort and case-control analyses in the Human Epidemiology and Response to SARS-CoV-2 cohort, we evaluated whether infection with common respiratory viruses protects against SARS-CoV-2 infections and investigated airway molecular mechanisms by which this protection is achieved. We tested 10,493 longitudinal nasal swabs from 1,156 participants for 21 respiratory pathogens. We performed RNA-sequencing on 147 swabs (N=144 participants) collected prior SARS-CoV-2 infection and 391 swabs (N=165 participants) during and before rhinovirus infection. RESULTS: Participants with rhinovirus infection in the previous 30 days were at 48% lower risk of SARS-CoV-2 infection (aHR:0.52, p=0.034). Among participants with SARS-CoV-2 infection, recent rhinovirus infection was associated with 9.6-fold lower SARS-CoV-2 viral load (p=0.0031). Higher pre-infection expression of 57 genes was associated with lower SARS-CoV-2 viral load, including 24 antiviral defense genes; 22 of these were induced by rhinovirus infections. Relative to adults, children expressed higher levels of the antiviral gene signature (p=0.014) and were at 2.2-fold increased risk for rhinovirus infections. CONCLUSIONS: Rhinovirus infections, which trigger increased expression of antiviral airway genes, are linked to a lower risk of SARS-CoV-2 infection. Frequent rhinovirus infections may enhance this protective gene profile, partially explaining why children experience milder SARS-CoV-2 infections compared to adults. TRIAL REGISTRATION NUMBER: NCT04375761.

Public Health Sciences

Nematullah M, **Fatma M**, Zhou G, Prajapati B, **Rashid F**, **Ayasolla K**, **Ahmed ME**, **She R**, **Mir S**, **Zahoor I**, **Hoda N**, **Rattan R**, and **Giri S**. Immune-responsive gene 1: The mitochondrial key to Th17 cell pathogenicity in CNS autoimmunity. *Proc Natl Acad Sci U S A* 2025;122(32):e2427052122. PMID: 40758870. Full Text

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Pathogenic Th17 cells play crucial roles in CNS autoimmune diseases such as multiple sclerosis (MS), but their regulation by endogenous mechanisms remains unknown. Through RNA-seq analysis of primary brain glial cells, we identified immune-responsive gene 1 (Irg1) as one of the highly upregulated genes under inflammatory conditions. Validation in the spinal cords of animals with experimental autoimmune encephalomyelitis (EAE), a preclinical MS model, confirmed elevated Irg1 levels in myeloid, CD4, and B cells in the EAE group, raising concerns as to whether Irg1 is detrimental or protective. Irg1 knockout (KO) mice exhibited severe EAE disease, increased mononuclear cell infiltration, and increased levels of triple-positive CD4+ T cells expressing IL17a, GM-CSF, and IFNγ. Adoptive transfer in Rag-1 KO and single-cell RNA sequencing highlighted the crucial role of Irg1 in shaping pathogenic Th17 cells. A lack of Irg1 in macrophages elevates Class II expression, promoting the polarization of myelin-primed CD4+ T cells into pathogenic Th17 cells via the NLRP3/IL-1β axis. Moreover, bone marrow chimeras revealed

that immune cells lacking Irg1 maintained pathogenic and inflammatory phenotypes, suggesting its protective role in autoimmune diseases, including MS.

Public Health Sciences
Orrego Villegas S, **Adjei Boakye E**, Arrieta J, Posada España K, Vanegas MN, and Prado Pinto G. Perspectives of healthcare providers on telemedicine implementation during the COVID-19 pandemic in Colombia: a mixed-method study. *Front Public Health* 2025;13:1643085. PMID: 40823239. Full Text

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BACKGROUND: The COVID-19 pandemic accelerated the adoption of telemedicine (TM) in Colombia as a tool for delivering healthcare for both chronic and non-chronic conditions. This study aimed to explore the perspectives of healthcare providers, directors, and managers on TM implementation within a major health plan provider covering 15% of the Colombia population. METHODS: Mixed-methods study was conducted, combining surveys and in-depth interviews with medical professionals and decision-makers. Thematic analysis of qualitative data and statistical analysis of survey responses provided insights into the challenges and opportunities of TM during the pandemic. RESULTS: Healthcare providers recognized TM as a valuable tool but identified key challenges to its optimization. Three main strategies were proposed: (1) enhancing medical training to improve remote diagnosis, (2) integrating wearables and digital technologies to support clinical decision-making, and (3) fostering a culture of TM use among patients and providers to ensure acceptance and sustainability. CONCLUSION: Telemedicine facilitated equitable healthcare delivery and contributed to reducing the digital gap in Colombia. However, to ensure long-term viability, national policies must improve internet connectivity and strengthen primary care infrastructure, particularly in underserved regions.

Public Health Sciences
Pflaum-Carlson J, **Redding A**, **Murphy D**, **MacLean L**, **Hamilton J**, and **Santarossa S**. Recruitment, retention and recouperation: lessons learned from a study aimed at assessing burnout mitigation in physician learners. *BMC Res Notes* 2025;18(1):376. PMID: 40890847. Full Text

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Public Health Sciences
Qadir H, **Palathingal Bava E**, **Gomez-Gelvez J**, **Liu W**, **Inamdar K**, **Wey E**, **Carey J**, **Shen Y**, **Kuriakose P**, and **Ghosh S**. BCL2-Rearrangment-Negative CD23+ Follicle Center Lymphoma and Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: A Rare Case of Biclonal Composite Lymphoma. *Cureus* 2025;17(7):e88727. PMID: 40861583. Full Text

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Composite lymphomas are rare and diagnostically complex, comprising two or more distinct lymphoma subtypes within the same anatomical site and often requiring a comprehensive diagnostic approach. Due to their rarity and varied presentations, further research is needed to better understand their pathogenesis, clonal relationships, and optimal management strategies. This case report highlights an unusual presentation of composite lymphoma involving the coexistence of BCL2-R-negative, CD23-positive follicle center lymphoma and chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).

Public Health Sciences

Schildroth S, Gaston SA, Harmon QE, Jackson CL, Wesselink AK, **Wegienka G**, Baird DD, and Wise Sc ML. A Prospective Study of Hair Dyes and Uterine Leiomyomata Incidence in the Study of Environment, Lifestyle, and Fibroids. *Fertil Steril* 2025; Epub ahead of print. PMID: 40783167. Full Text

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OBJECTIVE: To investigate associations between hair dye use and incident uterine leiomyomata (fibroids) among Black participants from the Study of Environment, Lifestyle, and Fibroids. DESIGN: Prospective cohort study. SUBJECTS: Reproductive-aged (26-39 years) individuals with an intact uterus residing in the Detroit, Michigan area (n=868). EXPOSURE: Self-reported hair dye use (any use vs. no use) in the previous 12 months queried on structured questionnaires. MAIN OUTCOME MEASURES: Fibroid incidence assessed by trans-vaginal ultrasounds. We fit Cox proportional hazard models to estimate hazard ratios (HRs) with 95% confidence intervals (CIs), adjusting for age, time on study, educational attainment, annual household income, occupational status, body mass index, age at menarche, parity, use of progestin-only injectable contraceptives within the past two years, alcohol consumption, and smoking status. RESULTS: One hundred and forty-nine incident fibroid cases were identified over 3,458 person-years of follow-up. After adjustment for confounders, use of any hair dye product (HR=1.44; 95% CI=0.91, 2.26) and rinses that fade (HR=1.98; 95% CI=1.04, 3.79) in the previous 12 months was associated with increased fibroid risk, compared with no use, though associations were generally imprecise. CONCLUSION: In this cohort, use of hair dye products was modestly associated with greater fibroid risk, which has important public health implications.

Public Health Sciences

So KC, Stolz L, Fam N, Ong G, Cheung A, Boone R, **Villablanca P**, **Jabri A**, Lam YY, Tchétché D, Oliva O, De Backer O, Møllller JE, Latib A, Scotti A, Coisne A, Sudre A, Dreyfus J, Nejjari M, Favre PE, Cruz-Gonzalez I, Estévez-Loureiro R, Barreiro-Perez M, Makkar R, Patel D, Leurent G, Donal E, Modine T, and Hausleiter J. Transjugular Transcatheter Tricuspid Valve Replacement in Patients With Cardiac Implantable Electronic Devices. *JACC Asia* 2025; Epub ahead of print. PMID: 40884522. Full Text

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BACKGROUND: Cardiac implantable electronic device (CIED)-related tricuspid regurgitation (TR) is common. Transcatheter tricuspid valve replacement (TTVR) is feasible with CIEDs in the right ventricle; however, data in this population are limited. OBJECTIVES: This study retrospectively analyzed patients undergoing compassionate-use transjugular TTVR with the LuX-Valve Plus for symptomatic TR with CIEDs from January 2022 to August 2024 at 17 international centers. METHODS: The primary endpoint was procedural TR reduction. Secondary endpoints included TR reduction, survival at 30 days, New York Heart Association functional class changes, and CIED function at follow-up. Non-CIED group was used for comparison. RESULTS: Of 99 patients, 36 (36.4%) had CIEDs. Baseline characteristics were similar, though the CIED group had a higher EuroSCORE (European System for Cardiac Operative Risk Evaluation) II score and more comorbidities. Procedural success (CIED vs non-CIED: 91.7% vs 95.2%; P = 0.781), 30-day mortality (5.6% vs 4.8%; P > 0.999), TR reduction (≤1+: 83.8% vs 84.9%; P > 0.999), and NYHA functional class I/II (80.8% vs 83.7%; P = 0.89) were comparable. The CIED cohort exhibited a higher numerical incidence of conversion to surgery (8.3% vs 1.6%) and tricuspid reintervention (11.5% vs 3.3%) within 6 months; however, these differences did not reach statistical significance (P = 0.267 and P = 0.160, respectively). Of the 22 patients with postoperative interrogation (median of 3.3 months), 9.1% of CIED patients exhibited worsening device parameters, with no need for lead replacement or extraction. CONCLUSIONS: Transjugular TTVR is safe and effective for managing TR and heart failure in patients

with CIEDs. Due to the small sample size, these findings highlight the need for larger, prospective studies to validate these outcomes.

Public Health Sciences
Stolz L, Fam N, Ong G, **Villablanca P**, **Jabri A**, de Backer O, Møllller JE, Tchétché D, Oliva O, So KC, Lam YY, Latib A, Scotti A, Coisne A, Sudre A, Dreyfus J, Nejjari M, Cruz-Gonzalez I, Estévez-Loureiro R, Barreiro-Perez M, Leurent G, Donal E, Bonnet G, Modine T, Makkar R, Patel D, Kresoja KP, Lurz P, and Hausleiter J. Transcatheter tricuspid valve replacement using the LuX-Valve Plus system: 1-year compassionate use outcomes. *Eur J Heart Fail* 2025; Epub ahead of print. PMID: 40879890. Full Text

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Public Health Sciences
Surie D, Self WH, Yuengling KA, Lauring AS, Zhu Y, Safdar B, Ginde AA, Simon SJ, Peltan ID, Brown SM, Gaglani M, Ghamande S, Columbus C, Mohr NM, Gibbs KW, Hager DN, Prekker M, Gong MN, Mohamed A, Johnson NJ, Steingrub JS, Khan A, Duggal A, Gordon AJ, Qadir N, Chang SY, Mallow C, Felzer JR, Kwon JH, Exline MC, **Vaughn IA**, **Ramesh M**, Papalambros L, Mosier JM, Harris ES, Baughman A, Cornelison SA, Blair PW, Johnson CA, Lewis NM, Ellington S, Grijalva CG, Talbot HK, Casey JD, Halasa N, Chappell JD, Rutkowski RE, Ma KC, and Dawood FS. RSV Vaccine Effectiveness Against Hospitalization Among US Adults Aged 60 Years or Older During 2 Seasons. *JAMA* 2025; Epub ahead of print. PMID: 40884491. Full Text

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IMPORTANCE: Respiratory syncytial virus (RSV) vaccines for adults aged 60 years or older became available in 2023. One dose is recommended for all adults aged 75 years or older and those aged 60 to 74 years at increased risk of severe RSV; however, duration of protection is unknown. OBJECTIVE: To evaluate RSV vaccine effectiveness against RSV-associated hospitalization among adults aged 60 years or older during 2 RSV seasons. DESIGN, SETTING, AND PARTICIPANTS: A total of 6958 adults aged 60 years or older were included in this test-negative, case-control study if they were hospitalized with acute respiratory illness at any of 26 hospitals in 20 US states during the October 1, 2023, to March 31, 2024, or October 1, 2024, to April 30, 2025, RSV seasons and had respiratory virus testing within 10 days of illness onset. Case patients tested positive for RSV only; control patients tested negative for RSV, SARS-CoV-2, and influenza. Demographic and clinical data were obtained through patient interview and electronic health records. EXPOSURES: Receipt of 1 RSV vaccine dose at least 14 days before illness onset. MAIN OUTCOMES AND MEASURES: Multivariable logistic regression was used to compare the odds of RSV vaccination among hospitalized cases and controls. Models were adjusted for age, sex, race and ethnicity, geographic region, and calendar month and year. Vaccine effectiveness was estimated as (1 - adjusted odds ratio) × 100%. Analyses were stratified by timing of RSV vaccine receipt (same vs prior season) relative to illness onset. RESULTS: Of 6958 adults aged 60 years or older, 821 (11.8%) were RSV cases and 6137 (88.2%) were controls. A total of 1438 patients were Black (20.1%) and 4314 were White (62.0%); 3534 were female (50.8%). Median age was 72 years (IQR, 66-80 years) and 1829 adults (26.3%) were immunocompromised. A total of 63 cases (7.7%) and 966 controls (15.7%) were

vaccinated. Estimated vaccine effectiveness against RSV-associated hospitalization was 58% (95% CI, 45%-68%) during 2 seasons and 69% (95% CI, 52%-81%) for same-season vaccination vs 48% (95% CI, 27%-63%; P = .06) for prior-season vaccination. Estimated vaccine effectiveness during 2 seasons was significantly lower among immunocompromised adults (30%; 95% CI, -9% to 55%) than immunocompetent adults (67%; 95% CI, 53%-77%; P = .02) and among those with cardiovascular disease (56%; 95% CI, 32%-72%) vs without (80%; 95% CI, 62%-90%; P = .03). CONCLUSIONS AND RELEVANCE: Respiratory syncytial virus vaccines prevented RSV-associated hospitalization during 2 seasons, although effectiveness was lower in patients with immunocompromise and cardiovascular disease than in those without these conditions. Ongoing monitoring is needed to determine the optimal RSV revaccination interval.

Public Health Sciences

Tao MH, **Wu T**, **Gordon SC**, **Zhou Y**, **Rupp LB**, **Trudeau S**, Schmidt MA, Daida YG, and **Lu M**. Antiviral treatment Reduces Risk of Development of Lung Cancer and non-Hodgkin Lymphoma in Patients with Chronic Hepatitis C. *Cancer Epidemiol Biomarkers Prev* 2025; Epub ahead of print. PMID: 40874910. Full Text

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BACKGROUND: Antiviral treatment for hepatitis C virus (HCV) has been shown to reduce risk of liver cancer, but there are few studies on its impact on the risk of non-liver cancers. We used a large cohort of HCV patients with extensive follow-up to investigate whether receipt of antiviral therapy affects the risk of extrahepatic cancers. METHODS: 17,485 HCV patients were followed until incidence of lung cancer, non-Hodgkin lymphoma (NHL), breast or prostate cancer, death, or last follow-up. We used multivariable modeling with time-varying covariates and propensity scores to adjust for treatment selection bias; we also applied generalized estimating equations (GEE) with a multinominal link function for discrete time-to-event data. Death was considered a competing risk. RESULTS: After 15 years of follow-up, we identified 408 incident cases of cancers, including 140 lung, 72 NHL, 81 breast (female), and 115 prostate. Compared to no treatment, patients who receive either direct-acting antivirals (DAA) or interferon-based (IFN) treatment had significantly lower risk of lung cancer (hazard ratio [HR]= 0.35, 95% CI 0.24-0.52 for achieving sustained virological response [SVR]; HR= 0.34, 95% CI 0.21-0.55 for treatment failure). Risk of NHL was reduced only among patients who achieved SVR. There were no significant associations between antiviral therapy and risks of breast and prostate cancer. CONCLUSIONS: Antiviral treatment for HCV independently reduced the risk of lung cancer, while the protective association with NHL was limited to patients achieving SVRs. IMPACT: Our findings support the importance of timely initiation antiviral therapy in patients with chronic HCV.

Radiation Oncology

Runge CL, Lyness JA, Gillison ML, Adelstein DJ, Harari PM, Ringash J, Geiger JL, Krempl GA, Blakaj DM, Bates JE, Galloway TJ, Jones CU, Gensheimer MF, Dunlap NE, Phan J, Caudell JJ, Pennington JD, Torres-Saavedra PA, Yom SS, Le QT, and **Movsas B**. Self-Perceived Hearing Outcomes with Radiation and Cisplatin or Radiation and Cetuximab for Patients with HPV-Positive Oropharyngeal Cancer - Results from xxxxx. *Int J Radiat Oncol Biol Phys* 2025; Epub ahead of print. PMID: 40829719. Full Text

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PURPOSE: xxxx was a noninferiority phase 3 trial comparing the efficacy of radiation with either cisplatin (RT+Cis) or cetuximab (RT+Cetux) for patients with HPV+ oropharyngeal cancer (OPC). Perceived hearing handicap was included as a patient reported outcome (PRO) secondary endpoint. The primary hypothesis was that perceived hearing handicap would be greater for patients receiving RT+Cis compared to RT+Cetux. METHODS AND MATERIALS: Perceived hearing handicap was measured at baseline, end of treatment, 3-, 6-, and 12-months post-treatment using the Hearing Handicap Inventory for Adults Screening Version (HHIA-S), a 10-item self-assessment questionnaire designed to measure patients' reactions to their hearing loss. Mixed ordinal logistic models were used to determine the treatment effect on HHIA-S scores and handicap categories (0.05 two-sided alpha). RESULTS: The PRO substudy included 375 eligible patients. No significant differences in patient/tumor characteristics were found between patients who participated in the HHIA-S study vs those excluded. For total HHIA-S scores and social and emotional subscales, RT+Cetux had significantly lower (i.e., better) scores from end of treatment. Change score from baseline to end of treatment for RT+Cis (4.32, 95% CI [2.57, 6.07]) was greater than RT+Cetux (0.08, 95% CI [-1.15, 1.31]). For hearing handicap category, RT+Cis had a significantly higher percentage of mild/moderate and severe cases at the end of treatment (32%) compared to RT+Cetux (20%) (p<.0001). Adjusted conditional odds of higher self-perceived hearing handicap category for RT+Cis compared to RT+Cetux was 3.73 (95% CI [2.10, 6.62]). CONCLUSION: Patients have significantly worse self-perceived hearing handicap after receiving RT+Cis treatment than with RT+Cetux. This was consistent across time through one-year post-treatment. These findings inform hearing-related outcomes for patients with HPV-associated OPC and indicate the need for ototoxicity monitoring with RT+Cis treatment.

Radiation Oncology
Shukla ME, Misono S, Amini A, Sieracki R, Takiar V, Ward MC, Bakst R, Chandra RA, **Chang SS**, Choi K, Galloway T, Hu KS, Robbins JR, **Siddiqui F**, Walker G, Witek ME, and Margalit DN. Executive Summary of the American Radium Society Appropriate Use Criteria for Management of Early Glottic Cancer: A Review. *JAMA Otolaryngol Head Neck Surg* 2025; Epub ahead of print. PMID: 40875219. Full Text

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IMPORTANCE: Stage I squamous cell carcinoma (SCC) of the glottic larynx carries a favorable prognosis after treatment with endoscopic surgery or radiation therapy (RT). In addition to tumor control, goals of therapy include preservation of voice quality, swallow function, and breathing. Multidisciplinary consensus guidelines are needed to assist clinicians in treatment selection and the appropriate use of both surgical and radiation-based techniques. OBSERVATIONS: Treatment of clinical T1N0 glottic SCC has evolved over time, with advances in both transoral laser microsurgery and RT designed to become more targeted and reduce the overall treatment burden for patients. When selecting a treatment option, consideration should be given to patient-specific factors, including tumor position/extent, age, and medical and psychosocial factors. This 16-member multidisciplinary American Radium Society (ARS) Head and Neck Cancer Appropriate Use Criteria (AUC) expert panel performed a review of the English-language medical literature from 2000 to 2022 to inform consensus guidelines. Clinical case variants were developed to represent commonly encountered clinical scenarios, and the RAND/UCLA appropriateness method was used to rate the appropriate use of various treatments. The modified Delphi method was used to reach consensus recommendations, which were approved by the ARS Executive Committee and subject to public comment per established ARS procedures. CONCLUSIONS AND RELEVANCE: Given the range of treatment options available, early glottic SCC management should be done in a multidisciplinary fashion including otolaryngologists and radiation oncologists. The ARS Head and Neck AUC expert panel created an appropriate-use consensus document by performing a literature review of the current treatment strategies for stage I glottic SCC, providing recommendations regarding the appropriateness of surgery or RT for various clinical scenarios and highlighting areas of controversy and uncertainty.

Radiation Oncology
Snyder KC, **DiCarlo A**, **Huang J**, **Zhao B**, **Huang Y**, and **Thind K**. Optimizing lung SBRT delivery: A hybrid approach combining dynamic conformal arc (DCA) and volumetric modulated arc therapy (VMAT) techniques. *J Appl Clin Med Phys* 2025;26(9):e70217. PMID: 40841188. Full Text

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PURPOSE: This study introduces and evaluates a hybrid dynamic conformal arc-volumetric modulated arc therapy (hDCA-VMAT) technique for lung stereotactic body radiotherapy (SBRT). The goal is to combine the planning efficiency of VMAT with the delivery robustness of dynamic conformal arc (DCA) techniques, particularly for low-density lung targets where motion and dose calculation uncertainties pose challenges. METHODS: Twenty-four previously treated lung SBRT cases were retrospectively replanned using hDCA-VMAT, conventional VMAT, and aperture controlled VMAT (VMAT_AC). hDCA-VMAT plans were initiated with a manually created DCA plan, followed by limited inverse optimization with constrained aperture modulation. Plans were created in Eclipse v16.1 and calculated using the AcurosXB algorithm. Dosimetric plan quality, beam complexity, and delivery efficiency were assessed. Complexity was quantified using aperture-based metrics (e.g., average leaf pair opening, beam area, modulation index). Pretreatment delivery accuracy was evaluated via EPID-based gamma analysis at 3%/1, 2%/1, and 1%/1 mm Gamma criteria. RESULTS: All techniques produced clinically acceptable plans. Target coverage and conformity indices were comparable, but hDCA-VMAT plans demonstrated reduced mid-dose spread and significantly lower modulation. hDCA-VMAT achieved the lowest modulation factor (2.1 ± 0.52) and shortest beam on time (1.74 ± 0.46 min), a 27%-30% reduction compared to VMAT and VMAT_AC. Beam complexity metrics confirmed larger, more circular apertures for hDCA-VMAT. Gamma pass rates were significantly higher for hDCA-VMAT across all criteria, particularly under stringent 1%/1 mm criteria. CONCLUSION: The hDCA-VMAT technique offers a practical, streamlined approach for lung SBRT planning that reduces modulation while maintaining high plan quality. By initiating with a DCA plan and applying limited optimization only when necessary, hDCA-VMAT minimizes planning complexity and improves delivery efficiency. These benefits are especially relevant for treating low-density lung tumors, where robustness to motion and delivery accuracy are critical.

Rehabilitation Services/Physical Therapy/Occupational Health
Wilson CM, **Boright LE**, Henshaw AM, and Naccarato A. Role of rehabilitation in palliative care after the COVID-19 pandemic: a narrative review. *Ann Palliat Med* 2025;14(4):379-392. PMID: 40769733. Full Text

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BACKGROUND AND OBJECTIVE: The coronavirus disease 2019 (COVID-19) pandemic resulted in an historic disruption and transformation of the healthcare system, including the management of individuals with serious illness. Rehabilitation for patients facing serious or life-threatening illness is underutilized and poorly understood, resulting in unwarranted suffering, disability, and poorly coordinated care. This narrative review aims to describe the impact of the COVID-19 pandemic on the role and scope of rehabilitation within the context of serious illness and palliative care. METHODS: A focused review of the literature included selected articles identified from three databases published from January 2020 to January 2025. Findings were synthesized narratively, with a focus on identifying themes and gaps in the literature related to two main topics: (I) the evidence related to rehabilitation for those with serious or life-threatening COVID-19 during the pandemic and (II) how rehabilitation for patients with serious illness has been transformed after emerging from the pandemic (including non-COVID diagnoses such as cancer, neurologic conditions, etc.). KEY CONTENT AND FINDINGS: The key themes identified during the COVID-19 pandemic emphasized the need for early rehabilitation, interdisciplinary care, and an emphasis on cardiopulmonary principles for rehabilitation. Themes identified during the pandemic also included the emerging role of telerehabilitation, and need for evidence and clinical guidelines for serious illnesses (including long COVID). Themes related to the transformative effect on palliative rehabilitation after the pandemic included an increased importance and focus on coordination of care and interdisciplinary care for those with serious illness and increased focus on mental health and social determinants of health (SDOH). Additionally, there appears to be increased infrastructure and activity related to research, advocacy, and awareness for palliative rehabilitation. CONCLUSIONS: The COVID-19 global pandemic highlighted the need for high quality, coordinated palliative care, including rehabilitation services, for patients facing a serious or life-threatening illness. Due to the benefits to a person's quality of life (QoL), dignity, and comfort, there is increasing evidence of the importance of seamless, ongoing access to rehabilitation services for patients with serious illness.

Rehabilitation Services/Physical Therapy/Occupational Health
Wu B, **Yang M**, Hu D, **Zhang R**, **Liu B**, **Hochstadt S**, **Lanfear DE**, Witonsky J, Kumar R, Hollenbach JA, Burchard EG, Ziv E, and **Williams LK**. HLA variation associated with peanut allergy and anaphylaxis among non-Hispanic Black individuals. *J Allergy Clin Immunol Glob* 2025;4(3):100485. PMID: 40476093. Full Text

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BACKGROUND: Peanut is a major cause of food allergy. HLA genes have been consistently associated with peanut allergy in association studies. To date, however, there have been very few genetic studies of

peanut allergy in non-Hispanic Black (Black) individuals, a group disproportionately affected by food allergy. OBJECTIVE: Our aim was to study the relationship between HLA alleles and peanut allergy among Black individuals. METHODS: The analysis consisted of Black participants from the Study of Asthma-Related Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE), a large cohort of individuals from metropolitan Detroit. At the time of enrollment, participants provided detailed food allergy histories, including symptoms. Four-digit resolution HLA allele calls were made using whole genome sequence data. RESULTS: The cases consisted of 119 individuals with reported peanut allergy and 59 individuals with peanut-related anaphylaxis; the comparison group consisted of 2640 individuals without reported food allergy. HLA-DRB1∗13:02 was the most significant allele associated with peanut allergy (adjusted odds ratio = 1.94 [95% CI = 1.28-2.93]), and HLA-DQA1∗01:02 was the top association with peanut-related anaphylaxis (aOR = 1.67 [95% CI = 1.14-2.44]). Amino acid polymorphisms at position 71 in the binding groove of HLA-DRB1 were associated with peanut allergy and estimated to affect peanut allergen binding affinity. CONCLUSIONS: In a cohort of Black individuals, this study independently identified the same associations of peanut allergy and HLA that were previously observed in non-Hispanic White individuals. Our findings suggest that specific HLA binding groove amino acid polymorphisms may confer similar peanut allergy risk across population groups and HLA alleles.

Research Administration

Chen J, Ngo A, Rodriguez-Cruces R, Royer J, Caligiuri ME, Gambardella A, Concha L, Keller SS, Cendes F, Yasuda CL, Alvim MKM, Bonilha L, Gleichgerrcht E, Focke NK, Kreilkamp BAK, Domin M, Von Podewils F, Langner S, Rummel C, Wiest R, Martin P, Kotikalapudi R, Bender B, O'Brien TJ, Sinclair B, Vivash L, Kwan P, Desmond P, Lui E, Duma GM, Bonanni P, Ballerini A, Vaudano AE, Meletti S, Tondelli M, Alhusaini S, Doherty CP, Cavalleri G, Delanty N, Kalviainen R, Jackson GD, Kowalczyk M, Mascalchi M, Semmelroch M, Thomas RH, **Soltanian-Zadeh H**, **Davoodi-Bojd E**, Zhang J, Lenge M, Guerrini R, Bartolini E, Hamandi K, Foley S, Rüber T, Bauer T, Weber B, Caldairou B, Depondt C, Absil J, Carr SJA, Abela E, Richardson MP, Devinsky O, Pardoe HR, Severino M, Striano P, Tortora D, Kaestner E, Hatton SN, Arienzo D, Vos SB, Ryten M, Taylor PN, Duncan JS, Whelan CD, Galovic M, Winston GP, Thomopoulos SI, Thompson PM, Sisodiya SM, Labate A, McDonald C, Caciagli L, Bernasconi N, Bernasconi A, Lariviere S, Schrader DV, and Bernhardt BC. Changes in Gray Matter Morphology and White Matter Microstructure Across the Adult Lifespan in People With Temporal Lobe Epilepsy. *Neurology* 2025;105(6):e213688. PMID: 40845263. Full Text

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BACKGROUND AND OBJECTIVES: Temporal lobe epilepsy (TLE) is commonly associated with mesiotemporal pathology and widespread alterations of gray and white matter structures. Evidence supports a progressive condition, although the temporal evolution of TLE is poorly defined. In this ENIGMA-Epilepsy study, we aim to investigate structural alterations in gray and white matter across the adult lifespan in patients with TLE by charting both gray and white matter changes and explore the covariance of age-related alterations in both compartments. METHODS: Mega-analysis of parcellated T1-weighted and diffusion MRI data across 18 international sites for patients with TLE was compared against healthy controls. We combined median-age split groupwise comparisons with cross-sectional sliding age-window analyses to explore gray (cortical thickness, subcortical volume) and white matter microstructure (fractional anisotropy, mean diffusivity) age-related changes. Five-year range age windows were constructed from mean z scores of all patients. Covariance analyses examined the coupled correlations of gray and white matter lifespan curves for each region. RESULTS: We studied 769 patients with TLE and 885 healthy controls across an age range of 17-73 years. Robust ($p(FDR) < 0.05$) gray matter thickness/volume decline ($d < -0.20$) was seen across a broad cortico-subcortical territory, extending beyond the mesiotemporal lobe throughout the adult lifespan in patients with TLE. White matter changes were also widespread across multiple fiber tracts with peak effects in temporolimbic fibers in fractional anisotropy ($d < -0.3$, $p(FDR) < 0.05$) and mean diffusivity measures ($d > 0.3$, $p(FDR) < 0.05$). Changes spanned the adult time window and effects exceeded typical aging-related processes in patients at the level of cortical thickness, subcortical volume, and diffusion measures, particularly in patients older than 55 years. Covariance analyses revealed strong associations across multiple white matter tracts, subcortical structures, and cortical regions within and beyond the temporolimbic system. DISCUSSION: This study highlights that patients with TLE exhibit more pronounced and widespread gray and white matter atrophy across the lifespan. The cross-sectional nature of our study limits definitive conclusions on whether the atrophy shown is progressive but emphasizes the importance of prompt diagnosis and intervention in patients. Collectively, our results motivate future longitudinal studies to clarify consequences of drug-resistant epilepsy.

Research Administration

Ngo A, Liu L, Larivière S, Kebets V, Fett S, Weber CF, Royer J, Yu E, Rodríguez-Cruces R, Zhang Z, Ooi LQR, Yeo BTT, Frauscher B, Paquola C, Caligiuri ME, Gambardella A, Concha L, Keller SS, Cendes F, Yasuda CL, Bonilha L, Gleichgerrcht E, Focke NK, Kotikalapudi R, O'Brien TJ, Sinclair B, Vivash L, Desmond PM, Lui E, Vaudano AE, Meletti S, Kälviäinen R, **Soltanian-Zadeh H**, Winston GP, Tiwari VK, Kreilkamp BAK, Lenge M, Guerrini R, Hamandi K, Rüber T, Bauer T, Devinsky O, Striano P, Kaestner E, Hatton SN, Caciagli L, Kirschner M, Duncan JS, Thompson PM, McDonald CR, Sisodiya SM, Bernasconi N, Bernasconi A, Gan-Or Z, and Bernhardt BC. Associations between epilepsy-related polygenic risk and brain morphology in childhood. *Brain* 2025; Epub ahead of print. PMID: 40811581. Full Text

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Extensive neuroimaging research in temporal lobe epilepsy with hippocampal sclerosis (TLE-HS) has identified brain atrophy as a disease phenotype. While it is also related to a complex genetic architecture, the transition from genetic risk factors to brain vulnerabilities remains unclear. Using a population-based approach, we examined the associations between epilepsy-related polygenic risk for HS (PRS-HS) and brain structure in healthy developing children, assessed their relation to brain network architecture, and evaluated its correspondence with case-control findings in TLE-HS diagnosed patients relative to healthy individuals We used genome-wide genotyping and structural T1-weighted magnetic resonance imaging (MRI) of 3,826 neurotypical children from the Adolescent Brain Cognitive Development (ABCD) study. Surface-based linear models related PRS-HS to cortical thickness measures, and subsequently contextualized findings with structural and functional network architecture based on epicentre mapping approaches. Imaging-genetic associations were then correlated to atrophy and disease epicentres in 785 patients with TLE-HS relative to 1,512 healthy controls aggregated across multiple sites. Higher PRS-HS was associated with decreases in cortical thickness across temporo-parietal as well as fronto-central regions of neurotypical children. These imaging-genetic effects were anchored to the connectivity profiles of distinct functional and structural epicentres. Compared with disease-related alterations from a separate epilepsy cohort, regional and network correlates of PRS-HS strongly mirrored cortical atrophy and disease epicentres observed in patients with TLE-HS, and highly replicable across different studies. Findings were consistent when using statistical models controlling for spatial autocorrelations and robust to variations in analytic methods. Capitalizing on recent imaging-genetic initiatives, our study provides novel insights into the genetic underpinnings of structural alterations in TLE-HS, revealing common morphological and network pathways between genetic vulnerability and disease mechanisms. These signatures offer a foundation for early risk stratification and personalized interventions targeting genetic profiles in epilepsy.

Research Administration

Wu B, **Yang M**, Hu D, **Zhang R**, **Liu B**, **Hochstadt S**, **Lanfear DE**, Witonsky J, Kumar R, Hollenbach JA, Burchard EG, Ziv E, and **Williams LK**. HLA variation associated with peanut allergy and anaphylaxis among non-Hispanic Black individuals. *J Allergy Clin Immunol Glob* 2025;4(3):100485. PMID: 40476093. Full Text

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BACKGROUND: Peanut is a major cause of food allergy. HLA genes have been consistently associated with peanut allergy in association studies. To date, however, there have been very few genetic studies of peanut allergy in non-Hispanic Black (Black) individuals, a group disproportionately affected by food allergy. OBJECTIVE: Our aim was to study the relationship between HLA alleles and peanut allergy among Black individuals. METHODS: The analysis consisted of Black participants from the Study of Asthma-Related Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE), a large cohort of individuals from metropolitan Detroit. At the time of enrollment, participants provided detailed

food allergy histories, including symptoms. Four-digit resolution HLA allele calls were made using whole genome sequence data. RESULTS: The cases consisted of 119 individuals with reported peanut allergy and 59 individuals with peanut-related anaphylaxis; the comparison group consisted of 2640 individuals without reported food allergy. HLA-DRB1∗13:02 was the most significant allele associated with peanut allergy (adjusted odds ratio = 1.94 [95% CI = 1.28-2.93]), and HLA-DQA1∗01:02 was the top association with peanut-related anaphylaxis (aOR = 1.67 [95% CI = 1.14-2.44]). Amino acid polymorphisms at position 71 in the binding groove of HLA-DRB1 were associated with peanut allergy and estimated to affect peanut allergen binding affinity. CONCLUSIONS: In a cohort of Black individuals, this study independently identified the same associations of peanut allergy and HLA that were previously observed in non-Hispanic White individuals. Our findings suggest that specific HLA binding groove amino acid polymorphisms may confer similar peanut allergy risk across population groups and HLA alleles.

Research Administration

Zhang R, **Liu B**, **Yang M**, **Wu B**, **Hochstadt S**, **Lanfear DE**, Witonsky J, Kumar R, Burchard EG, Ziv E, and **Williams LK**. Socioenvironmental factors associated with shrimp allergy and shrimp sensitization in a large and diverse patient population and cohort study from metropolitan Detroit. *J Allergy Clin Immunol Glob* 2025;4(3):100492. PMID: 40502543. Full Text

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BACKGROUND: Earlier studies have demonstrated significant differences in food allergy by race and ethnicity, particularly for seafood and shrimp. Shrimp allergy is particularly interesting given the potential for cross-reactive sensitization from other arthropods. OBJECTIVES: We characterized risk factors for shrimp allergy and shrimp sensitization. METHODS: Data from electronic health records were abstracted for food allergies among patients who sought care at a large health system between October 1, 2010, and April 1, 2024. Geocoded addresses were linked to US Census data to identify characteristics associated with shrimp allergy. Non-Hispanic Black participants from the Study of Asthma-Related Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE) were assessed for allergic sensitization using an IgE array, and survey data collected from participants were evaluated for association with shrimp, cockroach, and dust mite sensitization. RESULTS: Among 2,975,183 health system patients, 4,709 individuals reported shrimp allergy. Compared to White individuals, rates of shrimp allergy were significantly higher in Black, Asian/Pacific Islander, Native American, and Latino individuals. Shrimp allergy was higher with increasing age, female sex, and asthma, and it was inversely related to median household income. Among SAPPHIRE participants, sensitization to shrimp, cockroach, and dust mite was positively associated with total IgE levels and proportion of African ancestry, but inversely associated with head of household level of education. CONCLUSIONS: Both shrimp allergy and sensitization were associated with sociodemographic factors, suggesting that environmental exposures leading to cross-reactive sensitization may be important risk factors. Nevertheless, sensitization was also associated with ancestry, highlighting the potential importance of group-specific genetic risk factors.

Sleep Medicine

Ortiz LE, Morse AM, Thorpy MJ, Kushida CA, Harsh J, **Roth T**, Gudeman J, and Dauvilliers Y. Once-Nightly Sodium Oxybate Meets American Academy of Sleep Medicine Criteria for Treatment of Narcolepsy. *J Sleep Res* 2025;e70189. Epub ahead of print. PMID: 40851446. Full Text

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Data from the REST-ON trial were not available before the 2021 American Academy of Sleep Medicine (AASM) clinical practice guideline update, which included a literature review through August 2020. This post hoc analysis from REST-ON assessed participants who achieved clinically significant improvements on individual AASM clinical significance thresholds (CSTs). Composites of the coprimary endpoints and a secondary endpoint were also analysed. Participants with narcolepsy aged ≥ 16 years were randomised 1:1 to once-nightly sodium oxybate (ON-SXB) or placebo for 13 weeks. Coprimary endpoints were mean sleep latency on the Maintenance of Wakefulness Test (MWT), Clinical Global Impression of Improvement (CGI-I) rating, and number of cataplexy episodes; secondary endpoints included the Epworth Sleepiness Scale (ESS) score. Outcomes with ON-SXB treatment compared with baseline were assessed according to the CSTs, and for those who met CSTs, the proportions of participants who experienced clinically significant improvements on a composite of ≥ 2, ≥ 3, or 4 endpoints were calculated. For improvements from baseline with ON-SXB at Week 13 (9-g dose), mean sleep latency on the MWT increased 10.8 min (CST, ≥ 2-min increase), 92.8% rated improvement on the CGI-I (CST, ≥ 33% of participants reporting improvement), reduction in number of cataplexy episodes was 60.8% reduction (CST, ≥ 25% reduction), and reduction in ESS score was -6.5 (CST, ≥ 2-point decrease). At Weeks 3, 8 and 13, significantly more participants treated with ON-SXB versus placebo experienced clinical improvements on ≥ 2, ≥ 3, or 4 endpoints ($p \leq 0.05$). These data demonstrate the robust efficacy of ON-SXB across multiple clinically important narcolepsy symptoms per established CSTs, further supporting the use of ON-SXB in clinical practice. Trial Registration: This manuscript presents the results of a post hoc analysis from the REST-ON clinical trial (NCT02720744).

Sleep Medicine
Palagini L, Bruni O, Colizzi M, Comacchio C, Gemignani A, Nobili L, Balestrieri M, and **Drake CL**. Maternal vulnerability to insomnia: Relationship with poor newborn sleep and peripartum psychopathology. *Sleep Med* 2025;134:106732. PMID: 40795452. Full Text

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PURPOSE: Sleep reactivity, defined as the degree to which sleep is disrupted due to exposure to stress, serves as a distinctive trait and an indicator of an individual's vulnerability to insomnia. While insomnia may be a risk factor for maternal psychopathology, we aimed to study maternal insomnia vulnerability and its relationship with perinatal psychopathology and newborn sleep. METHOD: Pregnant women were recruited during their last routine assessment before being hospitalized for delivery at the Gynecological Unit of the University Hospital of Ferrara and Udine, Italy. The assessment included baseline evaluation (T0), and evaluations at 1 months (T1) in the postpartum period with specific questionnaires for insomnia vulnerability such as the Ford Insomnia Response to Stress Test (FIRST), Insomnia Disorder such as Sleep Condition Indicator (SCI), mood and anxiety symptoms such as Edinburgh Postnatal Depression Scale (EPDS), Mood Disorder Questionnaire (MDQ), State-Trait Anxiety Inventory (STAI) and newborn sleep Disturbance Scale for Children (SDSC). RESULTS: At T0, 151 pregnant women were included. Elevated sleep reactivity affected the 36.4 % at T0. Women with elevated prenatal sleep-reactivity were significantly more affected by prenatal, insomnia, anxiety and mood symptoms. Prenatal elevated sleep reactivity predicted post natal insomnia (OR 4.50,p = 0.014), anxiety (OR 3.44, p = 0.002) and depressive

symptoms (OR. 4.45, p = 0.008), It also predicted poor newborn sleep (OR 3.43, p = 0.032). CONCLUSIONS: Maternal vulnerability to insomnia is an important prenatal factor that may contribute to concurrent and postpartum psychopathology and to poor newborn sleep. Findings may suggest a potential hereditary aspect of insomnia in newborns born to women with insomnia disorder and exhibiting elevated sleep reactivity.

Surgery

Chamseddine H, **Halabi M**, **Shepard A**, **Nypaver T**, **Weaver M**, Hoballah JJ, **Kavousi Y**, **Onofrey K**, and **Kabbani L**. Popliteal-distal bypass versus infra-popliteal endovascular therapy for infra-popliteal occlusive disease. *J Vasc Surg* 2025; Epub ahead of print. PMID: 40769463. Full Text

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OBJECTIVE: Isolated infrapopliteal occlusive disease poses significant clinical challenges due to limited durable treatment options and poor limb salvage and survival rates. Although endovascular therapy (ET) has gained prominence for its minimally invasive approach, popliteal-distal bypass (PDB) provides an effective open approach that minimizes dissection and length of bypass required. This study aims to compare real-world outcomes of PDB vs infrapopliteal ET for chronic limb-threatening ischemia (CLTI) secondary to isolated infrapopliteal occlusive disease. METHODS: Patients who underwent a PDB or isolated infrapopliteal ET for CLTI between 2010 and 2024 were identified in the Vascular Quality Initiative. PDB was defined as a bypass using single-segment great saphenous vein originating from an above-knee or below-knee popliteal artery inflow; patients with a concomitant more proximal peripheral vascular intervention or bypass were excluded. Infrapopliteal ET was defined as transluminal balloon angioplasty, atherectomy, and/or stenting of a tibial artery; patients with a concomitant bypass or femoropopliteal intervention were excluded. Three-to-one nearest-neighbor propensity score matching without replacement was performed to ensure balance of covariates between the two comparison groups. Kaplan-Meier and Cox regression analysis were used to estimate long-term event rates and evaluate the association of type of intervention with the long-term outcomes of survival, amputation-free survival, primary patency, and major adverse limb events defined as the composite outcome of amputation and/or reintervention. RESULTS: A total of 3619 patients who underwent PDB were matched to 10,857 patients who underwent isolated infrapopliteal ET. All baseline characteristics and demographics were balanced after propensity score matching. The utilization of PDB for isolated infrapopliteal occlusive disease decreased from 25% to 5% between 2010 and 2023, whereas that of infrapopliteal ET increased from 75% to 95%. PDB was associated with a significantly longer hospital stay (6 days vs 1 day; P < .001) and higher rates of in-hospital mortality (1.4% vs 0.9%; P = .021), myocardial infarction (2.5% vs 0.4%; P < .001), acute kidney injury (7.2% vs 1.4%; P < .001), pneumonia (2.2% vs 0.7%; P < .001), and surgical site infection (2.9% vs 0.0%; P < .001) compared with infrapopliteal ET. At 1-year follow-up, PDB was associated with significantly higher survival (86.7% vs 83.9%; P < .001), amputation-free survival (72.6% vs 65.9%; P < .001), and primary patency (73.6% vs 69.0%; P = .002) and lower major adverse limb events (25.9% vs 30.1%; P = .007) compared with infrapopliteal ET. PDB was associated with significantly higher amputation-free survival compared with infrapopliteal ET for both above-knee PDB (73.6% vs 65.9%; P < .001) and below-knee PDB (71.9% vs 65.9%; P < .001), with no difference observed between above-knee and below-knee PDB (P = .407). Similarly, PDB was associated with significantly higher amputation-free survival compared with infrapopliteal ET for both PDB to a tibial artery (72.3% vs 65.9%; P < .001) and PDB to a pedal artery (72.6% vs 65.9%; P < .001), with no difference observed between PDB to a tibial artery and PDB to a pedal artery (P = .860). CONCLUSIONS: Although its use has declined over the past decade, PDB continues to provide superior long-term outcomes in amputation-free survival, patency, and limb salvage compared with infrapopliteal ET in patients with infrapopliteal occlusive disease, albeit with a higher rate of perioperative mortality and morbidity. Careful preoperative risk assessment and thoughtful patient selection are essential to optimize the outcomes of isolated infrapopliteal interventions, ensuring that immediate procedural risks are appropriately weighed against the potential for improved longer-term outcomes in this patient population.

Surgery

Hidalgo LG, Madill-Thomsen KS, Reeve J, Mackova M, Gauthier P, Demko Z, Prewett A, Lee M, Alhamad T, Anand S, Arnol M, Baliga R, Banasik M, Blosser CD, Bobba S, Brennan D, Bromberg J, Budde K, Chamienia A, Chow K, Ciszek M, Costa N, Dęborska-Materkowska D, Debska-Ślizień A, Domański L, Fatica R, **Francis I**, Fryc J, Gill J, Gill J, Glyda M, Gourishankar S, Gryczman M, Gupta G, Hruba P, Hughes P, Jittirat A, Jurekovic Z, Kamal L, Kamel M, Kant S, Kojc N, Konopa J, Kumar D, Lan J, Lowe D, Mazurkiewicz J, Miglinas M, Moinuddin I, Mueller T, Myślak M, Naumnik B, Pączek L, **Patel A**, Perkowska-Ptasińska A, Piecha G, Poggio E, Bloudíčkova SR, Regele H, Schachtner T, Shojai S, Sikosana MLN, Slatinská J, Smykal-Jankowiak K, Haler Ž V, Viklicky O, Vucur K, Weir MR, Wiecek A, Zaky Z, and Halloran PF. Improving the histologic detection of DSA-negative antibody-mediated rejection in kidney transplants. *Am J Transplant* 2025; Epub ahead of print. PMID: 40854490. Full Text

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Emerging treatments for antibody-mediated rejection (ABMR, NEJM391(2):122-132) have increased the importance of ABMR detection when donor-specific antibody (DSA) is negative. We addressed this issue in the Trifecta-Kidney study (ClinicalTrials.gov #NCT04239703) using three centralized tests in 690 kidney transplant biopsies: DSA (One Lambda Inc.), blood donor-derived cell-free DNA (dd-cfDNA, Prospera™ test, Natera, Inc.), and molecular biopsy assessment (MMDx). We used an "AutoBanff 2022" algorithm to model the impact of alternative DSA interpretations on the histologic diagnosis of "DSA-negative" ABMR following Banff guidelines, including agreement with dd-cfDNA and molecular ABMR.

Lowering MFI cutoffs for DSA-positivity did not improve detection of DSA-negative ABMR. However, simply calling all DSA positive allowed Banff 2022 guidelines to identify 46% more ABMR cases with no measurable DSA, and per Net Reclassification Improvement increased agreement between histologic diagnoses and both dd-cfDNA (P=7.72E-7) and molecular ABMR (P=7.69E-7). New ABMR cases were as strongly positive for dd-cfDNA and molecular ABMR as those found using the conventional DSA interpretation. A validation set analysis using INTERCOMEX study data (ClinicalTrials.gov NCT#01299168) confirmed these findings, and found that the new DSA-negative ABMR cases identified by calling all DSA positive had the same risk for graft loss as those found with conventional DSA interpretation. Trifecta-Kidney Study ClinicalTrials.gov #NCT04239703.

Surgery

King S, Williams KM, Hughes BD, and Newman EA. Health advocacy through translational science: an experimental model to quantify the impact of human social stressors on health outcomes. *Semin Pediatr Surg* 2025;35:151516. PMID: 40784038. Full Text

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Health status and outcomes are known to be impacted by social stressors, yet social-political change to improve health outcomes through social determinants of health is stagnant. The well understood associations between social stressors and health are often chronic in nature and are without causal evidence. A new model that demonstrates a clear cause and effect between food insecurity and accelerated tumor growth has the potential to change the way public health scientists and advocates frame their arguments for change. This model provides a novel framework for ethically sound, controllable, and translatable social determinants of health research based in objective science. Implementation of this model across other human stressors and pathologies will lay the groundwork for irrefutable evidence to support social-political change for improved health outcomes.

Surgery

Miller-Matero LR, **Pappas C**, **Christopher B**, **Grossi R**, **Vanderziel A**, Barnett NP, Moore RS, **Hamann A**, **Carlin AM**, **Varban OA**, and **Braciszewski JM**. A technology-based intervention to reduce alcohol use after metabolic and bariatric surgery: feasibility, acceptability, and preliminary outcomes. *Surg Obes Relat Dis* 2025; Epub ahead of print. PMID: 40885652. Full Text

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BACKGROUND: Patients who undergo metabolic and bariatric surgery (MBS) are at increased risk for an alcohol use disorder. A technology-based intervention, rooted in motivational interviewing, could broadly reach patients after MBS and has the potential to reduce alcohol use. OBJECTIVE: Examine the feasibility, acceptability, and preliminary outcomes of a technology-based intervention to reduce alcohol use delivered after MBS. SETTING: Health system. METHODS: Participants (N = 60) who were 3-18 months post-MBS were randomized to the intervention or treatment-as-usual control group. The tailored intervention consisted of 2 (15-minute) sessions of interactive web-based content followed by 3-months of daily text messaging. Participants completed baseline and a postintervention assessment (91.7% retention). RESULTS: Participants were primarily female (90%), White (55.0%) or Black (43.3%), with a mean age of 44.6 years (SD = 10.4). Of those randomized to the intervention (n = 24), 83.3% (n = 20) began the intervention and 95% (n = 19) completed it. The majority of participants rated all intervention

components positively and 100% agreed that other patients would use the intervention. The intervention group reported a significant increase in level of motivation to avoid alcohol use from baseline to postintervention (P = .02), whereas the control group did not show a significant change (P = .73). At the postintervention, the intervention group had significantly fewer participants endorsing alcohol use than the control group (43.5% versus 75%; X(2) = 5.63, P = .02). CONCLUSION: A technology-based intervention delivered after MBS was feasible, acceptable, and showed promising preliminary outcomes for increasing motivation to avoid alcohol use as well as reducing alcohol use.

Surgery

Nicksa GA, Chicoine N, Li LT, Jamshidi R, Lehane AJ, Raval MV, **King SD**, and Greenberg S. Protecting our patients' future through perioperative sustainability: Action and advocacy for the pediatric surgeon. *Semin Pediatr Surg* 2025;35:151518. PMID: 40812090. Full Text

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Climate change is a significant threat to human health and health equity. Marginalized populations, including children, are most impacted by our rapidly changing environment. Both the prevalence of pediatric surgical disease, as well as the ability to deliver surgical care, are affected by climate change. Ironically, healthcare systems have a significant, deleterious effect on the planet. However, there are many proven mitigation strategies to reduce the injurious climate impact of the delivery of surgical services, augment equity, and improve health. We describe five domains through which pediatric surgical care providers can act to generate more sustainable healthcare systems: reduce, repurpose, reuse, refuse, and recycle. We highlight successful examples instituted through various healthcare organizations and provide recommendations that pediatric surgical care providers can use to support the health of our planet through their daily work. These actions can increase sustainability, reduce cost, and promote equity for our patients and future generations.

Urology

Bertini A, **Stephens A**, Finocchiaro A, Viganò S, **Dinesh A**, **Guivatchian E**, Perri A, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Briganti A, Salonia A, Montorsi F, Sood A, Menon M, **Rogers C**, and **Abdollah F**. Long-term Cancer Control Outcomes After Robot-assisted Radical Prostatectomy in Pathologically Non-organ-confined High-risk Prostate Cancer: 20-year Report from a Single Tertiary Referral Center. *Eur Urol Focus* 2025; Epub ahead of print. PMID: 40774843. Full Text

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BACKGROUND AND OBJECTIVE: Exhaustive evidence on the long-term efficacy of robot-assisted laparoscopic prostatectomy (RALP) in non-organ-confined high-risk prostate cancer (PC) is still lacking. Our aim was to evaluate long-term oncological outcomes in this subset of patients treated with RALP at a single referral center. METHODS: We included 803 patients with pathologically non-organ-confined high-risk PC (≥pT3a and/or pN1) at RALP between 2001 and 2022 at Henry Ford Hospital (Detroit, MI, USA). All patient underwent RALP using the Vattikuti Institute technique, with or without extended pelvic lymph node dissection (external iliac, obturator, and internal iliac nodes). The Kaplan-Meier method was used to estimate overall survival (OS) and additional treatment-free survival. The probability of PC-specific survival (PCSS) was estimated via the competing-risks method. Competing-risk and Cox regression analyses were used to identify potential predictors of PC-specific mortality (PCSM), any-cause mortality (ACM), and additional treatment. KEY FINDINGS AND LIMITATIONS: We included 803 patients, of whom 415 (51.5%) had pT3a, 385 (47.9%) had ≥pT3b, 323 (40%) had pN1, and 670 (84%) had grade group 4-5 PC. Of the 635 patients with status information regarding additional treatment, 416 received further therapy after surgery. Specifically, 46, 110, and 260 underwent RT only, HT only, or RT + HT, respectively. Median follow-up was 72 mo (interquartile range 28-120). The 20-yr survival rates were 72.7% (95% confidence interval [CI] 56.8-86,5%) for PCSS and 45.2% (95% CI 29.1-60.1%) for OS. The rates of survival free from additional treatment were 31.3% (95% CI 26.1-36.5%) at 10 yr and 20.3% (95% CI 14.9-26.4%) at 15 yr. Multivariable regression revealed pT3b-4 stage as an independent predictor of PCSM (hazard ratio [HR] 2.50; p = 0.008), ACM (HR 1.84; p = 0.006), and additional treatment (HR 1.69; p < 0.001). CONCLUSIONS AND CLINICAL IMPLICATIONS: For patients with non-organ-confined high-risk PC, RALP achieves long-term oncological control. This study provides the longest follow-up after RALP as the primary local treatment for patients with truly aggressive PC forms and offers valuable insights for patient counseling on long-term outcomes.

Urology

Bertini A, **Stephens A**, Finocchiaro A, Viganò S, Perri A, Lughezzani G, Buffi N, Sorce G, Ficarra V, Briganti A, Salonia A, Montorsi F, Sood A, Menon M, **Rogers C**, and **Abdollah F**. Mortality and Additional Treatment Rates in Pathologically High-Risk Prostate Cancer With Prostate-Specific Antigen Persistence at Robot-Assisted Radical Prostatectomy: Long-Term Report From Single Tertiary Referral Center. *Prostate* 2025; Epub ahead of print. PMID: 40785187. Full Text

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BACKGROUND: Long-term cancer control efficacy of robotic-assisted laparoscopic prostatectomy (RALP) in men with pathologically high-risk prostate cancer and prostate-specific antigen (PSA) persistence remains poorly addressed in the literature. Our aim was to evaluate long-term survival and additional treatment (AT) rates in these individuals. METHODS: We included 803 patients who underwent RALP for pathologically high-risk PCa (pT ≥ 3a, pN0-1 or GG ≥ 4) between 2001 and 2022 at a single tertiary referral center (Henry Ford Hospital, Detroit). Patients without adequate information about PSA persistence were excluded from the analysis (n = 128). Kaplan-Meier curves estimated AT free-survival (ATFS) and all-cause mortality (ACM) free-survival, whereas the competing risk method was used to estimate cancer-specific mortality (CSM) free-survival, after stratification according to PSA persistence. Competing risk and Cox regression models tested the impact of PSA persistence on three endpoints: AT rates, CSM, and ACM. RESULTS: Our final cohort consisted of 675 who underwent RALP for pathologically high-risk PCa, 187 (27.7%) of whom had PSA persistence. The median age at surgery was 64 years (IQR 59-68), and the median follow-up duration was 75 months (IQR 33-125). Patients with PSA persistence were more likely to have higher PSA values at surgery (8 vs. 7 ng/mL, $p < 0.001$), pT3b-4 PCa (62.5% vs. 39.9%, $p < 0.001$), pN1 PCa (55.6% vs. 35.7%, $p < 0.001$), and positive surgical margins (PSMs) (65.2% vs. 43.4%, $p < 0.001$). Moreover, patients in the PSA persistence group had higher proportion undergoing only hormone therapy (HT) (24.1% vs. 11.9%, $p < 0.001$) and radiotherapy (RT) plus HT (50.8% vs. 31.1%, $p < 0.001$), reporting higher median PSA values at RT (0.6 vs. 0.2 ng/mL, $p < 0.001$), compared to patients with undetectable PSA. At 10 years after RALP, CSM-FS and ACM-FS were 79.7% versus 90.3% (Gray-test p-value = 0.001) and 72.1% versus 79.6% (log-rank p-value = 0.013), for persistent versus undetectable PSA, respectively. The 10-year rates of ATFS were 6.6% versus 33.2% (log-rank p-value < 0.0001), for persistent versus undetectable PSA, respectively. At MVA, persistent PSA was associated with AT (HR: 3.05, $p < 0.001$), but not with CSM (HR: 1.49, $p = 0.2$) or ACM (HR: 1.09, $p = 0.9$). CONCLUSION: Patients with pathologically high-risk PCa and PSA persistence after RALP, despite being at greater hazard of AT (HT and/or RT), did not have less favorable cancer control outcomes at 10 years than their counterparts with undetectable PSA levels. Our report provides the longest follow-up after RALP for this subset of patients, making it a valuable resource for counseling patients on the long-term oncologic outcomes of this procedure and postoperative adjuvant/salvage therapies.

Urology

Sion A, Rehfuss A, Millner R, Rose MJ, Patel H, and Ching CB. Bilateral Native Nephrectomy as a Successful Treatment for Persistent Polycythemia in a Pediatric Kidney Transplant Recipient: Case Report. *Pediatr Transplant* 2025;29(6):e70156. PMID: 40764705. Full Text

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INTRODUCTION: Polycythemia, characterized by elevated red blood cell counts, can lead to significant complications, especially in pediatric kidney transplant patients. In rare cases, persistent polycythemia is caused by excessive erythropoietin production from native kidneys post-transplant. We report a unique case in which bilateral native nephrectomy was a successful treatment for persistent polycythemia. METHODS: We present the case of a 23-year-old male with end-stage kidney disease due to an embolic event from an umbilical artery catheter resulting in bilateral kidney cystic dysplasia. The patient developed polycythemia at 22 months, initially treated with intermittent phlebotomy, which later transitioned to red cell depletion. Despite receiving a living donor kidney transplant at age 15, his hematocrit remained elevated due to continued erythropoietin production from his native kidneys. At age 17, he underwent robotic bilateral native nephrectomies. RESULTS/IMPORTANT CLINICAL FINDINGS: Following the nephrectomies, the patient's hematocrit was normalized within 2 months. The surgery was complication-

free, and the patient no longer required red cell depletion. Five years post-surgery, his hemoglobin and hematocrit remain stable. CONCLUSIONS: This case demonstrates that persistent polycythemia in pediatric kidney transplant recipients can be successfully treated with bilateral nephrectomies when caused by native kidney erythropoietin production. Surgical removal of native kidneys is a viable solution for refractory cases of post-transplant polycythemia, preventing complications like thromboembolic events and preserving long-term health. A multidisciplinary approach, including urology and nephrology, is essential in managing such complex cases.

Urology
Wang Y, Zhuo J, Christensen B, Chen K, Daignault-Newton S, **Hussain B**, Gammons M, Almajedi M, Grandy S, Matynowski A, Noyes SL, Mirza M, Shetty S, Jafri SMA, Tobert C, Brede C, **Rogers CG**, Lane BR, and Nelson R. Adoption and perioperative outcomes of single-port (SP) robotic partial nephrectomy in the state of Michigan: a MUSIC-KIDNEY analysis. *J Robot Surg* 2025;19(1):535. PMID: 40885878. Full Text

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Robotic partial nephrectomy (RPN) is a standard-of-care nephron-sparing intervention for clinical stage T1 renal masses (cT1RMs). We evaluated RPN outcomes performed using the da Vinci single port (SP) and multiport (Xi) platforms in a statewide quality improvement collaborative since SP introduction in Michigan. MUSIC-KIDNEY maintains a prospective registry of newly diagnosed cT1RM. Six surgeons from three practices within MUSIC have performed both. The perioperative data from patients undergoing SP and Xi RPN with these surgeons October 2020-August 2023 were analyzed. These surgeons completed a survey to assess reasons for choosing SP over Xi RPN. Of 828 RPNs performed by all MUSIC surgeons in the same duration, a total of 314 (38%) RPNs were completed by the six included surgeons who performed 121 (39%) RPNs with SP and 193 (61%) with Xi. SP RPN more commonly utilized the retroperitoneal approach than Xi RPN (80% vs. 6.1%, $p < 0.001$). When comparing perioperative outcomes, the experienced SP surgeon utilized same-day (55% vs. 9.5% vs. 5.7%, $p < 0.001$) and opioid-free discharge (77% vs. 22% vs. 18%, $p < 0.001$) significantly more than other urologists for both SP and Xi cases without a significant increase in positive surgical margins, ED visits, or readmissions. The survey results showed that surgeons early in the learning curve for SP RPN prefer to use SP for smaller, less complex masses. Although there has been limited adoption of SP RPN, initial experiences with SP RPN demonstrate procedural safety comparable to Xi RPN. Both robotic systems provide advantages, with SP mainly facilitating the retroperitoneal approach.

Urology
Zoltin K, **Shannon B**, **Timar R**, Blasdel G, and **Shakir N**. Orchiectomy and scrotectomy as genital gender-affirming surgery: novel surgical technique and patient-reported outcomes. *BMC Urol* 2025;25(1):217. PMID: 40849668. Full Text

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BACKGROUND: Gender-affirming orchiectomy is well described; however, a subset of patients may also seek scrotectomy to alleviate dysphoria related to the scrotum. Techniques and outcomes of gender-affirming orchiectomy and scrotectomy (GAOS) have not been described to date. METHODS: We retrospectively reviewed all patients who had undergone GAOS from 2021 to 2024 at our institution. The World Professional Association for Transgender Health criteria for surgical treatment were met preoperatively, and patients understood vaginoplasty was not recommended post-scrotectomy. Two approaches were offered: excision of a majority of scrotal tissue and primary closure of the perineal wound, or excision of all rugated skin with mons and groin (Y-flap) advancement. Patient-reported outcomes questionnaires from the PROMIS(®) Sexual Function and Satisfaction Measures, version 2.0, along with questions specific to post-scrotectomy anatomy, were sent postoperatively. RESULTS: Eight patients, median age 31 years, underwent GAOS with a preoperative hormone duration of 26.5 months. All patients reported dysphoria related to the scrotum and testes, and wished to preserve the phallus. Five elected for primary closure, three for Y-flap perineoplasty. At median 97-day follow-up, all reported satisfaction and dysphoria relief. One patient with Y-flap experienced wound dehiscence requiring operative revision. Four reported sexual activity with the ability to achieve erection and orgasm. CONCLUSIONS: GAOS is a well-tolerated procedure that can address dysphoria related to the scrotum and testes. Longer-term study of this emerging procedure is warranted. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1186/s12894-025-01867-8.

Administration
Huang-Vredevoogd J, **Doemer A**, **Siddiqui S**, **Shah MM**, **Asadi AA**, **DiCarlo A**, **Scarpace L**, **Robin A**, **Lee I**, **Moceri A**, and **Thind K**. PPP04 Expanding Treatment Options for Reirradiation: The First Case of Gammatile Implantation in the Spine. *Brachytherapy* 2025;24(4):S20-S21. Full Text

Purpose: GammaTile® surgically targeted radiation therapy is a form of low dose rate brachytherapy in which Cs-131 seeds are embedded into a resorbable collagen-based matrix, allowing the seeds to be easily placed along a resection cavity during surgery. GammaTile has been used in several intracranial applications including the treatment of recurrent glioblastomas, meningiomas, and brain metastases as well as newly diagnosed brain metastases. However, it has not been used extracranially. This study describes the first use of GammaTile in the spine, for a patient who had rectosigmoid adenocarcinoma with recurrent metastatic disease in the sacrum. They received their first course of radiation in 2022 with external beam (54Gy in 30 fractions), followed by fractionated stereotactic radiation therapy to the recurrent lumbosacral disease in 2023 (30Gy in 5 fractions), and presented with pain in the legs and progressive disease in the sacrum. Given the patient's two prior courses of external beam radiation therapy, off-label use of GammaTile was pursued due to its ability to minimize dose to the nearby thecal sac, cauda equina and sacral nerve roots. Methods: GammaTile workflow for cranial applications involves estimating the surface area of the resection cavity to calculate the expected number of tiles needed. However, for this novel application, the number of tiles was estimated using a mock-up of the anticipated tile configuration based on the patient's MRI (Figure 1b), as well as a personalized 3D-printed replica of the patient's spine (Figure 1a).Following surgical resection, which included a partial L5 laminectomy and partial sacrectomy (Figure 1c), four tiles (16 sources) were placed “upside down” from the typical orientation, i.e., with the larger 3mm spacing facing toward the thecal sac to maximize separation and minimize dose to the cauda. Additionally, Fibrin sealant and absorbable gelatin were placed in between the tiles and the thecal sac to create further separation. Immediately after surgery, CT images were acquired in the OR for post-implant dosimetry and to verify the desired tile placement. These images were then used to calculate the delivered dose to the patient using the Eclipse planning system, and MIM was used to convert physical dose to biological effective dose to the thecal sac (BED3Gy) using the linear quadratic model for a permanent LDR implant and published values for the repair time, potential doubling time, and alpha values.1 Results: The post-implant calculated BED3Gy distribution is shown in Figure 1d. The D0.035cc physical dose and BED3Gy dose to the thecal sac was 89.8Gy and 106.4Gy respectively. At a 3-month post-operative appointment, the patient reported improved pain and was able to ambulate for longer distances with a walker. Conclusions: This study presents our institution's experience with the first use of Gammatile for the spine, highlighting the ability of our multi-disciplinary team to offer a novel treatment technique for a patient faced with either disease progression or a more extensive, life-altering surgery.

Anesthesiology
Hannoudi A, **Gonte MR**, **Cannella C**, **Sawar K**, **Yono SS**, **Atisha NM**, **Walker EM**, **Bensenhaver J**, **Evangelista MS**, and **Atisha DM**. ASO Visual Abstract: The Effect of Oncoplastic Reduction Mammoplasty on the Incidence of Breast Lymphedema in Women Undergoing Breast-Conservation Surgery. *Ann Surg Oncol* 2025:2. Full Text

[Hannoudi, Andrew; Gonte, Madeleine R.; Sawar, Kinan] Wayne State Univ, Sch Med, Detroit, MI 48202 USA; [Gonte, Madeleine R.; Cannella, Cara; Yono, Summer S.; Atisha, Noah M.; Walker, Eleanor M.; Bensenhaver, Jessica; Evangelista, Maristella S.; Atisha, Dunya M.] Henry Ford Hosp, Div Plast & Reconstruct Surg, Detroit, MI USA
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Cardiology/Cardiovascular Research
Hawatian K, **Emakhu J**, **Morton T**, **Tuttle J**, **Sidani M**, **Nassereddine H**, **Krupp S**, **Cook B**, **Klausner H**, **McCord J**, and **Miller J**. 368 Hypertension Severity and Indeterminate High-Sensitivity Cardiac Troponin. *Ann Emerg Med* 2025;86(3):S160. Full Text

Study Objectives: Hypertension increases the risk of acute coronary syndrome (ACS) and major adverse cardiovascular events (MACE) (ie, myocardial infarction, all-cause mortality, and urgent revascularization), but its relationship with high-sensitivity cardiac troponin I (hs-cTnI) levels remains unclear. This study aimed to evaluate the association between hypertension severity and hs-cTnI levels and examined the impact of hypertension on 30-day MACE risk in patients with suspected ACS. Methods: We conducted a secondary analysis of a cluster randomized trial implementing a hs-cTnI early rule-out protocol. Patients were eligible for analysis who had suspected ACS and hs-cTnI testing and an electrocardiogram at a large, integrated health system consisting of ten emergency departments: five hospital-based and five free-standing facilities. We excluded patients without hs-cTnI values or values above the 99th percentile (18 ng/L). Patients were categorized into three hypertension severity groups: normotensive, defined as systolic blood pressure (SBP) less than 140 mmHg or diastolic blood pressure (DBP) less than 90 mmHg; moderately hypertensive, characterized by SBP between 140 mmHg and 180 mmHg or DBP between 90 mmHg and 110 mmHg; and severely hypertensive, where SBP was 180 mmHg or greater or DBP was 110 mmHg or greater. A generalized linear model assessed the relationship between hypertension severity and hs-cTnI levels, while multivariable logistic regression analyzed the effect of hypertension severity on 30-day MACE, adjusting for key confounders. Results: A total of 23,803 patients fit the inclusion criteria. Severe hypertension demonstrated an independent, statistically significant relationship with higher hs-cTnI levels ($\beta = 0.0645$; 95% CI: 0.047 to 0.082, $p < 0.001$). Likewise, severely hypertensive patients showed higher rates of elevated troponin levels (25.8% for 5-9 ng/L and 20.4% for 10-18 ng/L) compared to the other groups. After adjustment for confounders, the relationship between severe hypertension and 30-day MACE outcomes approached statistical significance (aOR: 1.61; 95% CI: 0.98–2.65, $p = 0.063$). Conclusion: This study revealed that patients with suspected ACS show increased hs-cTnI levels and higher 30-day MACE risks with worsening hypertension severity. Clinicians should interpret elevated troponin levels cautiously in hypertensive patients, prioritizing established risk factors such as coronary artery disease. No, authors do not have interests to disclose

Cardiology/Cardiovascular Research

Saleem M, **Qureshi MA**, and **Ananthasubramaniam K**. FDG-PET For Myocardial Viability Assessment: Does it Guide Decision Making For Revascularization In Real World Practice? A Single Center Experience. *J Nucl Cardiol* 2025;50. Full Text

Introduction: The incidence of heart failure driven by ischemic heart disease is increasing. Intuitively it makes sense that identification of ischemic viable myocardium could drive revascularization decisions and survival, but recent study evidence has not favored it. We sought to evaluate if FDG PET guides real world decision making for revascularization in ischemic cardiomyopathy and if it makes a difference Methods: This is a retrospective chart review study of PET ischemia and viability testing performed between 2020-2024 at our institution; Patients' baseline characteristics including comorbidities, ejection fraction and PET study results were evaluated. We compared baseline characteristics between positive viability and negative viability groups. Revascularization and changes in ejection fraction outcomes were assessed Results: Data of 111 patients who underwent PET ischemia and viability testing were analyzed; mean patients age is 69 yr old, M:F ratio 4:1, 64% white and 29% African American, all patients had HTN and HLD, 51 % diabetics and 53% were smoker. 78% of patients had a history of MI and 95% of patients have ischemic cardiomyopathy with a mean EF of 34%. The average SRS, SSS, SDS were 14, 13, 7 respectively. 99 patients received FDG for viability assessment. We found the following; First; 65 patients (67%) were positive for ischemic viable myocardium and 31 patients (31%) with non-viable myocardium. Second, there was no statistically significant difference in baseline characteristics of patients with positive viability and negative viability groups. Third, in the positive viability group (n=65); 37 patients (56%) had revascularization with PCI/CABG and 31 patients (43%) were treated medically and in the negative viability group, 19 patients (61%) were treated medically and only 11 patients (35%) received revascularization. Fourth, there is a significant improvement of the ejection fraction in the positive viability patients who underwent revascularization (mean baseline EF of 32%, mean post revascularization EF of 38% with P value =0.0004) and significant improvement in EF in the positive viability patient who were treated medically (mean baseline EF of 34%, mean EF post 3 months of medical therapy 37% with P value =0.005). Fifth, there is no significant improvement in the ejection fraction in the negative viability

patients who underwent revascularization (mean baseline EF of 32%, mean post revascularization EF of 23% with P value =0.39). Finally, symptoms were reported to be improved in 36 patients (52%) in the viability positive group. Conclusion: - Our single center experience shows that clinicians continue to believe in viability assessment and refer patients for FDG-PET testing.-FDG-PET viability studies can be utilized to guide management and decision making of revascularization which can predict functional recovery and symptoms improvement

Cardiology/Cardiovascular Research
Tondo C, De Potter T, Pickett R, Boersma LVA, Razak E, Tomassoni G, **Khan A**, Wimmer A, D'Souza B, Roy K, Christen T, Sutton B, and Wazni O. Randomized comparison of left atrial appendage closure and oral anticoagulation after catheter ablation for atrial fibrillation: subanalysis of AF type. *Europace* 2025;27(Supplement_1):i872. Full Text

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Background/Introduction: Cardiac ablation is effective at reducing the symptoms associated with arrhythmia. If anticoagulation is ceased postablation, contrary to clinical guidelines, patients are at increased risk of stroke due to the potential for asymptomatic atrial fibrillation (AF). Although left atrial appendage closure (LAAC) is an approved treatment to decrease the risk of thromboembolism from the left atrial appendage, it has not been well-studied following AF ablation. Purpose: OPTION compared the safety and efficacy of LAAC in a contemporary postablation clinical AF patient population at risk of stroke to contemporary oral anticoagulation (OAC). In this prespecified subanalysis, treatment characteristics and outcomes by AF type (paroxysmal and persistent) will be evaluated. Methods: OPTION is a multinational, multicenter, randomized, controlled trial. Catheter ablation patients were eligible if the procedure occurred 90 to 180 days prior to or was scheduled within 10 days of randomization. Patients were randomized 1:1 to ablation+LAAC versus ablation +OAC (95% DOAC) stratified by study site and ablation cohort (sequential or concomitant). The primary safety endpoint was non-procedural bleeding through 36 months based on International Society on Thrombosis and Haemostasis [ISTH] major bleeding or clinically relevant non-major bleeding definitions. The primary efficacy endpoint was the composite of all-cause death, stroke, or systemic embolism at 36 months. The secondary endpoint was ISTH major bleeding through 36 months. Additional endpoints include ablation and LAAC procedural characteristics, arrythmia recurrence, and quality of life. Results: A total of 803 patients were randomized to catheter ablation+LAAC and 797 to ablation+OAC. Overall, patients were 70±8 years old, one-third were women, mean CHA2DS2-VASc score was 3.5±1.3, and mean HAS-BLED was 1.2±0.8. Approximately 60% of patients had paroxysmal AF and 40% had persistent AF in each treatment arm. OPTION met its primary and secondary endpoints. In the subgroup of patients with paroxysmal AF, the primary efficacy endpoint occurred in 3.5% of LAAC and 4.0% OAC patients at 3 years. In patients with persistent AF, the rate was 8.0% in the LAAC and 9.0% in the OAC cohort. The primary safety endpoint occurred at a rate of 8.1% in LAAC and 18.1% in OAC-treated patients with paroxysmal AF. The rates were 8.9% in LAAC and 16.9% in OAC-treated patients with persistent AF. The rate of the secondary endpoint was 2.8% in the LAAC and 4.6% in OAC patients with paroxysmal AF. In patients with persistent AF, this rate was 5.5% in the LAAC and 5.8% in the OAC cohorts. Conclusion(s): In OPTION, among patients undergoing AF ablation, LAAC resulted in significantly less non-procedural bleeding than oral anticoagulation, while preserving similarly low rates of stroke, systemic embolism or death. Outcomes were consistent among patients with paroxysmal and persistent AF.

Dermatology
Belair N, and **Kerr HA**. Occupational Allergic Contact Dermatitis in Manicurists: A Systematic Review. *Dermatitis* 2025;36(4):e425. Full Text

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Objectives: Acrylates are a prevalent cause of allergic contact dermatitis (ACD) in both non-occupational and occupational settings. This is particularly evident in the artificial nail practice, where consumers and manicurists face increased sensitization risks. A focused analysis on occupational ACD among

manicurists is needed to identify industry trends and exposure risks. This study systematically reviews documented cases of occupational ACD in manicurists. Methods: A literature search was conducted in PubMed, Embase, and Scopus using appropriate MESH terms and keywords. 272 studies were identified, with 14 included for data analysis. Case studies that included individualized demographic data and patch testing results were included. Studies that did not focus specifically on professional manicurists or lacked patient data were excluded. Results: From the 272 studies, 14 articles detailing 17 patients were analyzed. A total of 100 positive patch tests were documented between all patients. Hydroxymethyl methacrylate (100% of patients), ethylene glycol dimethacrylate (76%), and hydroxypropyl methacrylate (41%) were the most common. Two patients left the profession due to ACD, allergen avoidance was advised for all, and specialty gloves recommended for four. Conclusions: This study highlights the risk of occupational ACD in manicurists, primarily from acrylates like hydroxymethyl methacrylate and ethylene glycol. The findings emphasize the need for improved safety protocols, including the use of specialty gloves, to reduce workplace allergen exposure. Standardizing nail product ingredient labels is crucial for allergen avoidance. Given that patients left the profession due to ACD, proactive measures are essential to protect workers and address the rise of occupational ACD in this industry.

Dermatology
Dimitrion P, **Krevh R**, **Veenstra J**, **Hamzavi**, **Adrianto**, **Zhou L**, and **Mi Q**. Proteomics identifies blood biomarkers associated with disease severity and genetic ancestry in hidradenitis suppurativa. *J Invest Dermatol* 2025;145(8):S118-S118. Full Text

[Dimitrion, P.; Krevh, R.; Veenstra, J.; Hamzavi, I; Adrianto, I; Zhou, L.; Mi, Q.] Henry Ford Hlth Syst, Dermatol, Detroit, MI USA; [Veenstra, J.; Adrianto, I; Zhou, L.; Mi, Q.] Michigan State Univ Hlth Sci, Henry Ford Hlth, Detroit, MI USA

Dermatology
Gold LS, Han G, Shahriari M, Choi O, Alkousakis T, Ma T, Chan D, Green L, Farberg A, Kwatra SG, and Alexis A. 63474 The VISIBLE study: Burden of comorbidities in participants with moderate-to-severe psoriasis across all skin tones. *J Am Acad Dermatol* 2025;93(3):AB92-AB92. Full Text

Dermatology
Gold LS, Strober B, Armstrong AW, Alkousakis T, Papp KA, Langley R, Choi O, Chan D, Jeyarajah J, Groysman V, and Lebwohl MG. 63736 SPECTREM: Guselkumab Demonstrates Consistent Significant Clearance Across the Full Range of Low Body Surface Area, Moderate Psoriasis With Special Sites Involvement. *J Am Acad Dermatol* 2025;93(3):AB301-AB301. Full Text

Dermatology
Shareef S, **Bhargava D**, and Ashack K. 60359 Utilizing Health Savings Accounts to Enhance Dermatological Care: Eligibility and Benefits. *J Am Acad Dermatol* 2025;93(3):AB340-AB340. Full Text

Emergency Medicine
Adeniran O, **Krambeck G**, **Assofi R**, **Bunting L**, **Etta G**, and **Jarou Z**. 403 Management of Emergency Department Patients With Low-Risk Deep Vein Thrombosis in the United States. *Ann Emerg Med* 2025;86(3):S175. Full Text

Study Objective: Historically, patients diagnosed with deep vein thrombosis (DVTs) were admitted for anticoagulation. In 2024, the American College of Emergency Physicians (ACEP) introduced a quality measure to encourage discharging patients with low-risk DVTs as part of the Merit-Based Incentive Payment System (MIPS). Patients with high-risk factors such as proximal DVT, concurrent PE, syncope, or those already on anticoagulation are excluded from the measure. The aim of our study is to evaluate retrospective adherence with ACEP's new DVT MIPS measure. Methods: Data from the National Hospital Ambulatory Medical Care Survey (NHAMCS) from 2016-2022 was analyzed, which contained ED visit information representing 1,867,690 patients diagnosed with DVT (ICD-10 codes: I82.4, I82.6, I82.5, I82.B). Bivariate and multivariable analyses examined associations between demographic factors, clinical characteristics (including DVT risk type and comorbidities), and disposition (admission versus discharge). Statistical tests used included Weighted Welch's T-Test and Rao-Scott Chi-Square Test. Results: Overall,

81.5% of patients were considered low-risk (95% CI, 73.9-87.3%). There was a significant difference in ED disposition by MIPS risk-type with 68.4% of low-risk patients being discharged (95% CI, 58.9-76.6%) compared to only 34.8% of high-risk patients being discharged (95% CI, 17.8-56.9%; p=0.005). Of the exclusion criteria in the MIPS measure, only concurrent PE was independently associated with admission (23.7% [95%CI 14-37%] admitted patients versus 3.17% [95% CI 0.71-13%] discharged patients, p=0.002), like due to infrequent reporting of other exclusion criteria. Additionally, we found several other factors associated with admission that are not currently built into the MIPS measure, such non-syncope other diagnoses associated with hemodynamic instability (hypotension [p <0.001], acute hypoxic respiratory failure [p=0.016]), composite risk of bleeding (p=0.007), acute blood loss anemia (p=0.033), and other comorbidities such as CKD/ESRD (p=0.008) and Alzeheimer's/dementia (p=0.003). Conclusions: Based on our study, opportunities exist to increase adherence with this measure. Additionally, opportunities exist to modify the measure to add additional exclusions for hemodynamic instability, risk of bleeding, or other comorbidities. No, authors do not have interests to disclose

Emergency Medicine
Emakhu J, **Hawatian K**, **Tuttle J**, **Etu EE**, **Berger D**, **Kea B**, **Mahler S**, and **Miller J**. 404 Association of Troponin Delta With 30-Day Major Adverse Cardiovascular Events. *Ann Emerg Med* 2025;86(3):S176. Full Text

Study Objectives: Evaluating chest pain and suspected acute coronary syndrome (ACS) heavily relies on high-sensitivity cardiac troponin assays. Analysis of dynamic troponin changes (troponin delta) is essential in this evaluation, yet the prognostic value of delta increases vs decreases are not well defined. This study examines how troponin delta categories (increase, decrease, and stable) correlate with 30-day all-cause mortality/myocardial infarction (MI) and coronary revascularization. Methods: The retrospective cohort study assessed adult patients who presented with chest pain to 10 Michigan emergency departments (ED) during 2020–2022. Patients eligible for the study received at least two high-sensitivity cardiac troponin (hs-cTnI) measurements taken in the emergency department (ED) (0, 1, and/or 3 hour), with all EDs using the same assay (Beckman Coulter hs-cTnI). We excluded those age <18 years and patients with ST-elevation MI. Troponin delta was defined as the percentage change between serial values: >20% increase, >20% decrease, or ≤20% change (stable). The primary outcome was a composite of 30-day mortality/MI, and the secondary outcome was revascularization. Logistic regression models adjusted for demographics, comorbidities, and clinical variables. We present adjusted odds ratios (aOR) and 95% confidence intervals (CI). Results: There were 21,912 patients included in the cohort with a mean age of 56 years and 52.7% female. The median and interquartile ranges in each troponin category are as follows: decrease (14.0 [8.0, 35.0] ng/L), increase (23.0 [6.0, 133.0] ng/L), and stable (4.0 [4.0, 6.0] ng/L). The primary outcome occurred in 33.2% of patients with a delta increase, 16.5% with a delta decrease, and 6.0% with a stable delta. A troponin delta increase was strongly associated with the primary outcome (aOR = 4.98; 95% CI: 4.35–5.71, p <0.001). A troponin delta decrease was modestly associated with the primary outcome (aOR = 2.61; 95% CI: 1.87–2.65, p < 0.001). Rates of revascularization were not statistically significant across delta categories. Conclusion: Troponin delta serves as an independent predictor for 30-day mortality/MI among patients experiencing chest pain in ED settings. While it had a more modest association, delta decrease was an independent predictor. No, authors do not have interests to disclose

Emergency Medicine
Farhat S, **Hagerman T**, **Nour M**, **Rammal JA**, **Lang T**, and **Miller J**. 124 Resident Physician Awareness of Barriers to Post-Discharge Care From the Emergency Department. *Ann Emerg Med* 2025;86(3):S53-S54. Full Text

Study Objective: Physician awareness of barriers to safe and effective transitions of care following emergency department (ED) discharge is crucial. Limited data exists evaluating the rates of resident physician awareness of these barriers. Our objective was to quantify this level of awareness in comparison to their patient's reality. Methods: We performed a secondary analysis of a prospective convenience sample of patients ≥18 years old at a single urban safety-net hospital with an EM residency program between 10/2024 and 1/2025. Barriers assessed included transportation difficulty, difficulty affording medications, need for assistance with activities of daily living, and lack of a primary care

physician. Low health literacy, risk for cognitive dysfunction, and patient understanding of discharge instructions were measured by use of the REALM-R, MiniCog, and scoring of recorded comprehension questionnaires, respectively. The discharging physician completed a brief written survey immediately after the patient was discharged. The primary outcome was physician detection of these patient reported barriers, reported as sensitivity (patients reporting barriers that are identified by physicians / all patients reporting the specific barrier). McNemar's test and Cohen's kappa statistics were utilized to evaluate patient-physician agreement. Results: The sample included 206 total patients [10 (5%) excluded for missing data] and 179 surveys completed by 36 different PGY 1-3 residents. Median patient age was 59 years; 48% female, and 87% black. Across all domains, patients reported barriers at a higher rate than physicians, including transportation difficulties (29.7% vs 22.2%), need for assistance with ADLs (26.1% vs 8.1%), difficulty affording medications (23.2% vs 5.6%), lack of a primary care physician (18.2% vs 8.7%), limited health literacy (60.4% vs 27.2%), cognitive dysfunction (46.5% of patients >=65 vs 12.7%), and poor understanding of discharge instructions (32.9% vs 3.0%). Sensitivity of resident identification was low across all barriers, with the highest for transportation difficulties (31.7%) and lowest for medication cost concerns (3.1%). Using McNamara's test, there was significant disagreement between patient reports and resident identification. Residents consistently under-identified barriers to ED discharge across all domains, except for transportation difficulty. Conclusions: Emergency medicine residents often underrecognize critical social and functional barriers that impact patient care after ED discharge. Poor agreement between patient-reported and physician-identified challenges, particularly in health literacy, the presence of a primary care physician, and financial constraints, suggesting a need for enhanced training, systematic screening, and interdisciplinary collaboration. Addressing these gaps is essential to improving discharge safety and reducing preventable adverse outcomes for vulnerable patients. [Formula presented] Yes, authors have interests to disclose Disclosure: SAEM Foundation Joseph Miller Grant Support SAEM Foundation

Emergency Medicine

Hawatian K, **Emakhu J**, **Morton T**, **Tuttle J**, **Sidani M**, **Nassereddine H**, **Krupp S**, **Cook B**, **Klausner H**, **McCord J**, and **Miller J**. 368 Hypertension Severity and Indeterminate High-Sensitivity Cardiac Troponin. *Ann Emerg Med* 2025;86(3):S160. Full Text

Study Objectives: Hypertension increases the risk of acute coronary syndrome (ACS) and major adverse cardiovascular events (MACE) (ie, myocardial infarction, all-cause mortality, and urgent revascularization), but its relationship with high-sensitivity cardiac troponin I (hs-cTnI) levels remains unclear. This study aimed to evaluate the association between hypertension severity and hs-cTnI levels and examined the impact of hypertension on 30-day MACE risk in patients with suspected ACS. Methods: We conducted a secondary analysis of a cluster randomized trial implementing a hs-cTnI early rule-out protocol. Patients were eligible for analysis who had suspected ACS and hs-cTnI testing and an electrocardiogram at a large, integrated health system consisting of ten emergency departments: five hospital-based and five free-standing facilities. We excluded patients without hs-cTnI values or values above the 99th percentile (18 ng/L). Patients were categorized into three hypertension severity groups: normotensive, defined as systolic blood pressure (SBP) less than 140 mmHg or diastolic blood pressure (DBP) less than 90 mmHg; moderately hypertensive, characterized by SBP between 140 mmHg and 180 mmHg or DBP between 90 mmHg and 110 mmHg; and severely hypertensive, where SBP was 180 mmHg or greater or DBP was 110 mmHg or greater. A generalized linear model assessed the relationship between hypertension severity and hs-cTnI levels, while multivariable logistic regression analyzed the effect of hypertension severity on 30-day MACE, adjusting for key confounders. Results: A total of 23,803 patients fit the inclusion criteria. Severe hypertension demonstrated an independent, statistically significant relationship with higher hs-cTnI levels ($\beta = 0.0645$; 95% CI: 0.047 to 0.082, $p < 0.001$). Likewise, severely hypertensive patients showed higher rates of elevated troponin levels (25.8% for 5-9 ng/L and 20.4% for 10-18 ng/L) compared to the other groups. After adjustment for confounders, the relationship between severe hypertension and 30-day MACE outcomes approached statistical significance (aOR: 1.61; 95% CI: 0.98–2.65, $p = 0.063$). Conclusion: This study revealed that patients with suspected ACS show increased hs-cTnI levels and higher 30-day MACE risks with worsening hypertension severity. Clinicians should interpret elevated troponin levels cautiously in hypertensive patients, prioritizing established risk factors such as coronary artery disease. No, authors do not have interests to disclose

Emergency Medicine

Jayaprakash N, **Gunaga S**, **Stevenson J**, **Sinkoff J**, **Spencer R**, **Stephens-Hoyer J**, **Rockoff S**, and **Bills G**. 579 Communicating Crowding Status: Developing and Validating a Traffic Light Framework for Surge Scores. *Ann Emerg Med* 2025;86(3):S249. Full Text

Study Objective: Quantifying levels of emergency department (ED) crowding that can be incorporated into healthcare system 'surge' description requires accounting for variation in hospital size and structure while still reflecting local levels of strain. The National Emergency Department Overcrowding Scale (NEDOCS) developed in 2004, is a validated communication tool used to quantify ED crowding. However, applying NEDOCS across diverse ED settings presents challenges related to generalizability. The objective of this project was to develop and validate a standardized approach for defining thresholds of ED crowding across variably sized EDs allowing more meaningful integration into a systemwide surge score. Methods: This study was conducted within a health system that includes an urban academic level 1 trauma center (D), four community and mixed academic hospital EDs (J, M, Wy, and WB), and five freestanding EDs (FSED) (B, C, F, P, S). Recognizing that the original NEDOCS variable, number of ventilated patients, underestimates the burden of critical care delivered in the today's ED's, we modified the score by substituting this variable with the number of critical care or ICU boarders. Initial validation began at the urban academic ED, which sees the highest patient volume in the system. ED crowding thresholds were defined using a traffic light-style color schema: Green, Yellow, and Red. Project stakeholders and hospital throughput leaders were mindful of the risk of desensitization if the Red threshold was set too low. An Excel-based modeling tool was used to create "what if" scoring scenarios across a wide range of variable combinations used in the modified NEDOCS (mNEDOCS) calculation. For modeling purposes, "ED Beds" and "Hospital Beds" were treated as fixed values. These "what if" scenarios were created to test our assumptions, identify leverage points, assess tactics and set thresholds. To validate thresholds across EDs in the system, each ED Medical Director selected one of two approaches: (1) prospective collection of mNEDOCS variables and perception of crowding at specific times of day to determine best-fit thresholds, or (2) use of the Excel-based "what if" tool to simulate score scenarios and identify Green, Yellow, and Red thresholds based on local conditions. Results: The urban academic level 1 trauma center was the first ED in the health system to validate the mNEDOCs model. Thresholds selected established a traffic light-based communication tool describing ED crowding, categorizing states as Green (not busy, busy, and extremely busy but not overcrowded), Yellow (overcrowded and severely overcrowded), and Red (dangerously overcrowded) (Figure 1). For system-wide expansion, each Medical Director selected the "what if" analysis tool for validation. Among the three highest-volume EDs (D, J, M), identical thresholds were set for all crowding categories. The next two mid-sized EDs (Wy, WB) established the same threshold for dangerously overcrowded, but this was 20 points lower than the larger EDs' threshold. Among the five freestanding EDs (FSEDs), there was significant variation in the dangerously overcrowded threshold, ranging from 106 to 180, a 75-point spread. The geometric mean threshold among FSEDs was 141.5 (SD = 23.8), with a median of 145. Conclusion: Development and validation of a standardized tool using a modified NEDOCS (mNEDOCS) score to describe ED crowding across a health care system is feasible. By establishing locally meaningful thresholds mapped to a traffic light schema, the tool enables consistent communication of crowding across diverse ED settings. In larger health systems with centralized coordination of transfers and bed placement, mNEDOCS has the potential to inform resource allocation, identify operational leverage points, andsupportsystemwide surge response. [Formula presented] No, authors do not have interests to disclose

Emergency Medicine

Khattab A, **Alhayek K**, **Vajda P**, **Christopher C**, **Joseph J**, **Sekhon R**, **Maroney A**, **Miller J**, and **Mitchell J**. 544 Study of the Impact of Virtual Simulation on Umbilical Vein Catheterization Among Emergency Medicine Residents. *Ann Emerg Med* 2025;86(3):S234. Full Text

Study Objectives: To assess whether Virtual reality (VR) technology has potential as a simulation tool for such procedures due to its ease of access, repeatability, and low relative cost; To survey EM residents on their perceptions around VR training in UVC placement; To analyze the performance of EM residents on the completion of simulated UVC placement on a mannikin; To teach EM residents to be proficient in high-acuity low opportunity (HALO) procedures including umbilical vein catheterization (UVC). Methods:

The study consisted of a non-randomized mixed convenience sample of EM residents (PGY 1-PGY 3) from an academic institution participating in didactic education on UVC placement. All residents were provided standard pre-learning education (n=27). The VR group received additional pre-learning with a VR UVC module (Vantari VR, Sydney AU) (n=9). The didactic session concluded with observed placement of a UVC on a task-trainer. Research assistants recorded time to completion for all learners. Standardized surveys were completed after VR pre-learning and UVC didactic simulation. Statistics using t-test or nonparametric testing were utilized where applicable. Results: All residents were successful in placement of UVC catheter on a mannikin. The mean completion time of the UVC hands-on simulation was 287 seconds in the VR group and 319 seconds in the control group (difference 32, 95% confidence interval -51 to 116 seconds, p=0.432). Participants in the VR group rated their confidence in UVC placement at 4.13 (1-5 scale) average as compared to 3.55 in the control group (p=0.150). Surveys revealed that participants strongly agreed that VR is a valuable training modality, but level of agreement was mixed on whether VR was more valuable than hands-on simulation. Conclusions: Qualitative data from the study shows that VR simulation increases confidence among residents in perception of procedural readiness and was shown to decrease their procedural time. The results of this small study did not reach statistical significance and further prospective research is needed to determine larger scale impact of VR on procedural training and patient-oriented outcomes. No, authors do not have interests to disclose

Emergency Medicine
Mirabal G, and **Jarou Z**. 508 Temporal Trends in Use of Social Determinants of Health Diagnoses in Emergency Department Patients. *Ann Emerg Med* 2025;86(3):S216. Full Text

Study Objective: Social determinants of health (SDoH) significantly impact patient outcomes. Recently, there has been a growing focus on identifying SDoH to enhance patient access to resources and improve the efficiency of healthcare systems. One method of capturing SDoH is using ICD-10 codes (Z55-65), introduced in 2015. These codes address issues related to education and literacy, employment, housing, economic stability, and psychosocial circumstances. We hypothesize that two recent significant events may have led to increased documentation of these ICD-10 codes: the passage of California Senate Bill 1152 in 2019, which requires addressing SDoH before discharging the patient from the hospital, and changes to billing and coding guidelines in 2023 that recognize SDoH as a factor in determining the complexity of medical decision-making. Methods: The California Health & Human Services Agency makes ICD-10 codes for all emergency department visits publicly available. To analyze the frequency of Social Determinants of Health (SDoH) diagnoses, we calculated the rate per 100,000 total diagnoses (dx/100k) annually. We divided the years into three periods based on significant events: 2016-2018, 2019-2022, and 2023. We employed a two-way ANOVA to compare the average frequency of SDoH diagnoses across these periods and ICD-10 groupings. We evaluated the differences between individual groups using Post-hoc Tukey HSD testing. A P-value of less than 0.05 was considered statistically significant. Results: Overall, there were statistically significant differences in the rates of Social Determinants of Health (SDoH) diagnoses across different periods ($p < 0.001$ for 2016-2018 vs 2019-2022; $p = 0.047$ for 2019-2022 vs 2023; $p < 0.001$ for 2016-2018 vs 2023) and in terms of ICD-10 grouping ($p < 0.001$). The SDoH category that exhibited the most significant increase in the relative rate of diagnoses when comparing 2023 to 2016 was “problems related to education and literacy” (Z55), which increased from 0.45 to 25.3 diagnoses per 100,000 people, representing a rate of 55.8. In 2023, the most frequently diagnosed SDoH were “problems related to housing/economic circumstances” (Z59) at 522.6 diagnoses per 100,000, followed by “employment/unemployment” (Z56) at 98.4, and “other psychosocial circumstances” (Z65) at 83.7 diagnoses per 100,000, respectively. Conclusions: The use of Social Determinants of Health (SDoH) diagnosis codes in California emergency departments has significantly increased. Further research is necessary to determine whether these trends exist in other settings. No, authors do not have interests to disclose

Emergency Medicine
Peltzer-Jones J, **Emakhu J**, **Etu E**, **LaBadie A**, **Kouam RW**, **Lakshmish-Kumar B**, **Moore D**, **Miller J**, **Gunaga S**, and **Al-Hage A**. 230 Evaluating Pediatric Behavioral Health Emergency Visits Before and After the COVID-19 Pandemic. *Ann Emerg Med* 2025;86(3):S98-S99. Full Text

Study Objective: Emergency departments (EDs) serve as a critical safety net for pediatric behavioral health (BH) emergencies. Even before the COVID-19 pandemic, pediatric BH visits were rising nationwide. The onset of the pandemic introduced profound psychosocial stressors—including school closures, social isolation, family economic hardship, and grief—that may have exacerbated existing conditions and triggered new mental health crises among youth. These disruptions destabilized both ED and inpatient pediatric BH operations, contributing to delays in evaluation, limited psychiatric bed availability, and increased strain on children, families, and frontline providers. While several studies have documented the impact of COVID-19 on pediatric BH care during the height of the pandemic, there remains limited literature describing how these patterns have evolved during the recovery period. This study analyzes trends in pediatric BH ED visits before and after the pandemic's onset, highlighting shifts in ED utilization and quality of care. Methods: We conducted a multi-center, retrospective cohort study of pediatric ED visits within a large integrated health system in Michigan, including nine urban and suburban EDs. Data were collected from January 2016 through February 2024 using electronic health records for patients under 18 years with visits coded for BH-related conditions using ICD classifications. The study period was divided into pre-pandemic (January 2016–February 2020) and post-pandemic (March 2020–February 2024) cohorts. Patient demographics, clinical characteristics, and ED operational variables were collected. Variables included visit frequency, ED length of stay (LOS), psychiatric and general medical admission rates, use of physical restraints (violent/self-harm vs non-violent), and frequency of patients leaving against medical advice (AMA). Trends were analyzed using descriptive statistics, two-tailed t-tests, and 12-month rolling averages for temporal visualization. Results: Across the study period, our health system recorded 3,469,947 ED encounters, of which 434,482 (12.5%) were pediatric visits. Among these, 12,307 visits (2.83%) were BH-related. Overall, monthly pediatric BH visits increased by 13.0% post-COVID (from 120.7 to 136.4/month, $p < 0.01$). Pediatric psychiatric admissions rose by 33.7% (21.1 to 28.2/month, $p < 0.01$). ED LOS for pediatric BH patients increased from an average of 475 minutes (7.9 hours) pre-pandemic to over 600 minutes (10+ hours) in the post-pandemic months, representing a 50% increase in ED boarding ($p < 0.01$). Use of violent/self-destructive restraints rose by 39.7%, from 3.7 to 5.17 incidents per month ($p < 0.01$), while non-violent restraint use remained rare and unchanged. AMA rates also rose significantly post-pandemic by 81.0%, from 1.84 to 3.33 cases per month ($p < 0.01$). These trends are visually summarized in the Figure, which highlights the sharp inflection points in BH ED visits, LOS, restraint use, psychiatric admissions, and AMA rates following the onset of the COVID-19 pandemic. Conclusion: The COVID-19 pandemic has had a profound and sustained impact on pediatric BH care in our EDs. The observed increases in visit volume, psychiatric admissions, LOS, restraint use, and AMA departures point to a rising acuity among pediatric BH patients and reflect escalating strain on ED operations. These findings likely highlight systemic gaps in pediatric psychiatric infrastructure and demonstrate the need for expanded pediatric mental health resources, including timely outpatient access, inpatient psychiatric capacity, crisis stabilization units, and enhanced ED support for BH care. Efforts to improve coordination between EDs and community mental health services will be critical to meeting the complex needs of this growing and vulnerable patient population. [Formula presented] No, authors do not have interests to disclose

Emergency Medicine

Saba R, **Jarou Z**, **Miles V**, **Olinger T**, and **McGuire D**. 543 Sonographer and Radiologist Agreement for DVT and Gallbladder Ultrasound in the Emergency Department. *Ann Emerg Med* 2025;86(3):S234. Full Text

Study Objectives: Prior studies have demonstrated high-rates of agreement between sonographer and radiologist interpretation of ultrasound images. In emergency medicine (EM), length of stay is an important quality measure. If the findings reported on sonographer worksheets are sensitive for conditions reported by radiologists, there may be opportunities to decrease length of stay. Methods: A retrospective study of adult patients (age 18+) presenting to the emergency departments at Henry Ford Providence Southfield and Novi was conducted, reviewing ultrasounds ordered for deep vein thrombosis (DVT) and abdominal studies ordered for cholelithiasis or cholecystitis. Sonographer worksheets were considered positive for cholecystitis if at least two of the following were documented: gallstones, positive Murphy's sign, pericholecystic fluid, and gallbladder wall thickening. Radiologist reads were considered positive for cholecystitis if the interpretation was definitive or reported findings suggestive of cholecystitis, or if further imaging was recommended (ie, HIDA scan). Sample size calculations were performed based on an

estimated 10% prevalence of disease, with an expected sensitivity of 95% for sonographer reads, using radiologist reads as the gold standard. The diagnostic accuracy of sonographer findings was assessed by constructing 2x2 tables. Results: Radiologist and sonographer's interpretations were extracted for 223 DVT and 186 abdominal ultrasounds. The prevalence of DVT was 11.2%, while the prevalence of cholelithiasis and cholecystitis was 38.7% and 14.0%, respectively. There was 100% agreement between sonographers and radiologists for DVT studies. For gallbladder ultrasounds, the sensitivity for cholelithiasis was 98.6% (95% CI, 97.4-100%) and 69.2% for cholecystitis (95% CI, 61.6-75.9%) Conclusions: At our institution, it may be reasonable to disposition patients awaiting results for DVT studies based on the sonographer worksheet alone. The same cannot be said for gallbladder ultrasounds. This discrepancy is likely caused by increased complexity of criteria for diagnosis of cholecystitis and that sonographers did not know their worksheets would be used for this purpose. Future studies should be performed to evaluate EM clinician willingness to disposition patients based on sonographer findings and the potential impact this may have on length of stay for various types of ultrasounds. No, authors do not have interests to disclose

Emergency Medicine

Vajda P, **Chien C**, **Al Karaki V**, **Gunaga S**, **Jayaprakash N**, **Klausner H**, **Miller J**, **Rammal JA**, **Rockoff S**, **Sinkoff J**, and **Betham B**. 361 Quantifying Changes in Daily Census Across Emergency Departments in 2018 and 2023: A Call to Action. *Ann Emerg Med* 2025;86(3):S156-S157. Full Text

Study Objective: To compare daily patient census data between academic, community and freestanding emergency departments (EDs) within a single health system in the pre- and post-COVID-19 era (2018-2023). Methods: This retrospective study was conducted across multiple EDs in a health system in southeastern Michigan. Operational data from three distinct ED settings (one academic, four freestanding, and four community) were reviewed for the years 2018 and 2023. The primary metric was the median treatment census by hour of the day for each site, assessing patient volume at specific times. The number of patients for each hour of the day was plotted along the Y- and X-axes. This analysis was performed separately for each year (2018 and 2023) and each ED setting. We calculated the percentage of variance between the lowest and peak patient census for each ED setting/year to assess daily variation. To compare daily census differences between 2018 and 2023, we focused on two time points: 7 am and 8 pm and calculated the relative percent increase in census between these times. Data from the four freestanding and four community EDs were aggregated and compared to the academic center using two-way analysis of variance (ANOVA). Results: The lowest daily census consistently occurred around 7 am, and the highest around 8 pm across all sites in both 2018 and 2023. Freestanding EDs exhibited the greatest fluctuations in census compared to other EDs ($p < 0.001$). In 2018, the freestanding EDs had a median census of 11 patients at 7 am and 51 patients at 8 pm, with a variability of 462%. In 2023, the median census at 7 am was 16, and at 8 pm, it was 62, representing a 387% variability. Community EDs exhibited similar trends but with lower variability. In 2018, the median census at community EDs was 59 at 7 am and 170 at 8 pm, reflecting a 288% increase. In 2023, the median census was 105 at 7 am and 196 at 8 pm, a 186% increase. The academic center had the least variability in daily census ($p < 0.001$). In 2018, the median census at the academic site was 48 at 7 am and 82 at 8 pm (a 121% increase), while in 2023, the census was 78 at 7 am and 92 at 8 pm (a 117% increase). Total yearly volume for the four freestanding EDs was 129,547 in 2018 and 128,156 in 2023. The community EDs had a total yearly volume of 244,753 in 2018 and 228,896 in 2023, while the academic center had 101,210 in 2018 and 84,792 in 2023. Conclusion: This study reveals consistent daily census fluctuations across ED settings, with freestanding and community EDs experiencing greater hourly variability than academic sites. Post-COVID trends show reduced total volume but persistently elevated hourly census, likely reflecting longer lengths of stay and delayed throughput. The academic ED's stable census pattern may indicate ongoing boarding challenges. These insights can guide EDs in adjusting staffing models, anticipating peak times, and developing targeted surge protocols across diverse care environments. [Formula presented] No, authors do not have interests to disclose

Gastroenterology

Aburumman R, **Tahmazian S**, **Nimri F**, and **Jafri S**. Management of Graft versus Host Disease Involving the Bone Marrow: Interventions and Outcomes. *Am J Transplant* 2025;25(8):S482. Full Text

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Purpose: Cytopenias can significantly impact patient outcomes in the immediate post-solid organ transplant period, and they can result from acute graft-versus-host disease (GVHD), though this is less frequent. This study aims to detail our single-center experience with GVHD with bone marrow involvement in patients who underwent liver transplantation (LT) over 10 years. Methods: We reviewed medical charts for patients who underwent LTs at Henry Ford Hospital Transplant Center from January 2014 to December 2023. We recorded all confirmed cases of GVHD with bone marrow involvement after LT. We collected information on their demographics, details of the liver transplant, and how GVHD was presented, diagnosed, and treated. Results: Out of 1,045 LTs performed at our center, 17 patients (1.6%) developed GVHD after transplantation. Of them, 8 had bone marrow involvement that presented in all patients as pancytopenia. Most of them were male (75%) and white (50%). The mean age at presentation was 67 ± 5. The most common indication for transplant was metabolic dysregulation associated steatotic liver disease (MASLD) in 50% of patients. All patients received liver from deceased donor. The average time from transplantation to first symptom reported was 34 days (± 16.4 SD). 7 out of the 8 patients also had skin involvement that presented as a rash (87.5%). Gastrointestinal tract involvement was seen in 62.5% of them and presented as diarrhea in all cases. One patient also had involvement of their central nervous system, which presented as altered mental status and diagnosed with a lumbar puncture. At presentation, a short tandem repeat (STR) test on patients' peripheral blood demonstrated the presence of a mean of 20.9% (± 31.1%) donor DNA. All patients received high-dose steroids as part of their treatment. 87.5% of them also received Etanercept as part of the treatment regimen, and half of them also received Photopheresis. Only one patient (12.5%) survived for more than 1 year after initial presentation, compared to 78% of patients with GVHD post LT who did not have bone marrow involvement. Conclusions: GVHD after solid organ transplantation typically presents with rash, diarrhea, fever, and pancytopenia 2 to 8 weeks after transplantation. Cytopenia has been described to confer a worse outcome. The lack of clinical trials for GVHD treatment limits an effective therapeutic strategy, and treatment outcomes of GVHD post liver transplant tend to be poor, with >85% mortality rate. [Formula presented] CITATION INFORMATION: Aburumman R., Tahmazian S., Nimri F., Jafri S. Management of Graft versus Host Disease Involving the Bone Marrow: Interventions and Outcomes AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: R. Aburumman: None.

Gastroenterology

Abusuliman M, **Kadouh A**, **Aburumman R**, **Rosario A**, **Pradeep A**, **Cox T**, **Rehman S**, **Klutke J**, **Saleem A**, **Alomari A**, Abusuliman A, Amreia M, **Arwani R**, **Dababneh Y**, **Khan M**, and **Jafri S**. Outcomes of Simultaneous Liver and Kidney Transplant vs. Liver Transplant Alone: Insights from a Midwest Transplant Center. *Am J Transplant* 2025;25(8):S471. Full Text

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Purpose: We aimed to evaluate long-term renal and survival outcomes in patients with chronic kidney disease (CKD) undergoing liver transplantation alone (LTA) versus simultaneous simultaneous liver and kidney transplant (SLK). Methods: A retrospective study included adult CKD patients (GFR <60 for ≥3 months pre-transplant) who underwent LTA or SLK at our center (2015-2022). Data collected covered demographics, comorbidities, liver disease, and dialysis status. The primary outcome was GFR at 3 months pre-transplant and 3, 6, 12, and 36 months post-transplant. Secondary outcomes included LOS, 1-year readmission, rejection, retransplantation, and mortality at 1, 3, and 5 years. Results: Our study included 231 patients: 67 underwent SLK, and 164 received LTA. Patient characteristics are in Table 1. Cirrhosis was the primary transplant indication in 193 patients (97%), mostly due to alcohol. The SLK group had higher creatinine on transplant day, pre-transplant HRS, and significantly lower pre-transplant

GFR (22.1 ± 11.7 vs. 47.8 ± 15.6, p < 0.001). Both groups showed GFR improvement (p < 0.01), but SLK had consistently higher post-transplant GFR, especially at 3 months (65.8 ± 24.5 vs. 52.3 ± 19.0, p < 0.01) (Figure 1). GFR decline was greater in LTA (p < 0.01). Mortality (28% vs. 20%, p = 0.14) and LOS (13 days, p = 0.3) were similar. Pre- or emergent post-transplant dialysis prolonged hospital stay (p < 0.01, p < 0.027). No significant differences were found in readmission (68% SLK vs. 63% LTA, p = 0.4) or re-transplantation (6.7% vs. 9.4%, p = 0.9). Graft rejection was higher in SLK (23% vs. 17%) but not significant (p = 0.3). Conclusions: Our study shows that SLK transplant provided better long-term renal preservation in patients with CKD. Mortality,LOS,readmission, and re-transplant rates were similar between groups,suggesting that SLK does not significantly increase perioperative risk or resource use. [Formula presented] CITATION INFORMATION: Abusuliman M., Kadouh A., Aburumman R., Rosario A., Pradeep A., Cox T., Rehman S., Klutke J., Saleem A., Alomari A., Abusuliman A., Amreia M., Arwani R., Dababneh Y., Khan M., Jafri S. Outcomes of Simultaneous Liver and Kidney Transplant vs. Liver Transplant Alone: Insights from a Midwest Transplant Center AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Abusuliman: None.

Gastroenterology

Alomari A, Althunibat I, **Saleem A**, **Abusuliman M**, **Omari Y**, **Jomaa D**, **Dababneh Y**, and **Jafri S**. Management of Patients with Vascular Reconstruction during Liver Transplantation. *Am J Transplant* 2025;25(8):S455. Full Text

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Purpose: Liver transplantation occasionally requires vascular reconstruction, such as arterial jump grafts or portal vein thrombectomy, to ensure adequate blood flow. Aspirin (ASA) and anticoagulation (AC) therapies are used to reduce thrombotic risk but may increase bleeding. Limited data exist on their impact in this context. This study evaluates the effect of ASA/AC use on survival, thrombotic events, bleeding, and retransplant rates, aiming to optimize care for this high-risk group. Methods: We performed a retrospective chart review of 400 patients who underwent liver transplant between 2019 and 2023. 66 patients received an arterial jump graft, a portal vein thrombectomy, or both. Demographic factors (age, gender, race), ASA/AC prescription at discharge, MELD scores at transplant, and clinical outcomes, including 1-year survival, ischemia/clots, bleeding events, and retransplant or death, were collected. Patients were stratified by ASA/AC prescription. Descriptive analysis was performed to identify trends in outcomes. Results: The study analyzed a cohort of 66 post-transplant patients with a median age of 62 years (range: 58-72). The majority were male (62%, n=41) and White (85%, n=56), with smaller proportions of Black (4%, n=3) and other racial backgrounds (11%, n=7). MELD scores at the time of transplant were higher in patients not on ASA/AC (median: 30, range: 23-40) compared to ASA/AC users (median: 24, range: 15-39). ASA/AC was prescribed at discharge to 87.87% of patients, while 12.12% did not receive ASA/AC. Clinical outcomes differed between groups: the 1-year survival rate was 96.5% in ASA/AC users compared to 75% in non-users. The incidence of ischemia/clots was comparable (27.6% vs. 25%), while bleeding events were more frequent in ASA/AC users (17.2% vs. 0%). Retransplant rates were 1.72% in ASA/AC users versus 12.5% in non-users. Among patients with clots, 16.7% experienced graft loss, with death occurring in 5.5% and retransplantation in 11.1% of these patients. In contrast, patients without clots had a 4.3% graft loss (death) rate and 0% retransplantation. Conclusions: ASA/AC use post-transplant is associated with improved 1-year survival rates, lower retransplant and death rates, and minimal impact on ischemia/clot incidence. Among patients with clots, graft loss, death, and retransplantation rates were notably higher than in patients without clots. These findings suggest ASA/AC may confer protective benefits in the post-transplant population, warranting further research to optimize its role in this context. CITATION INFORMATION: Alomari A., Althunibat I., Saleem A., Abusuliman M., Omari Y., Jomaa D., Dababneh Y., Jafri S. Management of Patients with Vascular Reconstruction during Liver Transplantation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES:

Gastroenterology

Alomari A, **Saleem A**, Althunibat I, **Abusuliman M**, **Dababneh Y**, **Jomaa D**, Abdulraheem A, **Mo J**, **Chen K**, and **Jafri S**. Association of Mean Arterial Pressure (MAP) with Mortality in Patients with Liver Cirrhosis Awaiting Transplantation. *Am J Transplant* 2025;25(8):S477. Full Text

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Purpose: Patients with liver cirrhosis listed for liver transplantation often experience hemodynamic changes, including changes in mean arterial pressure (MAP). Identifying the prognostic impact of MAP on mortality in this population may guide clinical decision-making. This study evaluates the association between MAP and mortality in patients listed for liver transplant. Methods: We conducted a retrospective cohort study of adult patients with liver cirrhosis listed for liver transplantation at a quaternary care center. To ensure comparability, only patients with a Model for End-Stage Liver Disease (MELD) score of 20-24 at the time of listing were included, while those with hepatocellular carcinoma (HCC) were excluded. Data collected included demographic information, mean arterial pressure (MAP) at listing, and clinical factors such as the use of antihypertensive medications, beta-blockers, and midodrine, as well as complications like hepatorenal syndrome (HRS), hepatic encephalopathy (HE), ascites, and variceal bleeding. We used logistic regression models to analyze the relationship between MAP and mortality on the waiting list, adjusting for medications and complications to isolate the independent effect of MAP. Additionally, a two-sample t-test was performed to compare the mean MAP between patients who died and those who survived Results: A total of 103 patients were analyzed. Higher MAP was significantly associated with lower odds of mortality on the waiting list (OR = 0.94, 95% CI: 0.89-0.99, p = 0.041). Each unit increase in MAP was associated with a 6% reduction in mortality risk. The mean MAP was significantly lower in patients who died (76.9 mmHg) compared to those who survived (83.2 mmHg) (p = 0.043). Additionally, higher MAP was associated with a decreased risk of HRS (OR = 0.94, 95% CI: 0.89-0.98, p = 0.011), but no significant associations were found between MAP and HE (OR = 0.97, 95% CI: 0.93-1.02, p = 0.247), ascites (OR = 1.00, 95% CI: 0.95-1.05, p = 0.847), or variceal bleeding (OR = 1.02, 95% CI: 0.95-1.09, p = 0.567). Conclusions: Lower MAP at the time of listing is an independent predictor of mortality in cirrhotic patients awaiting liver transplantation. The association remains robust after controlling for disease severity (MELD score), medications, and common complications. Additionally, low MAP was associated with a higher risk of developing HRS but not with HE, ascites, or variceal bleeding. These findings highlight the potential importance of hemodynamic optimization in this population. CITATION INFORMATION: Alomari A., Saleem A., Althunibat I., Abusuliman M., Dababneh Y., Jomaa D., Abdulraheem A., Mo J., Chen K., Jafri S. Association of Mean Arterial Pressure (MAP) with Mortality in Patients with Liver Cirrhosis Awaiting Transplantation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES:

Gastroenterology

Asfaw M, Garg A, Chalasani P, Vasireddy R, **Worley J**, and Kancharla P. Pancreatic cancer mortality trends (2018-2023): Exposing racial inequities in Michigan's cancer burden. *J Clin Oncol* 2025;43(16). Full Text

M. Asfaw

Background: Pancreatic cancer remains one of the most aggressive malignancies, with Black individuals facing significantly worse outcomes and a younger age of onset. Despite overall survival improvements in cancer care, racial disparities in pancreatic cancer continue to widen. This study analyzes Michigan's diverse population to quantify disparities and identify actionable solutions for healthcare equity. Methods: This observational study analyzed pancreatic cancer mortality patterns across Michigan in adults aged 25 and older were retrieved from the CDC WONDER database (2018-2023) using ICD-10 codes for malignant neoplasm of the pancreas. Crude mortality rates (CMRs) and Age-adjusted mortality rates

(AAMRs) per 100,000 were calculated by age, gender and race, with 95% confidence intervals (CI) for precision to assess racial disparities in mortality outcomes. Temporal trends and annual percentage changes (APCs) were analyzed using Joinpoint regression. Results: From 2018-2023, Michigan reported 10,162 pancreatic cancer deaths, with Black residents (14.1% of the population) accounting for 1,289 and White residents (who make up 78.9%) for 8,664 deaths. Overall, CMR was higher for White residents (18.26 per 100,000) than Black residents (15.21 per 100,000) who experienced a sharper rise in AAMR, increasing by 8.10% [14.36 (13.55-15.16)] compared to 4.92% [12.36 (12.10-12.63)] for White residents. For Black residents, CMRs increased with age, rising from 8.14 per 100,000 (45-54 years) to 105.78 per 100,000 (85+ years), peaking at 69.46 (65-74 years) and 95.37 (75-84 years). White residents had lower CMRs overall, starting at 1.48 per 100,000 (35-44 years) and gradually increasing to 115.28 per 100,000 in the 85+ group.In Washtenaw County, Black residents had a rate of 14.01 per 100,000 and White residents 15.79 per 100,000 with similar trends in Genesee, Wayne, and Ingham counties. Treatment inequities compounded these disparities: Black patients faced 38% lower odds of surgery, 45% longer delays for chemotherapy, and 27% lower clinical trial enrollment. These findings highlight significant racial disparities in pancreatic cancer mortality, treatment access, and outcomes, underscoring the need for targeted public health interventions. Conclusions: Our findings reveal significant racial disparities in pancreatic cancer outcomes in Michigan, with Black residents experiencing higher mortality rates and a younger age of death than White residents. These disparities reflect systemic barriers, including delayed diagnosis, fewer surgeries, and limited access to specialized care. Addressing these inequities requires bias training, targeted screening for high-risk Black populations, and expanded oncology services, while actionable solutions such as patient navigation and community-based screening programs can help bridge this healthcare gap and promote equity.

Gastroenterology

Chalasani P, Garg A, Vasireddy R, **Worley J**, and Kancharla P. Colorectal cancer mortality dynamics: Uncovering critical disparities in U.S. population health (2018-2023). *J Clin Oncol* 2025;43(16). Full Text

P. Chalasani

Background: Colorectal cancer(CRC) remains the third leading cause of cancer-related deaths in the United States, with a disproportionate burden on underserved populations. Despite established screening protocols and preventive measures, fewer than 35% of cases are detected early, significantly impacting survival rates. This study examines mortality patterns across demographic and geographic divides, revealing urgent public health priorities. Methods: This retrospective analysis was performed in adults aged 25 and older using the CDC WONDER database (2018-2023) using ICD-10 codes. We stratified mortality data by age, gender, race, geographic region and urbanization level to identify critical disparities and emerging trends. Crude mortality rates (CMRs) and Age-adjusted mortality rates (AAMRs) per 100,000 were calculated by age, gender, region and race, with 95% confidence intervals (CI) for precision. Temporal trends and annual percentage changes (APCs) were analyzed using Joinpoint regression. Results: From 2018 to 2023, among 313,744 deaths, mortality increased from 51,891 to 53,497, while theAAMR for CRC consistently declined from 12.92 to 12.44. The highestCMRwas in the 85+ group (156.11 per 100,000,95% CI: 153.05-159.17), followed by 75-84 (74.18,95%CI: 72.87-75.49), 65-74 (40.27, 95% CI: 39.58-40.96), and 55-64 (23.83, 95% CI: 23.37-24.30). The 45-54 group had a CMR of 11.74 (95% CI: 11.40-12.07), the 35-44 group 3.56 (95% CI: 3.38-3.74), the 25-34 group 0.77 (95% CI: 0.69-0.86), and the 15-24 group had the lowest at 0.09 (95% CI: 0.06-0.12). Males had a higher CMR of 17.23 per 100,000 (AAMR: 15.19, APC: -0.68, p = 0.21) than females, who had 14.42 per 100,000 (AAMR: 10.69, APC: -0.30, p = 0.56). The Midwest had the highest AAMR at 13.33 per 100,000 [APC: -0.78 (95% CI: -2.54 to 1.01, p = 0.31)], followed by the South at 13.54 [APC: 0.05 (95% CI: -0.80 to 0.92, p = 0.91)], the West at 11.90 [APC: 0.09 (95% CI: -0.79 to 0.95, p = 0.82)], and the Northeast at 11.54, with a significant decline in trends [APC: -1.90 (95% CI: -3.24 to -0.58, p < 0.01)]. Large central metro areas accounted for 25.3% of deaths (83,341), followed by large fringe metro areas (22.4%), medium metros (19.9%), micropolitan areas (10.0%), small metros (9.4%), and noncore areas (8.2%). Racial disparities showed White individuals with the highest CMR at 17.01 per 100,000 (AAMR: 12.69, APC: -0.78), while Black or African American individuals had a slightly lower CMR at 15.70 per 100,000 but the highest AAMR at 16.18 (APC: -1.63, p < 0.01), followed by American Indian or Alaska Native, Asian, Native Hawaiian, and other groups. Conclusions: These findings reveal critical gaps in CRC

prevention and care, disproportionately affecting young adults, males, and minorities. Public health initiatives must expand screening, improve access to care, and address regional inequities to reduce mortality and promote health equity.

Gastroenterology
Dunn W, Alkhouri N, Yip TCF, Castera L, Takawy M, Adams L, Verma N, Arab JP, **Jafri SM**, Zhong B, Dubourg J, Chen V, Singal AK, Diaz LA, Dunn N, Nadeem R, Wong VWS, Abdelmalek MF, Wang Z, Duseja AK, Almahanna Y, Bajunayd A, **Omeish HA**, Ye J, Harrison SA, Wong GLH, Arrese M, Robert S, and Shao C. Enhancing prediction of moderate fibrosis in MASLD patients for Resmetirom treatment via machine learning. *J Hepatol* 2024;80:S84. Full Text

Background and aims: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) affects approximately 30% of the global adult population and poses significant risks of disease progression particularly in patients with moderate to advanced fibrosis (stages 2–3). Following the FDA's approval of Resmetirom for treating Metabolic Dysfunction-Associated Steatohepatitis (MASH) in these stages, there is a need for a surrogate marker to refine the selection of patients for liver biopsy. The ALADDIN study introduces a novel machine learning-based web calculator to estimate the probability of stage ≥2 fibrosis in MASLD using routine laboratory parameters, with and without Vibration Controlled Transient Elastography (VCTE). Method: A total of 3708 patients with biopsy-confirmed MASLD from six centers worldwide were divided into Derivation and Internal Validation cohorts on a 1:1 basis, supplemented by 1289 patients from nine centers for External Validation. ALADDIN models, employing Random Forest, Gradient Boosting Machines, and XGBoost enhanced by Bayesian updates, were developed to evaluate moderate fibrosis (stage ≥F2). Results: The VCTE model achieved an Area Under the Curve (AUC) of 0.800 (95% CI 0.773–0.827) in external validation, significantly outperforming the FAST (AUC: 0.707, 95% CI 0.674–0.739, p < 0.0001) and Agile-3 (AUC: 0.764, 95% CI 0.735–0.793, p = 0.001) models. The model using routine laboratory parameters without VCTE reached an AUC of 0.757 (95% CI 0.730–0.783), comparable to FASTand Agile-3. The VCTE model model also demonstrated superior decision curve analysis, calibration, and classification accuracy, using a dual cut-off approach, and outperformed existing models in predicting moderate fibrosis. Conclusion: The ALADDIN study, via an international consortium has successfully developed and externally validated machine learning models that predict moderate fibrosis with notable accuracy. Our VCTE model, available at https://aihepatology.shinyapps.io/ALADDIN1/, and our routine laboratory parameter model without VCTE, available at https://aihepatology.shinyapps.io/ALADDIN2/ demonstrate statistical superiority and comparable performance respectively, against traditional models including Agile-3 and FAST. These algorithms will facilitate targeted liver biopsy in line with the new FDA approval for Resmetirom treatment.

Gastroenterology
Faisal M, **Faisal M**, **Saleem A**, **Karmo B**, **Hasso M**, **Chaudhary A**, **Shahzil M**, **Jafri S**, and **Zuchelli T**. Strategies for Success in Endoscopic Retrograde Cholangiopancreatography (ERCP) Intervention in Liver Transplant Patients with Biliary Complications and Altered Intestinal Anatomy. *Am J Transplant* 2025;25(8):S464-S465. Full Text

Purpose: Surgically altered anatomy in patients who undergo Liver Transplant (LT) offers a unique challenge to endoscopists. There is limited data regarding the optimal endoscopic approach for the management of biliary complications in this population. We aim to assess the safety, efficacy and outcomes of various endoscopic approaches to managing patients with altered anatomy following LT. Methods: Retrospective data was collected after study approval from our IRB. Individuals who had a history of LT and surgically altered anatomy who subsequently underwent an ERCP from 2017-2024 were selected. Individual charts were reviewed to collect demographic and procedural data. Outcomes included post-procedure complications and technical success. Results: 61 patients were identified who had surgically altered anatomy with a history of LT. Of these, 13 underwent ERCP, for a total of 29 procedures. 24 ERCPs were done in patients with hepaticojejunostomy (HJ), and 5 in Roux-en-Y gastric bypass (RYGB). For patients with HJ, 6(25%) ERCPs were done within 6 months of LT, whereas 2(40%) were done in this timeframe for RYGB. Indications for both groups included jaundice(N=11, 38%), stent management(N=9, 31%), sepsis(N=6, 21%), and others. For the two patients who had RYGB, one had EDGE procedure with same day ERCP and three subsequent ERCPs through the gastrogastric fistula via

the lumen apposing metal stent. The other patient had laparoscopy assisted ERCP. For patients with HJ anatomy, adult colonoscope was used in 15(26%) procedures, pediatric colonoscope for 4(17%) procedures, single balloon enteroscope for 4(17%) procedures and 1(4%) was done with a duodenoscope. Rigidizing overtube was used in 9(37.5%) of these procedures. Of these, 6(25%) were unsuccessful, with inability to reach HJ with colonoscope (N=3), excessive looping with single balloon enteroscope (N=1), and inability to locate HJ (N=2). Percutaneous Transhepatic Cholangiogram (PTC) drain placement was required in 3 of the unsuccessful procedures. Adverse events included esophageal mucosal breaks (N=2). Conclusions: We highlight the favorable success rate of endoscopic interventions in this population, with minimal adverse events. This suggest that ERCP can be a first step in managing biliary disease in post-LT patients with altered anatomy. Furthermore, successful interventions through ERCP can reduce the rate of PTC drain placement and the risk of infection related to PTC. Endoscopists should be aware of the various techniques and equipment available for technical success. Larger studies need to be done to establish guidelines for this indication. [Formula presented] CITATION INFORMATION: Faisal M., Faisal M., Saleem A., Karmo B., Hasso M., Chaudhary A., Shahzil M., Jafri S., Zuchelli T. Strategies for Success in Endoscopic Retrograde Cholangiopancreatography (ERCP) Intervention in Liver Transplant Patients with Biliary Complications and Altered Intestinal Anatomy AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Faisal: None.

Gastroenterology

Faisal M, **Garg N**, **Aburumman R**, **Saleem A**, Shahzil M, **Fatima M**, **Faisal M**, and **Jafri S**. Decreased Rate of Rejections Post Liver Transplant in Patients on a Glucagon-Like Peptide 1 (GLP-1) Analogue. *Am J Transplant* 2025;25(8):S487-S488. Full Text

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Purpose: Rejection is prevalent in patients undergoing liver transplant (LT), with studies showing a relation of Body Mass Index (BMI) to post transplant outcomes, including rates of rejection. Recently, Glucagon-like peptide-1(GLP-1) analogues are increasingly being used in post-transplant patients. We aimed to assess the association of semaglutide and tirzepatide with transplant rejection in patients with BMI > 30. Methods: Patients who underwent LTs at our institution were included from 1/2018-12/2023. Inclusion criteria was BMI > 30. We did a retrospective cohort study to assess whether they received GLP-1 analogues, including semaglutide and tirzepatide, after the liver transplant. Data including patient demographics and comorbidities was collected. The primary outcome was transplant rejection at 1 and 2-3 years. The secondary outcome was 3-year mortality. Results: 137 patients were included who underwent liver transplant from 01/2018-12/2023 with a BMI > 30. Of these, 33(24.1%) were exposed to semaglutide or tirzepatide while 104 (75.9%) had no such exposure after transplant. The mean age of the population was 58.86 +/- 8.2 in the case group and 62.08 +/- 9.2 in the control group. 23 (69.7%) were male in the case group while 69 (66.3%) were male in the control group. Comorbidities, including HTN, stroke and ESRD were comparable in both groups. 27 (87.9%) in the case group had diabetes while 37(35.6%) in the control group had diabetes (p=0.001). Mean BMI for the case group was 36.34 ± 4.81 and mean BMI for the control group was 33.9 ± 3.82 (p=0.01). Underlying liver disease prior to transplant was similar between the 2 groups, with Metabolic Dysfunction-Associated Steatohepatitis (MASH) being the most prevalent. For outcomes, 2(6.1%) patients in the exposed group had rejection within 3 years, compared to 24(23.1%) in the control group (p=0.03). Of these, both the patients in the control group had rejection within 1 year compared to 20(19.4%) patients in the control group who had rejection within 1 year. At 3 years, there were 0 deaths in the case group compared to 4 (3.9%) deaths in the control group (P=1.0). Conclusions: In our cohort, the use of semaglutide and tirzepatide was associated with a decreased incidence of liver transplant rejections in patients with BMI > 30. We were limited by single center and smaller number of patients. Further large scale, multicenter studies are needed to confirm the efficacy of these medications, possibly suggesting a more significant role post liver transplant. [Formula presented] CITATION INFORMATION: Faisal M., Garg N., Aburumman R., Saleem A., Shahzil M.,

Fatima M., Faisal M., Jafri S. Decreased Rate of Rejections Post Liver Transplant in Patients on a Glucagon-Like Peptide 1 (GLP-1) Analogue AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Faisal: None.

Gastroenterology
Faisal M, **Saleem A**, **Fatima M**, **Chaudhary AJ**, **Shahzil M**, **Faisal M**, and **Jafri S**. Impact of Glucagon Like Peptide-1 (GLP-1) Analogue Medications on Liver Transplant Risk Factors. *Am J Transplant* 2025;25(8):S462. Full Text

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Purpose: Patients who undergo liver transplantation are at higher risk of complications from diabetes and obesity. Recently, GLP-1 analogues have revolutionized management of these conditions and are increasingly being used in post-transplant patients. However, the safety of these agents in this population, particularly their association with cancer risk, is controversial. We aimed to assess the association of semaglutide and tirzepatide with cancer in patients who undergo liver transplant. Methods: All patients who underwent liver transplant at our institution were included from 1/2018-12/2023. We did a retrospective cohort study to assess whether they received GLP-1 analogues, including semaglutide and tirzepatide, after the liver transplant. Primary outcome was development of malignancy. Secondary outcomes were 1-and 3-year mortality. Results: 366 patients were included who underwent liver transplant from 01/2018-12/2023. Of these, 42(13%) were exposed to semaglutide or tirzepatide while 324(88%) had no such exposure. The mean age of the population was 58.12 +/- 7.6 in the exposed group and 58.44 +/- 11.5 in the control group. Comorbidities, including HTN, stroke and ESRD were comparable in both groups. 37(88.1%) in the exposed group had diabetes while 111(34.2%) in the control group had diabetes($p<0.001$). Similarly, 28(66.7%) patients in the exposed group had BMI>30 while 111(34.5%) patients in the control group had BMI>30($p<0.001$). The follow up period was 3.74 +/-1.3 years for the exposed group and 4.01 +/-1.5 years in the control group. For outcomes, 2(4.8%) patients in the exposed group were diagnosed with cancer in the follow up period versus 26(8.1%) in the control group ($p=0.76$). There was no cancer related mortality at one year while at 3 years, it was similar in both groups. For malignancies, 1(50%) patient in the exposed group had HCC, while 5(18%) patients in the control group had either HCC or cholangiocarcinoma. No patients in the exposed group were diagnosed with skin related malignancies including BCC, SCC and Malignant Melanoma, while 13(46%) patients in the control group were diagnosed with such malignancies. 1 patient in the exposed group was diagnosed with Post Transplant Lymphoproliferative Disorder. 11 patients in the control group were diagnosed with other malignancies including prostate cancer, lymphoma, follicular thyroid cancer, and leukemia. Conclusions: In our cohort, the use of GLP-1 analogues was not associated with cancer in patients who undergo liver transplantation. We were limited by single center and smaller number of patients. Further large scale, multicenter studies are needed to confirm the safety of these medications. [Formula presented]
CITATION INFORMATION: Faisal M., Saleem A., Fatima M., Chaudhary A., Shahzil M., Faisal M., Jafri S. Impact of Glucagon Like Peptide-1 (GLP-1) Analogue Medications on Liver Transplant Risk Factors AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Faisal: None.

Gastroenterology
Gordon SC, Jacobson I, Younes ZH, Silveira M, Drenth JPH, Morgera U, Dalekos G, Heo J, Yang K, Heusner C, Crittenden DB, and McWherter CA. Efficacy and safety of seladelpar in patients with primary biliary cholangitis and compensated liver cirrhosis in the open-label long-term ASSURE safety study: interim results. *J Hepatol* 2024;80:S20. Full Text

Background and aims: Seladelpar, a potent and selective PPAR-delta agonist (ie, a delpar), has anti-cholestatic and anti-pruritic activity in patients with primary biliary cholangitis (PBC). The ongoing international, phase 3 ASSURE study (NCT03301506) is an openlabel long-term study of seladelpar in patients with PBC who participated in a prior seladelpar study. Here we report interim efficacy and safety

results on a subset of patients with compensated liver cirrhosis. Method: Patients with PBC and cirrhosis were eligible for ASSURE if they had an inadequate response or intolerance to ursodeoxycholic acid (UDCA), previously participated in a seladelpar study, and had no history of hepatic decompensation. All patients received open-label seladelpar 10 mg oral daily. As of the data cutoff (29 June 2023), 174 patients from previous seladelpar studies (CB8025–21629 NCT02955602; CB8025-31731, NCT03301506; ENHANCE NCT03602560; CB8025-21838, NCT04950764) had enrolled, of whom 33 had compensated liver cirrhosis at study entry. Biochemical efficacy end points included the composite response of alkaline phosphatase (ALP) <1.67x upper limit of normal (ULN), ALP decrease ≥15%, and total bilirubin ≤ULN; ALP normalization; and change from baseline in ALP, total bilirubin, gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) all at Month 12. Results: Of the 33 patients with cirrhosis, most were female (91%) with a mean age of 60.4 years. Eight patients (24.2%) had portal hypertension, 93.9% were Child-Pugh (CP) class A, and 6.1% were CPB. Mean baseline liver stiffness by FibroScan was 19.3 kPa. At baseline mean ALP was 241.9 U/L, and total bilirubin was 0.92 mg/dL (27.3% >ULN). As of the data cutoff date, 23 patients with compensated cirrhosis had completed 12 months of treatment. Twelve out of 23 (52.2%) patients met the composite biochemical end point at Month 12. ALP normalization occurred in 39.1% (9/23 patients) at Month 12 and the mean percent change from baseline in ALP was −38.1% (absolute change: −99.5 U/L). Reductions were also observed in GGT and ALT (percent changes from baseline: −35.1% and −19.6% respectively) at Month 12; no change was observed in AST or total bilirubin. There were no serious adverse events that were liverrelated or related to study drug and no discontinuations due to adverse events. Conclusion: In this interim analysis of the ongoing ASSURE study PBC patients with compensated cirrhosis treated with seladelpar 10 mg for 12 months achieved clinically meaningful improvements in markers of cholestasis and liver injury. Seladelpar appeared overall safe andwell tolerated. These findings suggest that seladelpar has the potential to offer a safe and effective therapy for PBC patients with compensated cirrhosis.

Gastroenterology
Ismail M, **Chopra N**, Ahmad H, Kakakhel MZJ, Arshad MU, Qadri M, **Klein J**, Iftikhar Y, Jawad H, Afridi MS, and **Barawi M**. Cardiovascular disease and gastrointestinal cancers: Mortality trends and persistent disparities in the U.S. *J Clin Oncol* 2025;43(16). Full Text

M. Ismail

Background: Cardiovascular disease (CVD) is a significant contributor to mortality among patients with gastrointestinal tract (GIT) cancers. This study analyses changes in age-adjusted mortality rates (AAMRs) for CVD in GIT cancer patients in the U.S. from 1999 to 2020, focusing on demographic and geographic disparities. Methods: CVD-related deaths in GIT cancer patients aged ≥25 years were examined using CDC WONDER data. AAMRs per 100,000 individuals were calculated, and trends were assessed via annual percentage changes (APCs) and average annual percentage changes (AAPCs). Results: Between 1999 and 2020, 921,107 CVD deaths occurred among GIT cancer patients. The overall AAMRdecreased from 230.0 in 1999 to 190.7 in 2020, with an AAPC of -0.97∗ (p< 0.000001). Men had higher AAMRs (255.3) than women (144.4), though women experienced a greater decline (AAPC: -1.44∗, p< 0.000001) compared to men (AAPC: -0.88∗, p< 0.000001). Black individuals exhibited the highest AAMR (273.03), followed by Hispanics (199.3), Asians/Pacific Islanders (190.0), American Indians (182.75), and Whites (180.87). Asians/Pacific Islanders showed the steepest decline (AAPC: -2.56∗, p< 0.000001). Geographically, New York had the highest AAMR (318.73), while Utah recorded the lowest (98.05). Nonmetropolitan areas showed higher AAMRs than metropolitan areas but smaller declines (AAPC: -0.15∗, p = 0.003 vs. -1.13∗, p<0.000001). Conclusions: Despite overall declines in CVD mortality among GIT cancer patients, significant disparities persist by gender, race, and geography. Targeted interventions are needed to address these inequalities and further reduce the burden of CVD among this vulnerable population.

Gastroenterology
Ismail M, **Sardarova N**, Kakakhel MZJ, Singh P, Zaied MA, Ahmad H, Alsaadi MH, Ikram M, Riffat G, and **Barawi M**. From liver to life: The overlooked impact of MASLD on digestive cancer outcomes. *J Clin Oncol* 2025;43(16). Full Text

M. Ismail

Background: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is an increasing public health concern with the potential to increase the development of malignancy of the digestive tract and beyond. We aim to explore mortality trends of digestive cancer (DC) among MASLD patients. Methods: The CDC WONDER database was examined to extract age-adjusted mortality rates (AAMR) regarding DC among MASLD patients aged 25 years and older between 1999 and 2020. Data was stratified by age, gender, race, and U.S geographic regions. Results: 67616 deaths were documented from 1999 to 2020, with an overall AAPC of 2.8 (95% CI 1.99 to 3.62) and total AAMR of 13.6 (95%CI 13.5 to 13.7). Males showed higher mortality rates than females with an overall AAMR of 22.1 (95%CI 21.9 to 22.3). However, female gender showed higher AAPC with value of 3.6 (95%CI 2.88 to 4.32). Slight difference of AAPC between patients aged 55-64 and over 85 years as they showed the highest AAPC with value of 4.23 (95%CI 3.23 to 5.24) and 4.21 (95%CI 2.31 to 6.14) receptively. White race accounted for the highest AAPC followed by African American with 3.11 (95%CI 2.18 to 4.06) and 1.73 (95%CI 0.33 to 3.15) respectively. Conclusions: The highest AAPC was observed among Whites, older males, large central metropolitan residents and West residents. The observed disparities suggest the importance of improving outcomes for DC patients, particularly with MASLD. Keywords: Digestive cancer, MASLD, CDC WONDER, AAPC.

Gastroenterology

Malick A, **Tepe G**, **Nagai S**, **Muszkat Y**, **Beltran N**, **Pietrowsky T**, and **Jafri S**. Outcomes of Intestinal Biopsies Which Are Indeterminate for Rejection Following Intestine Transplant. *Am J Transplant* 2025;25(8):S839-S840. Full Text

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Purpose: We evaluated the impact of “indeterminate for rejection” (IFR) biopsy results and subsequent clinical outcomes. We aim to evaluate whether changes in immunosuppressive medications and cytomegalovirus (CMV) status at the time of IFR biopsy influence the likelihood of a subsequent biopsy also being classified as IFR or showing a definitive rejection outcome. Methods: Retrospective analysis of adult patients who underwent intestinal transplantation, including those who received multi-organ transplants with intestine with at least one biopsy classified as IFR. Data collected includes immunosuppressive changes, subsequent biopsy results, and infection status. Results: We evaluated 31 patients with long term follow-up following IFR biopsy. 17 (55%) were female. Mean age at time of transplant was 48 years (22-68). 18 (57.9%) patients had intestine transplant only, 13 had multiorgan transplant. There were 84 recorded instances of IFR biopsy results. 54 instances (64%) led to immunosuppression changes, while 30 (36%) did not. 4% of patients in the immunosuppression change group (ICG) and 7% in the no-change group (NCG) had positive CMV PCR at the time of biopsy. In ICG, 69% of cases were negative for rejection on follow-up biopsy. In NCG, 60% were negative for rejection on follow-up biopsy. Persistent indeterminate classification was observed in 9.3% of ICG cases and 20% of NCG. Mild rejection occurred in 20% of ICG cases and 17% of NCG cases. Moderate rejection was seen in 1.9% of ICG cases and 0% of NCG cases. Severe rejection was seen in 0% of ICG cases and 3.3% of NCG cases. There were no statistically significant differences between the two groups (Odds Ratio [OR] = 1.27, 95% Confidence Interval [CI]: 0.47-3.38, p = 0.6). A secondary analysis focused on only the first instance of an IFR biopsy for each patient. 71% of these cases were ICG. 77% of these ICG cases showed subsequent results negative for rejection. 44% of NCG cases showed negative subsequent results for rejection. Persistent IFR occurred in 4.5% of ICG cases and 22% of NCG. Mild rejection occurred in 14% of ICG cases and 22% of NCG. Moderate rejection occurred in 4.5% of ICG and 0% of NCG. Severe rejection occurred in 0% of ICG and 11% of NCG. Conclusions: While medication adjustments were frequently implemented following IFR biopsy, their effect on subsequent biopsy results was not statistically significant. The majority of patients who underwent immunosuppression changes had negative subsequent biopsy outcomes, similar to those without immunosuppression changes. The study highlights the complexity of managing IFR biopsy results in transplant recipients and underscores the

need for further research to better understand the appropriate response to IFR biopsy. CITATION INFORMATION: Malick A., Tepe G., Nagai S., Muszkat Y., Beltran N., Pietrowsky T., Jafri S. Outcomes of Intestinal Biopsies Which Are Indeterminate for Rejection Following Intestine Transplant AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Malick: None.

Gastroenterology
Nabaty R, **Muszkat Y**, **Nagai S**, **Beltran N**, **Pietrowsky T**, and **Jafri S**. Intestinal Transplantation for Short Bowel Syndrome from Gun Shot Wounds: A Case Series. *Am J Transplant* 2025;25(8):S843-S844. Full Text

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Purpose: Short bowel syndrome (SBS) is a malabsorption disorder leading to nutritional deficiencies and high morbidity. Gunshot wounds (GSWs) and other abdominal traumas are known causes of SBS. Intestinal transplantation offers a unique therapeutic option for this patient population; however, outcomes are not well elucidated. We present two cases of patients who developed SBS secondary to GSWs, underwent intestinal transplantation, and subsequently required transplant enterectomy. Methods: We evaluated patients with SBS due to GSW receiving an intestinal transplant at a single center for outcomes including rejection, infection, graft survival, and patient survival. Results: Two males sustained GSWs necessitating small bowel and colon resection, leading to SBS that became dependent on parenteral nutrition with multiple line-related complications. Both patients underwent isolated small bowel transplantation. Patient 1: A 21-year-old underwent transplant with post operative course remaining largely unremarkable for 102 months until he presented with abdominal pain and found to be in cellular and humoral rejection. He developed septic shock due to bacteremia and adenovirus enteritis and did not respond to medical management, necessitating eventual transplant enterectomy. Afterwards, he was managed with parenteral nutrition, however clinical course was complicated by multiple infections and opioid misuse. Patient ultimately expired 12 months post-transplant enterectomy. Patient 2: A 37-year-old underwent transplant and remained hospitalized for 41 days afterwards. Three weeks post-transplant he was noted to have cellular and humoral rejection requiring plasmapheresis and immunoglobulin. Approximately 12 months post-transplant, he presented with septic shock and multiorgan failure. Endoscopy revealed ulcerated and friable mucosa, leading to transplant enterectomy. Despite surgical intervention, his clinical status deteriorated, and he expired shortly thereafter. Conclusions: Patients undergoing intestinal transplantation for SBS secondary to GSW represent a unique and understudied population. These cases highlight the significant risks of rejection, transplant enterectomy, and morbidity. Despite these risks, outcomes are robust as illustrated with the first patient who had many years of normal bowel function, post-transplant. Further research is warranted to optimize management strategies and improve survival rates for this vulnerable population as advancements in transplantation continue. CITATION INFORMATION: Nabaty R., Muszkat Y., Nagai S., Beltran N., Pietrowsky T., Jafri S. Intestinal Transplantation for Short Bowel Syndrome from Gun Shot Wounds: A Case Series AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: R. Nabaty: None.

Gastroenterology
Patel T, John JD, Henna F, Alghaniem MMA, Abunamoos A, Cheema S, Arfin SMW, Nawaz A, Kalyandrug P, Sardarova N, **Barawi M**, Manahan K, and Geisler J. Extensive lymph node dissection and overall survival in colon cancer: A systematic review and meta-analysis. *J Clin Oncol* 2025;43(16). Full Text

T. Patel

Background: Colon cancer remains a leading cause of cancer-related mortality, with surgical resection and lymph node dissection (LND) being key to recovery treatment. Extensive lymph node dissection (ELND) in enhancing overall survival (OS) remains a subject of ongoing debate, as the evidence regarding its benefits versus associated risks is mixed or inconclusive. This meta-analysis aims to

evaluate whether ELND improves OS compared to standard lymph node dissection (SLND) in patients with colon cancer while assessing its impact on perioperative outcomes and lymph node retrieval. Methods: This Systematic Review and Meta-Analysis followed the PRISMA guidelines for evaluating the effectiveness of ELND, which analyzed seven articles containing 3,843 patients diagnosed with primarily local-stage (I-III) colon cancer, which met the inclusion criteria after screening 2797 articles, procured from a rigorous search strategy across bibliographic databases of PubMed, Medline, Pubmed Central, Scopus, Web of Science, and Embase until November 2024. Data analysis was performed using RevMan 5.4 software, which facilitated the computation of risk ratios, mean differences, and 95% confidence intervals (CIs). The assessment of heterogeneity was conducted using I2 statistics, while the evaluation of publication bias was carried out through the application of funnel plots. Results: ELND showcased significantly better overall survival rates than SLND with an RR of 0.34; 95% CI: 0.17-0.68; p = 0.002 with no observed heterogeneity (I2 = 0%). However, intraoperative complications between ELND and SLND were similar (RR: 0.90; 95% CI: 0.68-1.19; p = 0.45), although with substantial heterogeneity (I2 = 61%). As expected, given the nature of extensive dissection involved in ELND, it is expected to retrieve more lymph nodes, and statistically, there is an average difference of 10 nodes between the approaches (MD: 10.0; 95% CI: 0.10-10.0; p< 0.0001). However, this outcome exhibited significant heterogeneity (I2 = 100%), likely due to the variations in surgical technique and the definitions of 'extensive' dissection in each study included in the analysis. The survival benefit could be attributed to a more thorough removal of Lymph nodes, leading to improved disease staging and subsequent risk assessment and treatment planning. Conclusions: ELND provides promising oncological advantages through improved OS and enhanced staging accuracy without any difference in intraoperative complications. These findings suggest ELNDis a valuable technique in colon cancer surgery, specifically for local-stage disease. Further research can focus on having a standardized definition of 'extensive dissection' and further validate the study results.

Gastroenterology

Rehman S, Garg N, **Rahman T**, **Abusuliman M**, **Saleem A**, and **Jafri S**. Everolimus Does Not Alter Non-Hepatic Malignancy Following Liver Transplant. *Am J Transplant* 2025;25(8):S709. Full Text

Purpose: Malignancy after solid organ transplant especially skin cancers is common phenomenon and remains a major etiology of post-transplant mortality. Some case reports and small single center studies highlight various antioncogenic effects of mammalian target of rapamycin (mTOR) inhibitor class of immunosuppressants especially everolimus. This study aims to assess the effect of everolimus on the incidence of post-transplant skin malignancy and outcomes among liver transplant recipients. Methods: A retrospective chart review of post liver transplant patients at a large tertiary center in the midwest who received a liver transplant between 1/2015-12/2019 was conducted. Patients were split into 3 groups: not on everolimus post-transplant (group 1), started on everolimus within 1 year of transplant and discontinued before 3 years (group 2) and on everolimus for at least 3 consecutive years post-transplant (group 3). Demographic data including age, gender and etiology of cirrhosis was collected with primary outcomes assessing incidence of skin cancer. Secondary outcomes included other malignancy, transplant rejection, and death. Linear regression model used to compare these groups (group 1 vs. 3 and 2 vs. 3). Results: Among 381 liver transplant recipients, 59 patients were started on everolimus within 1 year of transplant and discontinued before 3 years (15.4%, group 2) and 65 patients were on everolimus for 3 consecutive years (17.1%, group 3). 25 patients in group 1 (9.7%), 6 in group 2 (6.8%) and 6 (9.2%) developed some skin malignancy with squamous cell carcinoma the most common among all three groups. 26 patients in group 1 (10.1%), 6 in group 2 (6.8%) and 5 (7.7%) developed some other type of malignancy with hematologic (23%) most common in group 1 and GI (67%) in group 2 and 3 (80%). There was no significant difference in incidence of skin malignancy (group 1 vs 3, p = 0.835; group 2 vs 3, p =0.513) or other malignancy across the groups. Similarly no significant difference in death (group 1 vs 3, p = 0.502; group 2 vs 3, p =0.611) or transplant rejection (group 1 vs 3, p = 0.30; group 2 vs 3, p =0.066). Conclusions: Our data demonstrates everolimus did not have a protective effect against skin malignancy, other malignancy, rejection or death among liver transplant patients. Whether these findings were related to a small sample size or time frame is unclear. Further investigations are warranted with a larger sample size and over a longer period to evaluate the long term benefit this immunosuppressant may have. CITATION INFORMATION: Rehman S., Garg N., Rahman T.,

Abusuliman M., Saleem A., Jafri S. Everolimus Does Not Alter Non-Hepatic Malignancy Following Liver Transplant AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Abusuliman: None.

Gastroenterology
Ronca V, Parente A, Lytvyak E, Hansen B, Hirschfield GM, Bonder A, Ebadi M, Elwir S, Alsaed M, Milkiewicz P, Janik M, Marschall HU, Burza MA, Efe C, Caliskan AR, Harputluoglu M, Kabaçam G, Terrabuio DR, Onofrio F, Selzner N, Pares A, Llovet LP, Akyildiz M, Arıkan C, Manns MP, Taubert R, Weber AL, Schiano T, Haydel B, Czubkowski P, Socha P, Ołdak N, Akamatsu N, Tanaka A, Levy C, Martin EF, Goel A, Sedki M, Jankowska I, Ikegami T, Rodriguez M, Sterneck M, Weiler-Normann C, Schramm C, Donato MF, Lohse AW, Andrade RJ, Patwardhan V, van Hoek B, Biewenga M, Kremer A, Ueda Y, Deneau M, Pedersen M, Mayo MJ, Floreani A, Burra P, Secchi MF, Terziroli B, Sciveres M, Maggiore G, **Jafri SM**, Debray D, Girard M, Lacaille F, Heneghan M, Mason AL, Oo YH, and Montano-Loza AJ. Recurrence of autoimmune hepatitis cholestatic variant syndromes after liver transplantation affects graft and patient survival in an international multicentre cohort. *J Hepatol* 2024;80:S374-S375. Full Text

Background and aims: A significant proportion of patients with variant syndromes (VS), namely AIH/PBC or AIH/PSC require liver transplantation (LT), despite treatment. The frequency of disease recurrence and the effect on graft survival is yet to be clarified. The aim of this international, multicentric, retrospective study is to evaluate risk factors associated with recurrence and the impact of the disease recurrence after LT on graft and patient survival. Method: We evaluated 172 patients undergoing LT for VS in 33 centres in North America, South America, Europe and Asia. Clinical data before and after LT, biochemical data within the first 12 months after LT, and immunosuppression after LT were analysed to identify patients with a higher risk of recurrence of autoimmune disease based on histological and radiological diagnosis. Cumulative probabilities of graft and overall survival after LT were calculated using semi-Markov model. Results: VS recurred after LT in 23% and 33% of patients after 5 and 10 years, respectively. An increased ALP and ALT at 12 months after LT (HR, 1.60; 95% CI, 1.13–2.25; $p < 0.01$, HR, 1.25; 95% CI, 1.01–1.53; $p = 0.03$) and acute rejection (HR 3.58; 95% CI, 1.60–7.73; $p < 0.01$) were found associated with a higher risk of VS syndrome recurrence, whilst the use of predniso (lo)ne was associated with a reduced risk (HR 0.30, 95% CI 0.14–0.64, $p < 0.01$). After adjusting for ALTand ALP at 12-months, the use of predniso (lo)ne was found to be independently and negatively associated with recurrent disease. The recurrence of VS was found significantly associated with graft loss and patients' survival at the multivariate Cox regression analysis with timedependent covariate. The 5-, 10- year probability of graft survival was 68% and 41% in patients with recurrent VS compared to 83% and 60% in patients without recurrent disease (p value, $p = 0.01$). The overall survival was significantly reduced in patients with recurrent disease ($p = 0.01$), with event probability at 5- and 10- years of 75% and 49 no% vs 84% and 60% in patients without recurrence. Conclusion: VS recurrence after LT is frequent and is associated with elevation of liver enzymes within the first year after LT and rejection episodes. VS recurrence negatively impacts graft and patient survival. Strategies are warrant to prevent VS recurrence or mitigate its negative effects.

Gastroenterology
Saleem A, **Al-Juburi S**, **Alomari A**, **Faisal M**, **Abusuliman M**, **Omeish H**, **Dababneh Y**, and **Jafri S**. Management in the Era Before Biomarkers: Long-Term Outcomes and Immunosuppression Strategies Following Liver Transplantation. *Am J Transplant* 2025;25(8):S488. Full Text

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Purpose: Post-liver transplantation survival has substantially improved over the last few decades. However, post-transplant management remains challenging due to the intricate balance between immunosuppression and its adverse effects. Excess immunosuppression is associated with metabolic disease, infection, readmission, and malignancy, whereas insufficient immunosuppression increases the

risk of rejection. Our study aims to delineate this balance to guide clinicians in safely minimizing immunosuppression without predisposing to rejection. Methods: Our study included patients who have had a 10-year liver transplant course starting in 2013 and were on tacrolimus immunosuppression. Patients who expired between 2018-2023 or lacked adequate clinical data were excluded. Mean 5-year tacrolimus troughs 5 years after transplant (2018 - 2023) were calculated. A mean trough level of 4 was used as a cutoff to subcategorize our patients into those with a 5 year mean trough of ≤4 or >4.We compared the incidence of rejection, infection, malignancies, hyperkalemia, nephrotoxicity, and hospital admissions between these groups during this time period. Results: Seventy-nine patients underwent liver transplantation at our center in 2013. Thirty-three patients expired or lacked sufficient data, leaving 44 for analysis, 17 females (39%) and 27 males (61%). The mean age was 54.6 with a standard deviation of 8.9 years. Etiologies of cirrhosis were Hepatitis C (45.45%), Alcohol (18.18%), Nonalcoholic Steatohepatitis (18.8%), Cryptogenic (9.09%), Primary Biliary Cirrhosis (4.55%), Primary Sclerosing Cholangitis (2.27%), and Cystic Fibrosis (2.27%). Tacrolimus troughs were >4 in 23 (52%) and ≤4 in 21 (48%). Rejection occurred in 6 patients in the >4 group and 3 in the ≤4 group. Hospitalization for infection occurred in 2 patients per group. Malignancy was identified in 2 patients in the >4 group and 3 in the ≤4 group. Nephrotoxicity was noted in 2 patients in the ≤4 group and 1 in the >4 group. The median overall hospital admission rate was 1 for both groups, with no statistically significant difference observed (p=0.667, Mann-Whitney test). No significant relationship between the mean 5-year trough and incidence of rejection, hyperkalemia, infection, cancer, overall hospital admission, and nephrotoxicity was found in our analysis (p>0.05). Conclusions: Our findings suggest that clinicians can safely down-titrate tacrolimus without an increased risk of rejection, infection, malignancy, nephrotoxicity, or readmission. Higher tacrolimus levels were also not associated with increased complications. These findings highlight the potential for individualized immunosuppression strategies to balance rejection risk and adverse effects. Larger studies are needed to improve generalizability. CITATION INFORMATION: Saleem A., Al-Juburi S., Alomari A., Faisal M., Abusuliman M., Omeish H., Dababneh Y., Jafri S. Management in the Era Before Biomarkers: Long-Term Outcomes and Immunosuppression Strategies Following Liver Transplantation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Saleem: None.

Gastroenterology

Saleem A, **Alomari A**, **Samad M**, **Ilyas O**, **Khaliq I**, **Abusuliman M**, **Chaudhary A**, **Omeish H**, **Faisal M**, **Dababneh Y**, **Affas S**, and **Jafri S**. Orthopedic Surgery in Liver Transplant Recipients: Does Surgical Urgency Influence Post Operative Morbidity. *Am J Transplant* 2025;25(8):S489. Full Text

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Purpose: Despite chronic immunosuppression, liver transplant recipients often require surgical interventions, with a growing demand for orthopedic procedures in this population. These surgeries present significant perioperative challenges, requiring a balance between maintaining immunosuppression and minimizing post-operative complications. However, the impact of surgical urgency on post-operative outcomes remains unclear. This study evaluates post-operative complications in liver transplant recipients undergoing elective versus emergent orthopedic surgeries and examines whether immunosuppressive regimens influence outcomes. Methods: A retrospective cohort study was conducted using SlicerDicer to identify liver transplant recipients who underwent orthopedic surgeries between 2013 and 2022. Patients were categorized based on surgical urgency as either elective or emergent. Collected data included demographics, type of surgery, and immunosuppressive regimen. Outcomes assessed included infection, transaminitis, acute kidney injury (AKI), and hospital readmission within one year post-operatively. Differences in outcomes among various immunosuppressive regimens were also examined. A descriptive analysis was performed to identify trends in post-operative complications based on surgical urgency and immunosuppressive regimen. Results: A total of 87 patients were included, with a mean age of 67.5 years and a mean transplant-to-surgery interval of 87 months.

The majority were male (59%, n=51) and White (82%, n=71), with smaller proportions of African American (16%, n=14) and other racial backgrounds (2%, n=2). Of these, 69 patients (79.3%) underwent elective orthopedic procedures, while 18 patients (20.7%) underwent emergent surgeries. Post-operatively, infection occurred in 7.2% of elective cases and 16.7% of emergent cases, transaminitis in 7.2% of elective cases and 11.1% of emergent cases, and AKI in 17.4% of elective cases and 16.7% of emergent cases. Hospital readmission within one year was observed in 36.2% of elective cases and 50.0% of emergent cases. These findings suggest a trend toward increased post-operative complications in patients undergoing emergent orthopedic surgery, particularly infections and transaminitis. Additionally, no significant differences in complication trends were observed among different immunosuppressive regimens. Conclusions: Orthopedic surgery in liver transplant recipients carries a risk of post-operative complications, with emergent procedures showing a trend toward systemic complications. While no differences were observed between immunosuppressive regimens, these findings highlight the need for careful perioperative management, particularly in emergent cases. Further studies with larger sample sizes are warranted to better define perioperative risks and guide clinical decision-making in this patient population. CITATION INFORMATION: Saleem A., Alomari A., Samad M., Ilyas O., Khaliq I., Abusuliman M., Chaudhary A., Omeish H., Faisal M., Dababneh Y., Affas S., Jafri S. Orthopedic Surgery in Liver Transplant Recipients: Does Surgical Urgency Influence Post Operative Morbidity AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Saleem: None.

Gastroenterology

Saleem A, **Obri M**, **Ilyas O**, **Alomari A**, **Faisal M**, **Abusuliman M**, **Chaudhary A**, **Rehman S**, **Franco-Palacios D**, **Nagai S**, **Venkat D**, and **Jafri S**. Outcomes and Risk Factors for Post-Operative Rejection and Transaminitis Following Dual Liver-Lung Transplantation: A Retrospective Cohort Study. *Am J Transplant* 2025;25(8):S468-S469. Full Text

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Purpose: Dual liver-lung transplantation (DLLT) is a rare and complex procedure, with limited data on post-operative rejection and liver function abnormalities. Understanding risk factors for acute cellular rejection and transaminitis is critical for optimizing immunosuppressive management. This study evaluates post-transplant outcomes in DLLT recipients and explores associations with recipient demographics, transplant indication, and underlying liver/lung disease etiology. Methods: A retrospective analysis was conducted on patients at our center who underwent DLLT between 2013 and 2024. Data collected included demographics, transplant indications, length of stay, incidence of acute rejection, and subsequent infections. Post-operative liver function tests (LFTs) beyond one month post-transplant were analyzed, and their relationship with age at transplant, liver disease etiology, and lung disease etiology was assessed. Results: A total of 10 patients (5 males, 5 females, mean age 53.7 years) underwent DLLT between 2013 and 2024. Liver disease etiologies were ethanol-related cirrhosis (n=2), hepatitis C (n=1), cryptogenic cirrhosis (n=1), autoimmune hepatitis (n=1), cystic fibrosis (n=1), and other unspecified causes (n=4). Lung transplant indications included idiopathic pulmonary fibrosis (n=5), pulmonary hypertension (n=2), other forms of interstitial lung disease (n=2), and cystic fibrosis (n=1).Post-operatively, 4 of 10 patients developed transaminitis beyond one month post-transplant, with liver biopsy confirming acute cellular rejection. Three patients received IV solumedrol, while one was managed with an oral steroid taper. Transaminitis resolved in all four cases after steroid treatment. Within three months, two patients treated with IV solumedrol developed infections from Candida and Aspergillus, though none developed CMV viremia. Two deaths occurred in the cohort. One patient passed away four years after transplant due to multifocal pneumonia, while the second patient passed away nine years post-transplant due to septic shock secondary to pneumonia in the setting of a new diagnosis of angiosarcoma. Neither patient had experienced rejection. Rejection and transaminitis were not significantly associated with age

at transplant, liver disease etiology, or lung disease etiology. Conclusions: This study provides one of the first detailed assessments of rejection and liver function abnormalities following DLLT. While transaminitis and acute cellular rejection occurred in 40% of patients, no clear predisposing factors were identified. IV solumedrol use for rejection was associated with increased infection risk, emphasizing the need for careful immunosuppressive management in this population. Further research with larger cohorts is essential to improve risk stratification and post-transplant care in DLLT recipients.

Gastroenterology

Saleem A, **Obri M**, **Ilyas O**, **Alomari A**, **Faisal M**, **Omeish H**, **Chaudhary A**, **Nagai S**, **Franco-Palacios D**, **Venkat D**, and **Jafri S**. Characterization and Risk Factors for Readmission and Emergency Department Presentations in Dual Liver-Lung Transplantation Patients. *Am J Transplant* 2025;25(8):S468. Full Text

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Purpose: Dual liver-lung transplantation (DLLT) is a rare procedure, with limited data characterizing patient demographics, risk factors, and post-transplant outcomes, particularly regarding hospital readmissions and emergency department (ED) presentations. This study aims to assess the rates of hospital readmission, ED presentations, and associated risk factors in DLLT recipients. Methods: A retrospective analysis was conducted on patients at our center who underwent DLLT between 2013 and 2024. Demographics, transplant indications, length of stay, acute rejection, causes of readmission, and ED presentations were analyzed. Readmission rates were categorized as occurring within 0-3 months and between 3 months and 1 year post-transplant. Mortality outcomes were also assessed. Results: Ten patients (5 male, 5 female) with a mean age of 53.7 years underwent DLLT. Liver disease etiologies were ethanol-related cirrhosis (n=2), hepatitis C (n=1), cryptogenic cirrhosis (n=1), autoimmune hepatitis (n=1), cystic fibrosis (n=1), and other unspecified causes (n=4). Lung transplant indications included idiopathic pulmonary fibrosis (n=5), pulmonary hypertension (n=2), interstitial lung disease (n=2), and cystic fibrosis (n=1). All patients (100%) were readmitted within 3 months, and 40% experienced additional readmissions within the first year. The most common causes of early readmissions (0-3 months) included infections (40%), diarrhea (20%), critical illness myopathy (20%), rejection (10%), and biliary stricture (10%). ED presentations within 1 year occurred in 50% of patients, with leading causes including melena (n=2), tachycardia (n=1), fever (n=1), and gastrostomy tube dysfunction (n=1). Initial length of stay, lung transplant etiology, liver disease etiology, and age at transplantation were not associated with readmission or ED presentation rates ($p>0.05$). Two patients (20%) died within 10 years post-transplant, one at 4 years and one at 8 years. Readmission within 1 year was not significantly associated with mortality at 5 or 10 years. Conclusions: DLLT recipients experience high rates of early readmission, with infections being the leading cause. ED presentations are common, with gastrointestinal and infectious concerns predominating. No significant associations were found between transplant etiology, initial hospital stay, or age at transplantation and readmission or ED presentation rates. Long-term mortality was not associated with early readmission. These findings underscore the need for enhanced post-transplant surveillance and targeted interventions to mitigate early complications. CITATION INFORMATION: Saleem A., Obri M., Ilyas O., Alomari A., Faisal M., Omeish H., Chaudhary A., Nagai S., Franco-Palacios D., Venkat D., Jafri S. Characterization and Risk Factors for Readmission and Emergency Department Presentations in Dual Liver-Lung Transplantation Patients AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Saleem: None.

Gastroenterology

Saleem A, **Samad M**, **Khaliq I**, **Ilyas O**, **Farah B**, **Alomari A**, **Faisal M**, **Abusuliman M**, **Omeish H**, and **Jafri S**. Infectious Morbidity and Mortality in Small Intestine Transplantation: A Decade of Experience. *Am J Transplant* 2025;25(8):S845. Full Text

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Purpose: Small intestine transplant (SIT) is a life-saving procedure for patients with intestinal failure; however, long-term success is challenged by post-transplant infections due to immunosuppressive therapy. Despite advancements in transplantation, SIT recipients remain at high risk for infectious complications significantly impacting morbidity and mortality. Identifying patterns of infection and survival outcomes in these patients is critical for optimizing post-transplant care and developing targeted preventive strategies. This study aims to evaluate the incidence, timing, and mortality associated with infectious complications in SIT recipients, providing insight into the most vulnerable periods and the need for enhanced surveillance and intervention. Methods: A retrospective cohort study was conducted at a single urban quaternary care center in the Midwestern United States, analyzing 27 SIT recipients from 2012 to 2022. Data collected included age at transplant, sex, and causal organisms of infection. Patients were stratified into three groups based on the onset of infection: within six months, 6-12 months, and beyond 12 months post-transplant. Primary outcomes included one- and three-year survival rates. Results: The cohort included 27 patients (62% female, mean age 49 years). Intra-abdominal infections were the most common (29.6%, n=8), with 88% occurring within six months, yielding an 86% one- and three-year survival. CMV viremia (19%) occurred mostly beyond 12 months (80%), with a 100% three-year survival; however, cases arising within 6-12 months had 0% survival at three years. Pneumonia (15%) primarily developed within six months, with 100% three-year survival, except for one case (6-12 months) with no survival at three years. Upper respiratory and skin infections accounted for 7.4% and 11.1% of cases, respectively, both demonstrating favorable three-year survival except for late-onset skin infections (6-12 months), which had 0% survival at three years. Conclusions: Intra-abdominal infections were the most frequent and occurred predominantly within six months post-SIT. CMV viremia, while the second most common, showed variable outcomes based on timing. Larger multicenter studies are needed to better characterize infectious risks and optimize post-SIT management. CITATION INFORMATION: Saleem A., Samad M., Khaliq I., Ilyas O., Farah B., Alomari A., Faisal M., Abusuliman M., Omeish H., Jafri S. Infectious Morbidity and Mortality in Small Intestine Transplantation: A Decade of Experience AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Saleem: None.

Gastroenterology

Stratton P, **Fitzmaurice M**, **Jakupovic L**, **Moonka D**, **Tong M**, and **Poparad-Stezar A**. Rejection Outcomes in Simultaneous Liver-Kidney Transplant versus Liver Transplant Alone in Recipients with Chronic Kidney Disease. *Am J Transplant* 2025;25(8):S773. Full Text

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Purpose: As more patients with renal dysfunction receive liver transplants, chronic kidney disease (CKD) has been identified as a risk factor for post-transplant morbidity and mortality. Since the addition of serum creatinine in the Model of End Stage Liver Disease (MELD), the number of simultaneous liver kidney transplants (SLKT) have increased by 177% (Thompson, 2009). Despite the vast number of SLKTs performed across the country, there is no standardized immunosuppression (IS) strategy. Our study aims to compare outcomes of recipients of SLKT to liver transplant alone (LTA) with pre-existing CKD. Methods: This retrospective analysis evaluated SLKTs compared to LTAs with pre-existing CKD from January 2018-December 2023. LTA patients had diagnosed CKD with an estimated glomerular filtration rate (eGFR) of 30-44 mL/min/1.73 m2 (CKD stage 3b). The primary outcome was acute rejection (AR) within 1 year (antibody and T-cell mediated), and secondary outcomes included maintenance IS, AR

treatment, infection, renal function, malignancy, and death, assessed for 1 year. Results: 51 SLKT patients and 31 LTA patients were included, with baseline characteristics evenly matched, however patients in the SLKT were younger with worse renal function (table 1). Table 2 contains secondary outcomes. Patients in the SLKT group had higher rates of AR compared to LTA (21.6 vs 12.8%; p=0.282). 3 drug IS regimens were more common in SLKT (27.5 vs 17.9%; p=0.291) and use of mammalian target of rapamycin inhibitors (mTORi) was higher in LTA (11.8 vs 43.6%; p<0.001). Tacrolimus troughs were significantly higher in the SLKT group at 6-12 months. Clostridiodes difficile infections and a composite infection endpoint (cytomegalovirus, blood stream, urinary tract, and intra-abdominal infections) were higher in SLKT (76.5 vs 59%; p=0.076). eGFR was significantly higher for the SLKT group through 1 year. LTA patients' eGFRs were maintained around their pre-LTA baseline. Malignancy and mortality rates were low, but the SLKT group had more deaths (2.6 vs 11.8%; p=0.134). Conclusions: Despite significantly improved eGFR post-transplant, the SLKT group suffered more complications including AR, infection, malignancy, and mortality, possibly in part due to differences in IS management. The SLKT group had greater IS requirements. This suggests that although there is evident renal benefit of SLKT, there may be unknown factors that heighten the risk of non-renal complications. Future studies can work to establish optimal IS regimens in this complex dual-organ population to help mitigate these risks. [Formula presented] CITATION INFORMATION: Stratton P., Fitzmaurice M., Jakupovic L., Moonka D., Tong M., Poparad-Stezar A. Rejection Outcomes in Simultaneous Liver-Kidney Transplant versus Liver Transplant Alone in Recipients with Chronic Kidney Disease AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: P. Stratton: None.

Gastroenterology

Toiv A, **Justus H**, Lee V, Altamura-Murgia G, Horslen S, Weiner J, Schiano T, Segovia M, and **Jafri S**.
Glucagon-Like Peptide-2 Therapy Outcomes Following Intestinal and Multivisceral Transplantation: A Multicenter Experience. *Am J Transplant* 2025;25(8):S844. Full Text

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Purpose: Glucagon-like peptide-2 (GLP-2) plays a critical role in intestinal adaptation, mucosal growth, and nutrient absorption. While GLP-2 therapy has shown benefits in patients with short bowel syndrome, its effects following intestinal transplantation (IT) and multivisceral transplantation (MVT) remain unknown. This study aims to describe the clinical outcomes of patients who received GLP-2 therapy after IT or MVT, providing insights into its potential role in post-transplant recovery and long-term outcomes. Methods: A retrospective analysis was conducted on sev7en patients who received GLP-2 therapy following IT or MVT across four transplant centers between 2014 and 2024. Results: Among the 7 transplant recipients, there were 2 men and 5 women. 5 patients underwent IT alone, while 2 underwent MVT. The median age at transplantation was 46 years (mean 45, range 19-62), with a median transplant waitlist time of 71±109 days. 71% of recipients developed short bowel syndrome due to bowel resection, while 29% had dysmotility as the underlying cause. All patients received teduglutide, with 57% starting treatment prior to undergoing IT. At GLP-2 initiation, 71% of patients were dependent on total parenteral nutrition (TPN), and with treatment, 67% successfully transitioned off TPN. GLP-2 therapy was eventually discontinued in 71% of patients, with bowel obstruction being the most common reason (67%). Notably, all patients retained their colons post-transplant. No patients had a history of colon polyps or colon cancer, and no polyps were detected during follow-up colonoscopies. Only one patient died 66 days post-transplant due to septic shock from a leg abscess, which occurred 10 days after discontinuing GLP-2 treatment. The remaining patients surpassed the 1- and 3-year survival milestones and did not have any infectious complications on treatment. Conclusions: GLP-2 therapy may play a beneficial role in intestinal

adaptation and post-transplant recovery, potentially facilitating independence from TPN in IT and MVT recipients. Bowel obstruction appears to be the main complication leading to therapy discontinuation and occurred in the majority of patients undergoing GLP-2 therapy. Despite these challenges, survival outcomes were generally favorable, warranting further investigation into the long-term benefits and risks of GLP-2 therapy in transplant recipients. CITATION INFORMATION: Toiv A., Justus H., Lee V., Altamura-Murgia G., Horslen S., Weiner J., Schiano T., Segovia M., Jafri S. Glucagon-Like Peptide-2 Therapy Outcomes Following Intestinal and Multivisceral Transplantation: A Multicenter Experience AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Toiv: None.

Gastroenterology

Toiv A, **Justus H**, Sarowar A, Lee V, Marquez J, Altamura-Murgia G, Horslen S, Weiner J, Schiano T, Segovia M, and **Jafri S**. Outcomes Following Graft Enterectomy After Intestinal and Multivisceral Transplantation: A Multicenter Analysis. *Am J Transplant* 2025;25(8):S843. Full Text

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Purpose: Graft enterectomy following intestinal transplantation (IT) or multivisceral transplantation (MVT) is a critical event that significantly impacts patient morbidity, survival, and long-term nutritional dependence. Data on IT failure requiring enterectomy and outcomes following enterectomy remain poorly defined. This study aims to describe the clinical outcomes of patients who underwent enterectomy after IT or MVT, providing insights into the post-enterectomy course. Methods: Retrospective analysis of 20 patients who underwent IT or MVT and subsequently required graft enterectomy from four transplant centers between 2012 and 2024. The primary outcome was patient survival analyzed by Kaplan-Meijer analysis. Secondary outcomes included retransplantation and infection within 3 months. Results: Among the 20 patients who underwent graft enterectomy following IT or MVT, there were 10 men and 10 women, with 55% receiving their transplants before the age of 18. The average age of the cohort at the time of enterectomy was 21 years, with a median age of 7 years. The average age of the pediatric patients was 4, and adult patients was 45. IT alone accounted for 75% of transplants, while 25% were MVT. Rejection was the primary indication for enterectomy in 100% of cases. MVT recipients were significantly more likely to undergo re-transplantation compared to IT recipients (p=0.01) and showed a trend toward improved survival (p=0.40). At 6 months and 1-year post-enterectomy, survival rates were 73% and 67% for IT recipients and 80% and 80% for MVT recipients, respectively. The pediatric transplant recipients had significantly increased survival compared to the adults (p=<0.01). There was no significant difference between IT and MVT recipients in their development of PTLD or infection within 3 months of enterectomy. Conclusions: Graft enterectomy remains a significant event following IT and MVT, with rejection being its most common indication. MVT demonstrated a trend of higher survival and significantly higher re-transplantation rates compared to IT alone after enterectomy. Pediatric transplant recipients had higher survival rates than adult transplant recipients. Our findings highlight the need for improved immunosuppressive protocols and post-transplant monitoring to mitigate the risk of graft failure. Further research is warranted to enhance long-term survival and quality of life in this complex population. CITATION INFORMATION: Toiv A., Justus H., Sarowar A., Lee V., Marquez J., Altamura-Murgia G., Horslen S., Weiner J., Schiano T., Segovia M., Jafri S. Outcomes Following Graft Enterectomy After Intestinal and Multivisceral Transplantation: A Multicenter Analysis AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Toiv: None.

Gastroenterology

Toiv A, **O'Brien HB**, **Andrews T**, and **Jafri S**. The Effects of Demographic Factors Upon Intestinal Transplant Outcomes. *Am J Transplant* 2025;25(8):S840-S841. Full Text

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Purpose: Demographic factors are increasingly recognized as potential influences on transplant outcomes. Limited data exist on the impact of demographic factors on intestinal transplantation (IT) and multivisceral transplantation (MVT) outcomes. This study aims to evaluate the impact of both sex and age on IT and MVT post-transplant outcomes. Methods: Retrospective chart review of all patients who underwent IT or MVT at an academic transplant center from 2010 to 2023. Patients were stratified by sex (male vs. female) and age (<50 vs. ≥50 years). The primary outcome was patient survival, analyzed using Kaplan-Meier analysis. Secondary outcomes included graft failure (GF), reoperation rates, moderate-to-severe rejection, and the development of chronic kidney disease (CKD). Results: Among 50 IT recipients, there were 20 men and 30 women. When stratified by age, 21 were <50 years old, while 29 were ≥50 years old. IT alone accounted for 58% of transplants, while 42% were MVT. Survival analysis revealed no significant mortality difference between the groups when analyzed by sex (p=0.28) or when comparing IT alone to MVT (p=>0.05 in all subgroups). Male IT recipients showed a higher need for reoperation within 1 month (p=0.01), though this difference did not persist at 3 months (p=0.44). No significant differences were observed between the sexes for GF, rejection rates, or CKD. In contrast, age was a significant predictor of survival, with recipients ≥50 years old demonstrating significantly lower survival rates than younger recipients (p<0.01). Older recipients had a trend towards higher incidence of reoperation within 3 months and an increased risk of developing CKD. No significant differences were found between age groups in terms of GF or rejection rate. Conclusions: While transplant recipient sex did not significantly impact survival or transplant-related outcomes, age ≥50 years was associated with significantly lower survival rates following IT. Further studies are needed to explore immunosuppression modifications and infectious surveillance strategies that may help reduce the incidence of CKD and improve mortality outcomes in these populations. CITATION INFORMATION: Toiv A., O'Brien H., Andrews T., Jafri S. The Effects of Demographic Factors Upon Intestinal Transplant Outcomes AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Toiv: None.

Gastroenterology

Toiv A, **O'Brien HB**, **Sarowar A**, **Andrews T**, and **Jafri S**. Liver Transplant Outcomes and Complications for Metabolic- Dysfunction Associated Alcohol Related Liver Disease (MetALD). *Am J Transplant* 2025;25(8):S493. Full Text

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Purpose: Metabolic alcohol-associated liver disease (MetALD) describes the coexistence of alcohol-associated liver disease (ALD) and metabolic dysfunction-associated steatotic liver disease (MASLD), two leading indications for liver transplantation (LT). However, the impact of this increasingly recognized dual pathology on LT recipient outcomes has not been thoroughly investigated. Our aim was to determine whether LT recipients with MetALD had less favorable postoperative outcomes than those with isolated ALD. Methods: A retrospective cross-sectional study of all patients who underwent LT for the primary indication of ALD at a high-volume academic transplant center between January 1, 2014, and September 26, 2023. Patients were stratified into 2 groups: LT recipients with isolated ALD and those with MetALD based on the presence of metabolic comorbidities. Kaplan-Meier analysis was used to compare mortality and graft survival rates between groups. Results: Of 381 LT recipients with ALD, 159 (42%) had isolated ALD, and 222 (58%) had MetALD. The MetALD group had a significantly higher median age (58 vs 50 years; p<0.001) and was predominantly female (77% vs. 45%). Comorbidities in the MetALD group

included diabetes (37% vs. 0%), hyperlipidemia (23% vs 0%), hypertension (77% vs. 0%), and coronary artery disease (27% vs. 0%) (all p<0.001). Despite the greater prevalence of baseline metabolic comorbidities in the MetALD group, no significant differences in postoperative mortality was observed between groups at 1 (94% vs 96%), 3 (91% vs. 90%), or 5 years (90% vs. 88%) after LT. Furthermore, no significant differences in graft failure were observed between groups at 1 (91% vs 95%), 3 (88% vs 89%), or 5 years (99% vs 87%) after LT. Rejection rates and surgical complications were also comparable between groups. Conclusions: Despite being older and having a significantly higher prevalence of metabolic and cardiovascular comorbidities including diabetes, hyperlipidemia, hypertension, and coronary artery disease, LT recipients with MetALD demonstrated positive patient and graft survival outcomes comparable to those in patients with isolated ALD. These results highlight the value of LT as a treatment option in this complex patient population and suggest that the presence of MetALD should not preclude consideration for LT. CITATION INFORMATION: Toiv A., O'Brien H., Sarowar A., Andrews T., Jafri S. Liver Transplant Outcomes and Complications for Metabolic- Dysfunction Associated Alcohol Related Liver Disease (MetALD) AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Toiv: None.

Gastroenterology
Trivedi PJ, **Gordon SC**, Gulamhusein A, Villamil A, Lawitz EJ, Vierling JM, Londoño MC, Kremer AE, Bowlus CL, Proehl S, Zhuo S, Crittenden DB, and McWherter CA. LONG-TERM SAFETY OF SELADELPAR 10 MG WITH UP TO 5 YEARS OF TREATMENT IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS. *Gut* 2025;74:A228. Full Text

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Introduction The Phase 3, placebo-controlled RESPONSE study (NCT04620733) of seladelpar, a first-in-class delpar (selective PPAR-delta agonist), in primary biliary cholangitis (PBC) patients with an inadequate response or intolerance to ursodeoxycholic acid demonstrated significant improvements in cholestatic markers and pruritus with seladelpar over 1 year and similar proportions of adverse events (AEs) and serious AEs (SAEs) between the seladelpar and placebo groups. To assess long-term safety, data from all PBC patients exposed to seladelpar 10 mg in 6 studies with similar entry criteria were pooled. Methods AE data from 2 placebo-controlled and 4 open-label studies were pooled for all patients treated with seladelpar 10 mg as of 31 Jan 2024, beginning with first exposure to seladelpar, including all exposure periods and excluding treatment gaps. Placebo exposure was pooled from the 2 placebo-controlled studies. Exposure-adjusted patient incidences of AEs, SAEs, and AEs of interest (defined as liver-, muscle-, and renal-related AEs) were calculated. Results As of the data cutoff, a total of 486 patients received seladelpar 10 mg: 355 were treated for ≥1 year; 170, ≥2 years; 66, ≥3 years; 36, ≥4 years; and 10, ≥5 years. The exposure-adjusted patient incidence (per 100 patient-years) for seladelpar 10 mg was 48.3 for AEs, 8.0 for SAEs, 9.8 for Grade ≥3 AEs, and 6.1 for liver-related AEs (table 1). There were no treatment-related SAEs. Muscle and renal AEs occurred in <7 patients per 100 patient-years. Placebo exposure included 152 patients: 117 were treated for ≥12 weeks, 84 for ≥6 months, and 57 for 12 months of placebo treatment in RESPONSE. The exposure-adjusted patient incidence (per 100 patient-years) for patients treated with placebo was 132 for AEs (rate reflective of shorter exposure time for placebo patients), 7.8 for SAEs, 12.2 for Grade ≥3 AEs, and 13.3 for liver-related AEs (with other AEs of interest occurring at lower rates). AEs leading to treatment discontinuation occurred in 2.9 patients per 100 patient-years in seladelpar patients and 5.6 per 100 patient-years in placebo patients. Conclusions Analysis of a large safety database for seladelpar in PBC patients with exposure through 5 years indicated that seladelpar was well tolerated with a safety profile similar to placebo.

Gastroenterology
Trivedi PJ, Levy C, Kowdley KV, **Gordon SC**, Bowlus CL, Londoño MC, Hirschfield GM, Gulamhusein A, Lawitz E, Villamil A, de Guevara ALL, Mayo MJ, Younes ZH, Shibolet O, Yimam K, Pratt D, Heo J, Morgera U, Andreone P, Kremer AE, Corpechot C, Goel A, Peyton A, Elbeshbeshy H, Crittenden DB, Heusner C, Proehl S, Zhou S, and McWherter CA. Long-term efficacy and safety of open-label seladelpar treatment in patients with primary biliary cholangitis (PBC): interimresults for 2 years from the ASSURE study. *J Hepatol* 2024;80:S98. Full Text

Background and aims: Seladelpar, a potent and selective PPAR-delta agonist, has been shown to reduce biochemical markers of cholestasis and pruritus in PBC patients. ASSURE (NCT03301506) is an ongoing, open label, long-term phase 3 trial of seladelpar in patients rolling over from the phase 3 registrational study RESPONSE (NCT04620733) or with prior participation in legacy studies: phase 3 ENHANCE (NCT03602560) study; CB8025–21629 (NCT02955602); CB8025-31731 (NCT03301506); and CB8025-21838 (NCT04950764). Here, we report interim 2-year efficacy and safety results for 337 enrolled patients. Method: Patients with insufficient response or intolerance to first line PBC treatment ursodeoxycholic acid and prior participation in a seladelpar clinical trial could enroll in ASSURE. Key end points were the composite biochemical response (alkaline phosphatase (ALP) <1.67x upper limit of normal (ULN), ALP decrease ≥15%, and total bilirubin ≤ULN) and ALP normalization. Pruritus was reported using a numerical rating scale (NRS; 0–10). Baseline for participants who entered ASSURE from RESPONSE was entry to RESPONSE, analyzed as continuous seladelpar or crossover from placebo. Legacy patients were analyzed separately with baseline set as the entry to ASSURE. Results: As of 31 January 2024, 158 patients from RESPONSE and 179 patients from legacy studies had received 10 mg seladelpar, daily, for up to 155 weeks in ASSURE. In RESPONSE, 61.7% (79/128) of seladelpar patients met the composite end point at Month 12 vs 20% (13/65) for placebo.With continued treatment in ASSURE, 61.8% (63/102) at 6 months in ASSURE and 72.4% (21/29) at 12 months in ASSURE met the composite end point. Among placebo patients crossing over to seladelpar, 75% (39/52) at 6 months and 93.8% (15/ 16) at 12 months met the composite end point. ALP normalized in 25% of seladelpar and 0 placebo patients at Month 12 in RESPONSE. With continued treatment, 33.3% (6 months) and 17.2% (12 months) had ALP normalization. For crossover patients, 26.9% and 50% had ALP normalization at these timepoints. The change in pruritus NRS with seladelpar in ASSURE was similar to RESPONSE: −3.8 and −3.7 change from baseline at 6 months in continuous and crossover patients, respectively, corresponding to the key secondary end point in RESPONSE. Among legacy patients, 73.2% (120/164) and 69.7% (69/ 99) met the composite end point at Month 12 and Month 24 in ASSURE. Normalization of ALP was achieved by 42.1% at 12 months and 42.4% at 24 months. Reduction in pruritus NRS in this group was −3.8 at Month 12 and −3.1 at Month 24. The safety profile was favorable with no treatment-related serious adverse events. Conclusion: Continuous treatment with seladelpar for RESPONSE and legacy patients led to sustained effects on biochemical markers and pruritus. Seladelpar appeared safe and well tolerated with longterm use.

Gastroenterology

Younossi Z, Yilmaz Y, Yu ML, Isakov V, Fernández MIC, Wong VWS, Eguchi Y, Romero-Gómez M, Méndez-Sánchez N, Duseja AK, Keklikkiran C, George J, Bugianesi E, Singal AK, Hamid SS, Alswat KA, Chan WK, Fan J, Papatheodoridis G, **Gordon SC**, El-Kassas M, Roberts S, Lam B, Racila A, Henry L, Alqahtani S, and Stepanova M. Fatigue is an Important Driver of Work Productivity Loss and Impairment of Patient-Reported Outcomes (PROs) among Patients with Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). *J Hepatol* 2024;80:S643-S644. Full Text

Background and aims: MASLD is associated with fatigue which can have negative impact on clinical outcomes and PROs. We assessed fatigue among MASLD patients seen in real-world practices. Method:We used data [demographics, medical history, FIB-4 scores, liver stiffness by transient elastography and PRO scores (FACIT-F, CLDQ-NASH, WPAI)] collected by the Global NASH Registry™. Presence of clinically overt fatigue was determined from medical history (MH-based fatigue) or using Fatigue Scale of FACIT-F PRO instrument (FS<30 on a 0–52 scale; PRO-based fatigue). Results: We included 6783 MASLD patients from 18 countries (Australia, China, Cuba, Egypt, Greece, Hong Kong, India, Italy, Japan, Saudi Arabia, Malaysia, Mexico, Pakistan, Russia, Spain, Taiwan, Turkey, USA): age 51 ± 13 years old, 44% male, 47% employed, 68% obese, 41% type 2 diabetes (T2D), 51% hypertension, 19% with advanced fibrosis (biopsy or transient elastography ≥9.5 kPa or FIB-4 ≥2.67), 24% history of depression, 29% sleep apnea, 20% abdominal pain. Of all patients, 39% had MH-based fatigue and 26% had PRObased fatigue by FACIT-F. Concordance between the two fatigue definitions was 68%, with 44% of those with MH-based fatigue also having PRO-based fatigue (vs. 9% among those without MH-based fatigue). Regardless of the definition, MASLD patients with fatigue were younger (50 vs. 52 years), more commonly female (67% vs. 49%), obese (75% vs. 64%) with T2D (45% vs. 38%), depression (34% vs. 17%) and abdominal pain (33% vs. 10%) (all $p < 0.05$). Patients with fatigue also reported a substantial impairment in other PRO scores: total CLDQ-NASH score 4.49 (SD 1.08) vs. 5.51 (0.96) in patients with

vs. without MH-based fatigue (impairment of −1.02, or −17% of range size), compared to 3.83 (0.91) vs. 5.44 (0.89) in those with vs. without PRO-based fatigue (impairment −1.61, or −27% of range size); similarly total FACIT (4 generic domains of FACIT-F) was −11% by MH-based fatigue and −20% by PRO-based fatigue, and excessive work productivity impairment (WPI) was −13% by the presence of MH-based fatigue and −25% by PRO-based fatigue. After adjustment for clinico-demographic confounders, association of lower PRO scores with fatigue remained significant for all studied PRO scores, with the effect size again being greater for PRO-based fatigue than MH-based fatigue: −20% vs. −10% for total CLDQ-NASH, −16% vs. −6% for FACIT-F, and −21% vs. −7% for WPI (all $p < 0.0001$). Other predictors of lower PRO scores in MASLD included younger age, female sex, advanced fibrosis, non-hepatic comorbidities, and lack of regular exercise ($p < 0.05$). Conclusion: MASLD patients experience substantial fatigue burden that is partially captured by medical history and more accurately asserted by a fatigue-specific PRO instrument (FACIT-F). Fatigue is associated with a significant impairment of other PROs and work productivity with its negative economic impact.

Gastroenterology

Yuen MF, Heo J, Nahass RG, Wong GLH, Burda T, Bhamidimarri KR, Hu TH, Nguyen TT, Lim YS, Chen CY, **Gordon SC**, Holmes J, Chuang WL, Kohli A, Alkhouri N, Gray K, Thi EP, Medvedeva E, Eley T, Ganchua SC, Iott C, Eill E, Espiritu CL, Anderson M, Fortney T, Cloherty G, and Sims KD. Imdusiran (AB-729) administered every 8 weeks in combination with 24 weeks of pegylated interferon alfa-2a in virally suppressed, HBeAg-negative subjects with chronic HBV infection leads to HBsAg loss in some subjects at end of IFN treatment. *J Hepatol* 2024;80:S809-S810. Full Text

Background and aims: Functional cure of CHB will require suppression of viral replication, reduction of HBsAg and use of an immunomodulator such as pegylated interferon alfa-2a (IFN) to enhance HBV-specific immunity. Imdusiran (AB-729) is a GalNAcconjugated single trigger siRNA that targets all HBV RNA transcripts and reduces all viral antigens including HBsAg. AB-729-201 is an ongoing Phase 2a study assessing 24 weeks of imdusiran followed by 12 or 24 weeks of IFN ± additional imdusiran doses in HBeAgnegative CHB subjects virally suppressed on nucleos (t)ide analogue (NA) therapy. Interim data through the end of the IFN treatment period (EOT) is available for all subjects. Method: Forty-three subjects received imdusiran 60 mg every 8 weeks (wks) for 24 wks (4 doses) during the lead-in phase. After Wk 24, subjects were randomized to 1 of 4 sub-groups: A1 (24 wks IFN + 2 imdusiran doses + NA; N = 12), A2 (24 wks IFN + NA; N = 13), B1 (12 wks IFN + 1 imdusiran dose + NA; N = 8) or B2 (12 wks IFN + NA; N = 10). After completing IFN ± imdusiran treatment, subjects continued NA therapy for 24 wks and stopped NA therapy if ALT <2 × upper limit of normal, HBV DNA undetectable and HBsAg <100 IU/ml. Safety, antiviral and immunologic assessments were obtained. HBsAg was assessed via Roche Cobas Elecsys HBsAg II assay (lower limit of quantitation [LLOQ] = 0.05 IU/ml) and results <LLOQ were analyzed by Abbott HBsAg Next assay (sensitivity cutoff = 0.005 IU/ml). Results: Baseline characteristics were described previously. All subjects have completed IFN dosing, and 18/43 subjects have been assessed for NA discontinuation (d/c) atWk76 or 64. In groups A1/A2, 7/25 (28%) subjects had HBsAg ≤LLOQ at EOT (Wk 52) and 5/7 were confirmed to be non-reactive with the Abbott Next assay. All 7 subjects had concurrent anti-HBs levels >10 IU/L, and 5/7 had levels >100 IU/L. In groups B1/B2, 0/18 subjects had HBsAg ≤LLOQ at EOT (Wk 40), although 2 reached <LLOQ during IFN treatment but subsequently rebounded. Group A1 had more profound HBsAg mean (±SE) log10 change from baseline at EOT than other groups; A1 = −2.85 (0.41) log10, A2= −1.44 (0.43) log10, B1= −1.85 (0.38) log10, and B2 = −1.68 (0.17) log10. Imdusiran treatment was well-tolerated with no serious adverse events (AEs) or AEs leading to d/c; IFN-related AEs were like those reported previously. Nine of 18 subjects have stopped NA therapy; 1 subject has HBsAg and HBV DNA <LLOQ after 6 months off NA therapy suggestive of functional cure, and 1 subject restarted therapy after 8 wks due to confirmed HBV DNA >20, 000 IU/ml with normal ALT levels. Conclusion: HBsAg ≤LLOQ with detectable anti-HBs was observed at EOT in 28% of subjects who received 4 or 6 doses of imdusiran plus 24 weeks of IFN, but in 0 subjects who received 4 or 5 doses of imdusiran plus 12 weeks of IFN. The study remains ongoing and additional EOT data, durability of EOT HBsAg loss, and preliminary immunology data for a subset of study subjects will be presented.

Hematology-Oncology
Abdelrahim M, **Khan G**, Hatoum H, Zervoudakis A, Dayyani F, Zhang L, Li J, Maxwell F, O'Reilly EM, Wainberg ZA, and Bounetheau Peters ML. Impact of UGT1A1∗28 polymorphism on tolerability in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) treated with NALIRIFOX in NAPOLI 3. *J Clin Oncol* 2025;43(4_Suppl):717-717. Full Text

M. Abdelrahim

Background: SN-38, the active metabolite of irinotecan, is cleared by the liver enzyme uridine diphosphate glucuronosyltransferase 1A1 (UGT1A1) and biliary excretion. UGT1A1∗28 (genotype 7/7) homozygosity is associated with reduced activity of UGT1A1 and a recommendation for dose adjustment of non-liposomal irinotecan, a component of the FOLFIRINOX regimen. In this post-hoc analysis, we analyzed the impact of UGT1A1∗28 homozygosity on the incidence and profile of treatment-emergent adverse events (TEAEs) among patients enrolled in NAPOLI 3 (NCT04083235). Methods: Patients (N = 770) with confirmed untreated mPDAC were randomized (1:1) to receive liposomal irinotecan 50 mg/m2 + oxaliplatin 60 mg/m2 + leucovorin 400 mg/m2 + 5-fluorouracil 2400 mg/m2 (NALIRIFOX) on days 1 and 15 of a 28-day cycle or nab-paclitaxel 125 mg/m2 and gemcitabine 1000 mg/m2 (Gem+NabP) on days 1, 8 and 15 of a 28-day cycle. UGT1A1∗28 status was evaluated in all patients before enrollment. All patients, regardless of UGT1A1∗28 status, received the full starting dose of liposomal irinotecan and followed the same dose reduction rules. This exploratory analysis of TEAEs by UGT1A1∗28 status was descriptive; statistical analyses were not performed. Results: Overall, 83 patients (11.0%) were homozygous for UGT1A1∗28, among whom the incidence of TEAEs was similar to patients with non-homozygous status (Table). The most frequently reported TEAEs (≥ 40%) among the homozygous group (vs the overall NAPOLI 3 population) were diarrhea (59.0% vs 70.5%), nausea (56.4% vs 59.5%), vomiting (46.2% vs 39.7%) and anemia (41.0% vs 26.2%) in the NALIRIFOX arm and nausea (45.5% vs 42.7%), fatigue (45.5% vs 37.7%), diarrhea (45.5% vs 36.7%) and anemia (40.9% vs 40.4%) in the Gem+NabP arm. Conclusions: The incidence of TEAEs, including TEAEs leading to death, was similar between patients with homozygous and non-homozygous UGT1A1∗28 status, in both treatment arms. The profile of TEAEs was consistent with that of the overall NAPOLI 3 population. UGT1A1∗28 status did not substantially influence the safety profile or subsequent need for dose reductions of liposomal irinotecan in NAPOLI 3. (Table Presented).

Hematology-Oncology
Amaria RN, Duvivier HL, Tsai KK, Momtaz P, Galamaga RW, Pisick EP, Patrick Doonan B, **Weise AM**, Langr N, Winkler JD, Dave HP, Diamond JR, and Sullivan RJ. Nautilus, a phase 1b/2 trial of combining oral HDAC inhibitor (HDACi) with MEK inhibitor (MEKi) in patients with NRAS-mutated metastatic melanoma (MM). *J Clin Oncol* 2025;43(16). Full Text

R.N. Amaria

Background: Activating NRAS mutations occur in 15-20% of MM cases. The MEK inhibitor binimetinib has modest single agent activity with 15% objective response rate (ORR) and 2.8 month progression-free survival (PFS). Bocodepsin (OKI-179) is a novel Class Iselective, oral histone deacetylase inhibitor that was found to have synergistic efficacy with MEKi in preclinical models of NRAS-mutated melanoma. Cells displayed unrepaired double strandDNAbreaks and cellular apoptosis, while regressions were observed in xenograft models. Here we present the results of the phase 2 portion of a clinical trial of this combination in NRASmutantMM(NCT05340621). Methods: In this Phase 2 study, only patients with NRAS-mutant MM previously treated with immunotherapy were enrolled and treated with bocodepsin at the recommended phase 2 dose (300mgdaily, 4 days on, 3 days off, continuously) with binimetinib (45 mg twice daily, continuously). Primary endpoint was ORR, with secondary endpoints including safety and PK analyses. Results: As of 1/3/2025, 36 total patients were enrolled; 14 in phase 1b dose escalation and 22 in phase 2, including a total of 24 NRAS-mutant melanoma patients. Median age of NRAS-mutant MM patients was 69 years, and 47% of patients were males. Median numbers of prior therapies was 3 and LDH elevations were found in 41% of patients. There were no grade 3/4 toxicities seen in .10% of patients, including no episodes of high grade rash. Of the 20 evaluable patients with NRAS-mutant MM, ORR was 30%. The median PFS was 7.25 months (5-92 weeks). Conclusions: The combination of

bocodepsin and binimetinib in patients with NRAS-mutant melanoma is tolerable with manageable AEs and no high grade rash. Initial response data in patients with NRAS-mutant melanoma are supportive of potential combinatorial activity of a MEK inhibitor and HDACi bocodepsin. Further investigation is crucial asMMpatients with disease progression after immunotherapy remain in need of rational therapeutic options. Thus, MEKi + HDACi warrants further study in a larger patient cohort.

Hematology-Oncology
Bellon A, Gambardella V, Paz-Ares LG, Navarro A, Jain P, María López-Picazo J, De Miguel MJ, **Gadgeel SM**, Bhatti SA, Rocha P, Ke A, Massiere F, Imedio ER, and Dozio V. In silico evaluation of the interaction of P-gp and 3A4 substrates with the WEE1 inhibitor Debio 0123 and clinical application in the Debio 0123-104 combination trial with carboplatin and etoposide. *J Clin Oncol* 2025;43(16). Full Text

A. Bellon

Background: Debio 0123 is an oral, brain-penetrant, highly selective WEE1 kinase inhibitor currently being investigated in several clinical trials in patients with advanced solid tumors both as monotherapy and in combination. In vitro, Debio 0123 can inhibit and induce cytochrome P450 (CYP) 3A4 and inhibit P-gp. Methods: A physiologically-based pharmacokinetic (PBPK) model using Simcyp Population Based Simulator was developed for Debio 0123 to evaluate its perpetrator effect on sensitive substrates of CYP3A4 and P-gp. A second model was developed for etoposide as victim drug. Both were combined to assess the risk of clinical drugdrug interaction (DDI) between Debio 0123 and etoposide. Plasma etoposide concentrations were simulated following single and three daily doses of etoposide 100 mg/m2 IV administered concomitantly with, or without, 520 mg oral (PO) Debio 0123. The Debio 0123 model was developed using in vitro and clinical data from previous Debio 0123 clinical trials. Results: No clinically significant DDIs were predicted between Debio 0123 given for 3 consecutive days and the CYP3A4 probe substrate, midazolam. When PO or IV administration of midazolam was simulated, the 90%CI of the geometric mean ratio (GMR) for AUCinf and Cmax, alone versus in combination with Debio 0123, entirely fell within 0.9 and 1.3. A weak DDI was predicted towards the P-gp probe substrate dabigatran etexilate. When given orally, AUCinf and Cmax GMR of dabigatran with, or without, Debio 0123 were 1.87 and 1.93, respectively. Administration, for 3 consecutive days, of Debio 0123 combined with IV etoposide was predicted to have no effect on etoposide exposure (90%CI of GMR for both AUC and Cmax within 0.80-1.25). Accordingly, the design of Debio 0123-SCLC-104 trial with Debio 0123 administered in combination with carboplatin and etoposide (NCT05815160 - ASCO 2025 # 495064) was developed with standard doses of IV etoposide. To confirm the absence of DDI, PK samples were collected in the trial. No major changes were noted in the observed etoposide exposure across Debio 0123 dose levels (200 to 400 mg) after one or three days of co-administration in adult SCLC participants that recurred or progressed after previous platinum treatment. Etoposide PK observed in the study was also in line with literature data (US label Etopophos 2011). Debio 0123 PK was consistent with data previously reported for monotherapy (Abstract #3120 ASCO 2024). Conclusions: Overall, these results indicate that there is no relevant PK interaction between Debio 0123 and IV etoposide. For concomitant medications that are P-gp substrates, only a weak DDI is expected with Debio 0123. Furthermore, the absence of significant DDIs predicted with CYP3A4 substrates suggests that Debio 0123 can be combined with a wide range of therapies.

Hematology-Oncology
Camidge DR, Girard N, Lu S, **Gadgeel SM**, Cuppens K, Lee SH, Horinouchi H, Kim TM, Delmonte A, Pons-Tostivint E, Jotte RM, Aanur N, Coburn H, Jiang Q, Jennaro TS, Navas T, Li Y, and Goldman JW. Phase 1b/2 study evaluating telisotuzumab adizutecan (ABBV-400; Temab-A) in combination with budigalimab in patients (pts) with advanced non-squamous (NSQ) non-small cell lung cancer (NSCLC) with no prior treatment for advanced disease and no actionable genomic alterations. *J Clin Oncol* 2025;43(16). Full Text

D.R. Camidge

Background: c-Met (MET) protein expression is frequently increased in NSCLC and is associated with poor prognosis. 24% of pts with NSQ EGFR wildtype (WT) NSCLC exhibit increased c-Met protein expression, ie, ≥25% 3+ via IHC. Addition of programmed cell death (ligand) 1 (PD-[L]1) inhibitors to

chemotherapy (CT) has improved treatment of NSCLC regardless of PD-(L)1 expression. However, more-effective therapies are needed, particularly for pts with no known actionable genomic alterations. Temab-A is an antibody-drug conjugate comprising the c-Met protein-targeting antibody telisotuzumab and the potent topoisomerase 1 inhibitor adizutecan payload attached via a stable cleavable linker. In an ongoing phase 1 study (NCT05029882), Temab-A monotherapy demonstrated manageable safety and promising efficacy in pts with advanced/metastatic (a/m) NSQ EGFR WT NSCLC in second line and later, with an objective response rate (ORR) of 48% (23/48) across all c-Met expression levels and clinical benefit rate of 85% (41/48) (De Miguel et al. Ann Oncol. 2024;35:S805-S806). Herein, we describe a study evaluating Temab-A in combination with the PD-1 inhibitor budigalimab. Methods: This multicenter, global, open-label, phase 1b/2, randomized (in part 2) study (NCT06772623) will enroll ~172 pts (≥18 yr) with a/m NSQ NSCLC. Eligible pts have ECOG 0 or 1, measurable disease per RECIST v1.1, and documented EGFRWTand PD-L1 status. Primary objectives are to evaluate safety and tolerability, assess efficacy as measured by ORR by blinded independent central review, and select the recommended phase 3 dose of Temab-A combined with budigalimab. Secondary objectives include assessment of efficacy outcomes (PFS, DOR, OS, and disease control rate), characterization of PK and immunogenicity, and evaluation of PD and potential predictive biomarkers. The study has 2 parts: a safety dose-escalation part 1 and a dose-optimization part 2. Part 1 enrolls ~12 pts who have received #1 prior systemic therapy for a/m NSCLC, including platinum-based CT, an immune checkpoint inhibitor, or targeted therapy. Pts receive escalating doses of Temab-A IV Q3Wguided by BOIN design in combination with a fixed dose of budigalimab IV Q3W. Dose-limiting toxicities are evaluated during cycle 1. Part 2 enrolls ~160 pts who have not received prior systemic therapy for a/m NSCLC. Pts are randomized 1:1:1:1 to Temab-A at 1 of 2 doses determined in part 1 + budigalimab, to budigalimab + CT, or to SOC (pembrolizumab + CT) arms. Randomization is stratified by PD-L1 expression and history of brain metastases. Treatment continues until disease progression, intolerable toxicity, or other discontinuation criteria are met. The first dosing of the first patient enrolled is planned in March 2025.

Hematology-Oncology

Choueiri TK, Ornstein MC, Barata PC, Matrana MR, Merchan JR, Gedye C, **Hwang C**, Kumar R, Lee JL, Guan Y, Ghasemi M, Quadri S, Negro C, Chen J, Foster PG, Monga M, McGregor BA, Rha SY, and Drakaki A. Combination casdatifan plus cabozantinib expansion cohort of phase 1 ARC-20 study in previously treated patients with clear cell renal cell carcinoma. *J Clin Oncol* 2025;43(16). Full Text

T.K. Choueiri

Background: Hypoxia-inducible factor 2-alpha (HIF-2a) is highly dysregulated in clear cell renal cell carcinoma (ccRCC), resulting in increased expression of proteins involved with angiogenesis, proliferation, and cancer cell survival. Casdatifan is an orally bioavailable small-molecule HIF-2a inhibitor. We investigated the safety and efficacy of casdatifan in combination with the anti-vascular endothelial growth factor receptor tyrosine kinase inhibitor (VEGFR-TKI) cabozantinib in previously treated patients with ccRCC in an expansion cohort (casdatifan + cabozantinib) of the phase 1, open-label ARC-20 (NCT05536141) trial. Methods: Patients enrolled in the casdatifan + cabozantinib expansion cohort were previously treated with immunotherapy (IO) alone or with anti-VEGF therapies. Casdatifan 100 mg and cabozantinib 60 mg were given orally once daily. Endpoints included the incidence of treatment-emergent adverse events (AEs) and objective response rate (ORR) by RECIST v1.1. This study is ongoing; data as of January 3, 2025, are reported. Results: Overall, 27 patients with a median (range) follow-up of 2.9 (0.1-6.8) months were enrolled. At data cut off, prior treatment settings included adjuvant only (n = 5/26) and metastatic (1L n = 17/26; 2L n = 4/26). Prior therapies included IO only (n = 15/26) or IO plus VEGFR-TKI (n = 11/26). All grade AEs occurred in 89% of patients with the most common being anemia (n = 16 [59%]) and fatigue (n = 15 [56%]). Most common (.10%) grade≥3 AEs were anemia (n = 7 [26%]) and hypoxia (n = 3 [11%]). No cardiac events were reported. AEs leading to casdatifan-only, cabozantinib-only, or both casdatifan + cabozantinib dose reductions occurred in 3 (11%), 7 (26%), and 2 (7%) patients, respectively. Only one (4%) pt discontinued due to an AE, hypoxia related to casdatifan. Responses continue to be observed among the efficacy evaluable population (n = 22; as of January 27, 2025) with ORR of 41% (n = 1 complete response; n = 8 partial response). Activity was seen across all IMDC risk groups. Conclusions: In previously treated patients with ccRCC, casdatifan 100 mg in

combination with cabozantinib 60 mg had a manageable AE profile with promising clinical activity. These data support continued evaluation of this combination in the phase 3 PEAK-1 clinical trial.

Hematology-Oncology
Dasari A, Yu G, Kopetz S, Puhalla SL, Lucas PC, Sahin IH, Deming DA, **Philip PA**, Hong TS, Rojas-Khalil Y, Loree JM, Wolmark N, Yothers G, George TJ, and Lieu CH. Colon adjuvant chemotherapy based on evaluation of residual disease (CIRCULATENORTH AMERICA): NRG-GI008. *J Clin Oncol* 2025;43(16). Full Text

A. Dasari

Background: Currently, there are no biomarkers validated prospectively in randomized studies for resected colon cancer (CC) to determine need for adjuvant chemotherapy (AC). However, circulating tumor DNA (ctDNA) represents a highly specific and sensitive approach (especially with serial monitoring) for identifying minimal/molecular residual disease (MRD) postsurgery in CC patients (pts), and may outperform traditional clinical and pathological features in prognosticating risk for recurrence. CC pts who do not have detectable ctDNA (ctDNA-) are at a much lower risk of recurrence and may be spared the toxicities associated with AC. Furthermore, for CC pts with detectable ctDNA (ctDNA+) who are at a very high risk of recurrence, the optimal AC regimen has not been established. We hypothesize that for pts whose CC has been resected, ctDNA status may be used to risk-stratify for making decisions about AC. Methods: In this prospective phase II/III trial, up to 1,912 pts with resected stage IIB, IIC, and III CC will be enrolled. Based on the post-operative ctDNA status using personalized and tumor-informed assay (Signatera™, bespoke assay), those who are ctDNA- (Cohort A) will be randomized to immediate AC with fluoropyrimidine (FP)+oxaliplatin (Ox) for 3-6 mos per established guidelines v serial ctDNA monitoring. Patients who are ctDNA+ post-operatively, or with serial monitoring (Cohort B), will be randomized to FP+Ox v more intensive AC with addition of irinotecan (I) for 6 mos. One cycle of chemotherapy is allowed while awaiting ctDNA testing results for cohort assignment. The primary endpoints for Cohort A are time to ctDNA+ status (phase II) and disease-free survival (DFS) (phase III) in the immediate v delayed AC arms. The primary endpoint for Cohort B is DFS in the FP+Ox v FP+Ox+I arms for both phase II and phase III portions of the trial. Secondary endpoints include prevalence of detectable ctDNA post-operatively, time-to-event outcomes (overall survival and time to recurrence) by ctDNA status, and the assessment of compliance to adjuvant therapy. Biospecimens including archival tumor tissue, as well as post-operative plus serial matched/normal blood samples, will be collected for exploratory correlative research. Active enrollment across the NCTN started in June 2022 with CCTG sites joining in August 2023. Current accrual (as of 1-27-2025): 647/1,912. NCT: 05174169. Support: U10 CA180868, -180822; -180888; UG1 CA189867; Natera, Inc.

Hematology-Oncology
Deluca C, Stapp J, Kriz C, Massey J, **Loss T**, **Kafri Z**, Beyer M, Marshall J, Ying Y, Treisman J, and Ali Z. Fusing quality improvement and education frameworks to reduce delays in tumor genotyping at community cancer centers. *J Clin Oncol* 2025;43(16). Full Text

C. Deluca

Background: Delays in obtaining tumor genotyping results hinder the ability of communitybased oncologists to develop timely and effective treatment plans for patients with metastatic colorectal cancers (mCRC).Based on these identified challenges, a quality improvement educational intervention was developed to improve genotyping workflows and enhance clinicians' ability to incorporate timely biomarker testing results into treatment planning for patients with mCRC. Methods: Educational workshops were conducted at five US community cancer centers to address delays in tumor genotyping and their impact on treatment planning. These workshops aimed to enhance clinician knowledge and practice strategies for molecular testing protocols and treatment planning. Physician champions at each center facilitated learner engagement, encouraged multidisciplinary collaboration, and promoted institutional change by driving discussions tailored to their centers' specific challenges and baseline performance metrics. To date, pre- and post-intervention data have been collected from a mix of tumor board captured-metrics and case data compiled in spreadsheets. Baseline and follow-up analyses of

patient cases (pre N = 96, post N = 62) evaluated changes in molecular testing rates enabling insights into the effectiveness of the intervention. Results: 90 clinicians participated in the educational workshops, collection of case data is ongoing. Results collected thus far show an overall average reduction of 20.6 days for tumor genotyping results being ready (51.7 days pre vs 31.1 days post). Physician champions report increased consistency in ordering molecular profiling earlier after the education. However, unresolved challenges remain, including insufficient tissue sampling that delay genotyping results as well as the initiation of chemotherapy while awaiting results, which may limit the immediate use of targeted therapies. Conclusions: Cases collected to date suggest that targeted educational workshops addressing genotyping delays formCRCat community cancer centers can drive measurable improvements in molecular testing workflows and reduce time to results. These changes highlight the potential of such interventions to enhance treatment planning timelines in order to optimize therapeutic decision-making. However, persistent barriers limiting further reductions in treatment initiation time underscore the need for continued efforts to address systemic challenges.

Hematology-Oncology
Doi T, Satoh T, Yamamoto N, **Hwang C**, Hamid O, Olszanski AJ, Zeng F, Katsube T, Chisamore MJ, and Harada T. Preliminary results of a first-in-human phase 1b (aCCeleR8-001) study of S- 531011, a humanized anti-CCR8 monoclonal antibody, in patients with advanced solid tumors. *J Clin Oncol* 2025;43(16). Full Text

T. Doi

Background: C-C motif chemokine receptor 8 (CCR8) is selectively upregulated in tumorinfiltrating regulatory T cells (TI-Tregs) in multiple cancers, inhibiting anti-tumor activity of the host immune system. S-531011, a humanized IgG1 monoclonal antibody, is anticipated to deplete CCR8-positive TI-Tregs, restoring anti-tumor immunity without inducing autoimmunity. Methods: An aCCeleR8-001 study is a Phase 1b/2, multicenter, open-label study of S-531011 which consists of Phase 1b Dose Escalation part (Parts A-1 and A-2) and Phase 2 Dose Expansion part. The safety/tolerability, pharmacokinetic (PK), pharmacodynamic, and anti-tumor activity of S-531011 as monotherapy and in combination with pembrolizumab (Merck & Co., Inc.) were evaluated in patients with various types of locally advanced or metastatic solid tumors. S-531011 monotherapy was administered at 8, 24, 80, 240, 800, or 1600 mg/kg intravenously every 3 weeks (Q3W) in Part A-1, whereas patients in Part A-2 received S-531011 at 80, 240, 800, or 1600 mg/kg in combination with pembrolizumab 200 mg/ kg Q3W. The data were analyzed when all patients in Dose Escalation cohorts completed the dose-limiting toxicity (DLT) observation period. Results: As of the data cutoff date (30 Sep 2024), 40 and 35 patients were enrolled in Parts A-1 and A-2, respectively. No DLTs were reported at any dose level and themaximumadministered dose of S-531011 was 1600mgin both parts. One patient reported an infusion-related reaction in Part A. Immune-related adverse events (irAEs) were reported in two patients (5.0%; Grade 1/2 only) in Part A-1, whereas 15 irAEs were reported in 10 patients (28.6%; including four Grade 3 irAEs in four patients) in Part A-2. PK of S-531011 was approximately dose proportional with a terminal elimination half-life of 10 to 12 days regardless of dose level. CCR8 receptors in PBMCs were occupied at doses of 80 mg or higher. PK/CCR8 receptor occupancy modeling analysis indicated that > 90% of receptors in tumor tissues were occupied in the range of 80 to 800 mg. Multiplex immunohistochemistry analysis demonstrated proof of mechanism as evidenced by CCR8-positive Treg depletion in tumor tissue at doses of 24mgor higher. Among 62 evaluable patients dosed at 80 to 1600mgin Part A, four patients (6.5%) had confirmed partial response, three of whom had colorectal cancer (CRC). Twenty patients (32.3%) had disease control for≥6 weeks. Response rate was not correlated with dose (80 to 1600 mg). Following a comprehensive data review, tentative recommended Phase 2 doses were determined to be 80 to 800 mg in both parts. Conclusions: S-531011 was well tolerated up to 1600 mg as monotherapy and in combination with pembrolizumab. A higher response rate in patients with CRC warrants further exploration of this tumor type in Phase 2 Dose Expansion part. Phase 2 CRC cohorts are currently ongoing.

Hematology-Oncology
Ghimire B, **Jamil M**, **Rogers LR**, and **Girgis M**. Efficacy of systemic therapy in breast cancer with CNS metastases: “Real-world” experience. *J Clin Oncol* 2025;43(16). Full Text

B. Ghimire, Henry Ford Health System, Detroit, MI, United States

Background: The incidence of CNS metastases in breast cancer is rising. While local therapies such as surgery and radiation remain standard, data on upfront systemic therapies for active brain metastases, especially HER2-negative patients, is limited. This study examines upfront systemic therapy efficacy for CNS metastases in breast cancer patients at a single institution, including a majority African American (AA) population. Methods: A retrospective chart review included breast cancer patients with CNS metastases treated at Henry Ford Health (January 2014-July 2024). Eligible patients had not received concurrent local therapy; prior local therapy was permitted if unrelated to the studied lesions. CNS response was to be assessed using RANOBM (defines measurable disease as lesions > 10 mm) for parenchymal and modified RANO-LM criteria for leptomeningeal disease (LMD). Results: Among 35 patients (20 AA, 13 Caucasian), with a median age of 54 years, HER2-positive was the most common receptor type (49%), followed by HR-positive (37%) and triple-negative (14%); nearly half (46%) had HER2-low disease. Parenchymal metastases were predominant (86%); three had co-existing LMD, and two others had only LMD. Most metastases were multiple; 91% had lesions < 10 mm. 43% had prior WBRT or SRS to unrelated lesions. HER2-positive patients had the highest CNS overall response rate (ORR, 53%) and disease control rate (DCR, 94%), followed by HR-positive (ORR 31%, DCR 69%) and triple-negative (ORR and DCR 20%). Median PFS did not significantly differ between receptor groups (p = 0.130). Trastuzumab-deruxtecan (T-Dxd) was the most common regimen (10/35) and within HER2-positive and HR-positive groups. T-Dxd achieved CNS ORR of 60%, DCR of 90%, and median PFS of 16 months. Tucatinib-based regimens showed a 100% DCR with median PFS of six months. Other therapies, including sacituzumab, abemaciclib, and trastuzumab-emtansine, showed stable disease as the best response. Among AAs, HR-positive was the most common receptor type (50%). These patients had ORR of 35% and DCR of 65%. TDxd maintained ORR of 60% and DCR of 80%. Of five patients with LMD, three were HER2- positive, and two were HR-positive, with an ORR of 60%, and DCR of 80%. Conclusions: This “real-world” experience highlights that, at our institution, most patients with breast cancer and CNS metastases considered for upfront systemic therapy lack measurable disease (91% having lesions < 10 mm) typically required for clinical trials. Nonetheless, the response rate aligns with published experiences. In addition, we included patients with LMD, who are often excluded in trials. Our data also suggests impressive CNS responses with T-Dxd, both overall and in AA patients. The management of brain metastases and LMD in these patients is best approached in a multidisciplinary format.

Hematology-Oncology

Gor D, **Rehman T**, **Pradeep A**, **Ghosh S**, and **Kuriakose P**. MM-259: Impact of the International Myeloma Working Group (IMWG) SLiM Criteria on Multiple Myeloma Management: A Tertiary Care Center Experience. *Clin Lymphoma Myeloma Leuk* 2025;25:S911. Full Text

Multiple myeloma (MM) is a hematologic malignancy characterized by the proliferation of plasma cells. IMWG's introduction of the SLiM criteria in 2014 expanded the diagnosis of MM. Our retrospective study evaluated the adoption and impact of these criteria at Henry Ford Cancer Institute (HFCI), focusing on patient demographics and outcomes of those diagnosed exclusively using the SLiM criteria. Methods: Electronic medical records at HFCI (January 2015–December 2023) were reviewed to identify MM patients meeting at least one SLiM criterion (≥60% plasma cells, free light chain (FLC) ratio >100, or MRI lesion), excluding those with CRAB features. Data on demographics, staging, treatment, and outcomes (through December 2024) were analyzed. Results: Between 2015 and 2023, 495MMpatients were diagnosed; 190 met at least one SLiM criterion. After excluding 177 with CRAB features, 13 patients remained who were diagnosed solely by SLiM criteria. Of these, 6 had plasma cells >60%, 11 had FLC ratio >100, and 3 met MRI criteria. The mean age was 63.6 years; 53.8% were female, 53.8% African American, and 38.4% Caucasian. High-risk cytogenetics were present in 53.8% patients. By Revised International Staging System (R-ISS) staging, 61.5% of patients had stage 1, 30.7% had stage 2, and 7.6% had stage 3 disease. Twelve patients received treatment with induction regimen, which included bortezomib, lenalidomide, dexamethasone (VRd) (n = 9), daratumumab-VRd (n = 1), carfilzomib, lenalidomide, dexamethasone (KRd) (n = 1), or bortezomib, dexamethasone (Vd) (n = 1), all starting treatment at diagnosis. Among them, there was one death (hospice, age/comorbidities), two relapses (both in remission after second-line therapy), and nine remained in remission. One patient, diagnosed in

2017, has not required treatment to date. Conclusion: Our study highlights real-world data on the impact of the IMWG SLiM criteria for MM diagnosis. Patients diagnosed solely based on SLiM criteria, who would previously have been classified as having smoldering myeloma, were treated at diagnosis, reflecting real-time adoption of the updated guidelines. This underscores the positive impact and practical applicability of the revised criteria. Interestingly, one untreated patient has not progressed, suggesting the need for appropriately powered randomized studies to better understand outcomes in this specific subset of patients.

Hematology-Oncology
Hamilton EP, Han HS, Kalinsky K, Abuhadra N, McAndrew NP, Spira AI, Chan N, Starks D, Wulf GM, Chaudhry A, Kelley K, Parajuli R, Wang JS, O'Shaughnessy J, **Weise AM**, Richardson DL, Roque DR, Ferrarotto R, Zizlsperger N, and Giordano A. Initial phase 1 dose escalation data for emiltatug ledadotin (Emi-Le), a novel B7-H4- directed dolasynthen antibody-drug conjugate. *J Clin Oncol* 2025;43(16). Full Text

E.P. Hamilton

Background: B7-H4 is a transmembrane protein over-expressed in breast (BC), ovarian (OC), endometrial (EC), and adenoid cystic carcinoma type 1 (ACC-1) cancers, with limited expression in healthy tissues. Emi-Le (XMT-1660) is a B7-H4-directed Dolasynthen ADC designed with a proprietary auristatin F-HPA microtubule inhibitor payload with controlled bystander effect. Methods: The Phase 1 trial is investigating Emi-Le monotherapy in adult patients (pts) with advanced/metastatic TNBC, HR+/HER2- BC, OC, EC and ACC-1. In dose escalation, eligible pts received Emi-Le at doses of 7.2-115 mg/m2 per cycle, with all collected data informing the recommended doses for the expansion (EXP) portion of the trial. Tumors were evaluated retrospectively for B7-H4 expression by IHC, with the preliminary high cutoff set at TPS≥70. Results: As of December 13, 2024, 130 pts were dosed. Across all tumor types, median age of pts was 55; median 4.5 prior lines of therapy (range 0-15). B7-H4 status was evaluated for 103 pts, with 44% determined to be B7-H4 TPS high. Overall, Emi-Le was generally well tolerated. The most common TRAEs were transient AST increase (38%, G3 14%), proteinuria (31%, G3 9%), nausea (29%, G3 1%) and fatigue (28%, G3 0%). The only G3 TRAEs in ≥5% of pts were AST increase and proteinuria. No G4 or 5 TRAEs were reported. No observed dose-limiting treatment-related neutropenia, neuropathy, ocular toxicity, interstitial lung disease or thrombocytopenia. TRAEs leading to discontinuation were observed in 2.3% of pts. Clinical activity was correlated with both dose and B7-H4 expression. For pts treated with doses ranging from 38.1-67.4 mg/m2 per cycle (intermediate dose range), the confirmed ORR in evaluable pts with high B7-H4 expression was 23% (6/26), including a 23% (3/13) confirmed ORR in evaluable pts with TNBC, with all 13 pts having previously received at least one topoisomerase-1 inhibitor (topo-1) ADC. At doses ≥76.2 mg/m2 per cycle (high dose range), the confirmed ORR in evaluable pts with high B7-H4 expression was 22% (2/9), with 78% (7/9) having ≥30% reduction in target lesions. Of the 8 pts with confirmed responses at doses ≥38.1 mg/m2, 5 had reduction in target lesions > 60%, including 1 CR. All 4 pts with high B7-H4 expression treated at the initial EXP dose of 67.4mg/m2 Q4W had tumor reductions and were on treatment with durations of ≥16 weeks as of data cutoff. Conclusions: Based on the initial reported data, Emi-Le appears to have encouraging clinical activity and tolerability in a heavily pretreated population. Further clinical development is ongoing in the EXP portion of the trial at a dose of 67.4 mg/m2 Q4W in pts with advanced/metastatic TNBC who have received 1-4 prior lines of systemic therapy, including at least one topo-1 ADC. Dose exploration is ongoing to identify a potential second higher EXP dose.

Hematology-Oncology
Han HS, Kalinsky K, Abuhadra N, Giordano A, Starks D, Wulf GM, McAndrew NP, O'Shaughnessy J, Spira AI, Chan N, Kelley K, Parajuli R, **Weise AM**, Chaudhry A, Wang JS, Richardson DL, Roque DR, Meric-Bernstam F, Rogalski C, and Hamilton EP. Emiltatug ledadotin (Emi-Le): A B7-H4-directed dolasynthen antibody-drug conjugate (ADC) being investigated in phase 1 dose expansion in patients with triple negative breast cancer who received at least one prior topoisomarase-1 inhibitor ADC. *J Clin Oncol* 2025;43(16):Tps1141-Tps1141. Full Text

H.S. Han

Breast cancer is the leading cause of cancer death for women worldwide, with triple-negative breast cancer (TNBC) considered one of the more aggressive breast cancers, accounting for ~15% of all cases. Unfortunately, there remains an unmet medical need for effective and well-tolerated treatments for advanced/metastatic TNBC; in heavily pretreated patients, standard-of-care single-agent chemotherapy has limited efficacy, with response rates of ~5%, PFS ~7 weeks. Emiltatug ledadotin (Emi-Le; XMT-1660) is a B7-H4-directed Dolasynthen ADC designed with a precise, target-optimized drug-to-antibody ratio (DAR 6) and a proprietary auristatin F-HPA microtubule inhibitor payload with controlled bystander effect. The FDA has granted Emi-Le two Fast Track designations for the treatment of adult patients with breast cancer, including patients with TNBC who have previously been treated with topoisomerase-1 inhibitor (topo-1) ADCs. Initial dose escalation clinical data from the ongoing Phase 1 trial at doses ranging from 38.1-67.4 mg/m2 per cycle demonstrated a 23% confirmed response rate in patients with B7-H4 high TNBC who were heavily pretreated all of whom received at least one prior topo-1 ADC. Methods: Based on encouraging clinical activity and tolerability data in the initial dose escalation data, the expansion portion (EXP) of the Phase 1 trial has been initiated and is actively enrolling patients. EXP has a Simon 2-stage design and will evaluate two doses in patients with advanced/metastatic TNBC who have received 1-4 prior lines of systemic therapy, including at least one topo-1 ADC. Patients will be evaluated for B7-H4 expression prospectively by IHC and will be stratified into B7-H4 TPS high and B7-H4 TPS low cohorts. The first EXP dose is 67.4 mg/m2 Q4W. Dose exploration is ongoing to identify a potential second higher EXP dose. The protocol includes the option for multiple additional indications, including HR+/HER2- breast cancer, endometrial cancer, ovarian cancer, and ACC-1.

Hematology-Oncology
Hannoudi A, **Gonte MR**, **Cannella C**, **Sawar K**, **Yono SS**, **Atisha NM**, **Walker EM**, **Bensenhaver J**, **Evangelista MS**, and **Atisha DM**. ASO Visual Abstract: The Effect of Oncoplastic Reduction Mammoplasty on the Incidence of Breast Lymphedema in Women Undergoing Breast-Conservation Surgery. *Ann Surg Oncol* 2025:2. Full Text

[Hannoudi, Andrew; Gonte, Madeleine R.; Sawar, Kinan] Wayne State Univ, Sch Med, Detroit, MI 48202 USA; [Gonte, Madeleine R.; Cannella, Cara; Yono, Summer S.; Atisha, Noah M.; Walker, Eleanor M.; Bensenhaver, Jessica; Evangelista, Maristella S.; Atisha, Dunya M.] Henry Ford Hosp, Div Plast & Reconstruct Surg, Detroit, MI USA
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Hematology-Oncology
Jindal D, **Hirko K**, **Cassidy-Bushrow A**, **Ghosh S**, **Susick L**, **Latack K**, **Shetty P**, and **Neslund-Dudas C**. Racial differences in prevalence of coronary artery calcification among patients undergoing lung cancer screening. *J Clin Oncol* 2025;43(16). Full Text

D. Jindal

Background: Coronary artery calcification (CAC) is a known risk factor for coronary heart disease. Lung cancer screening (LCS) with low-dose computed tomography (LDCT) can detect lung cancer at earlier stages and reduce mortality. Additionally, CAC are common incidental findings among patients undergoing LDCT for LCS. However, racial differences in incidental findings of CAC among LCS patients have not been thoroughly investigated. We examined the association between race and presence of moderate to severe CAC among patients undergoing LDCT for LCS. Methods: We conducted a retrospective analysis of electronic health records (EHR) from Henry Ford Health (2016-2023) among patients undergoing LDCT for LCS. CAC was classified as moderate or severe (vs. none or mild). Race was categorized as Black, White, Asian, American Indian/Alaskan Native, Other and Unknown. We focused on Black and White patients, owing to the small sample size in the other groups. Multivariable logistic regression was used to examine the association between race and presence of moderate to severe CAC, adjusting for age, sex, and tobacco smoking status. Results: A total of 15,911 patients who were eligible for LCS and completed at least one screen during our study period were included. Of these, 79.6% were White and 20.4% were Black. The mean age of patients was 63.865.8 years; 50.4% were

male and 61.4% reported current tobacco smoking. Demographic comparisons show that White patients were more frequently male compared to Black patients (50.9% vs 47.9%, p = 0.002). In addition, Black patients were slightly older (64.365.7 vs 63.665.8 years) and reported a higher current tobacco smoking status (67.9% vs 59.7%, p < 0.0001) compared to White patients. The prevalence of moderate to severe CAC was 10.9% overall and was higher among Black vs White patients (16.1% vs 9.6%, p < 0.0001). After covariate adjustment, Black patients had significantly higher odds of moderate to severe CAC compared to White patients (odds ratio [OR] = 1.8, 95% CI 1.6-1.9, p < 0.0001). Conclusions: The study findings suggest significant racial differences in the prevalence of CAC among patients undergoing LCS. Race may be an important factor when assessing cardiovascular risk in patients undergoing LCS and may have implications for screening protocols and preventive strategies. Future research is needed to explore the impact of these differences on risk and mortality from cardiovascular diseases.

Hematology-Oncology
Kitchens CS, Shi Q, Dasari A, Garcia-Aguilar J, Sanoff HK, George TJ, Hong TS, Yothers G, **Philip PA**, Baghdadi TA, Alese OB, Bercz A, George M, O'Reilly EM, Meyerhardt JA, Shergill A, Horvat N, Romesser PB, Hall WA, and Smith JJ. Trials in progress: Alliance A022104/NRG-GI010-A randomized phase II/III trial testing the efficacy of triplet versus doublet chemotherapy regarding clinical complete response and disease-free survival in patients with locally advanced rectal cancer (LARC; the Janus Rectal Cancer trial). *J Clin Oncol* 2025;43(16). Full Text

C.S. Kitchens

Background: A total neoadjuvant therapy (TNT) approach improves compliance with chemotherapy and increases rates of tumor response compared to neoadjuvant chemoradiation (CRT) alone in those with locally advanced rectal cancer. Recent data indicate that optimal sequencing of TNT involves consolidation (rather than induction) chemotherapy to improve complete response rates. The use of FOLFIRINOX has shown to improve response and outcomes compared to CRT and surgery alone. Data have also shown that patients with clinical complete response (cCR) after TNT may be managed with a watch and wait approach (WW) instead of preemptive total mesorectal resection (TME). However, the optimal consolidation chemotherapy regimen to improve cCR rates has not been established, and a randomized clinical trial has not robustly evaluated cCR as a primary endpoint. We designed this NCI-sponsored study of chemotherapy intensification to address this and to increase cCR rates, provide opportunity for organ preservation, and survival outcomes. Methods: In this multigroup randomized, seamless phase II/III trial (1:1), up to 760 patients with LARC, T4N0, any T with node positive disease (any T, N+) or T3N0 requiring abdominoperineal resection or coloanal anastomosis and distal margin within 12 cm of anal verge will be enrolled. Stratification factors include tumor stage (T4 vs T1-3), nodal stage (N+ vs N0) and distance from anal verge (0-4; 4-8; 8-12 cm). Patients will be randomized to receive neoadjuvant long-course chemoradiation (LCRT) followed by consolidation doublet (mFOLFOX6 or CAPOX (control arm)) or triplet chemotherapy (FOLFIRINOX (experimental arm)) for 3-4 months. LCRT in both arms involve 4500 cGy in 25 fractions over 5 weeks +900 cGy boost in 5 fractions with a fluoropyrimidine. Patients will undergo assessment 8-12 (64) weeks post-TNT completion. The primary endpoint for the phase II portion will compare cCR between treatment arms. A total number of 312 patients (156 per arm) will provide statistical power of 90.5% to detect a 17% increase in cCR rate, at a onesided alpha = 0.048. The primary endpoint for the phase III portion will compare disease-free survival (DFS) between arms. A total of 285 DFS events will provide 85% power to detect an effect size of hazard ratio 0.70 at a one-sided alpha of 0.025, requiring enrollment of 760 patients (380 per arm). Secondary objectives include overall survival, organ preservation time, time to distant metastasis, and adverse event rates.

Hematology-Oncology
Le X, Piotrowska Z, Spira AI, Baik CS, Baggstrom MQ, Falchook GS, Neal JW, **Gadgeel SM**, Lopes G, Johnson ML, Riess JW, Nguyen D, Morelli L, Sandino D, Margossian S, Upadhyay V, and Santini F. NVL-330, a selective HER2 tyrosine kinase inhibitor, in patients with advanced or metastatic HER2-altered non-small cell lung cancer: The phase 1 HEROEX-1 study. *J Clin Oncol* 2025;43(16). Full Text

X. Le

Background: Oncogenic mutations and gene amplifications in the HER2 receptor tyrosine kinase are detected in approximately 2-4% and 1-5% of non-small cell lung cancers (NSCLC) in the US, respectively. Exon 20 insertion mutations (exon20ins) are the predominant HER2 mutations in NSCLC, and ~50% of patients with HER2-mutant metastatic NSCLC develop brain metastases. The antibody drug conjugate (ADC) trastuzumab deruxtecan (T-DXd) has received FDA accelerated approval for HER2-mutant NSCLC, but no tyrosine kinase inhibitors (TKIs) are currently approved for this indication. NVL-330 is a novel, brain-penetrant, HER2-selective investigational TKI, designed to address the medical need of targeting HER2-mutant tumors, and treating brain metastases, while minimizing treatment related adverse events due to off-target inhibition of wild-type EGFR. Methods: HEROEX-1 (NCT06521554) is a first-inhuman, Phase 1a/1b trial. The Phase 1a dose escalation portion employs a Bayesian optimal interval design with a 3+3 run-in, followed by a Phase 1b dose expansion. The study population includes adult patients with advanced or metastatic NSCLC with a HER2 oncogenic mutation (Phase 1a/1b) or amplification (Phase 1a only) determined by local testing. Eligible patients must have received at least one prior systemic therapy including platinum-based chemotherapy with or without immunotherapy, or are unsuitable candidates for available therapies. Prior HER2-directed antibodies and HER2-directed ADCs are allowed. Prior HER2 TKIs are allowed in Phase 1a only. Patients will receive NVL-330 by oral administration once or twice daily. The primary objectives are to evaluate safety and tolerability, determine the recommended Phase 2 dose, and, if applicable, the maximum tolerated dose of NVL-330. Additional objectives include assessment of preliminary activity and characterization of the pharmacokinetic and pharmacodynamic profiles of NVL-330. Analyses will be performed to evaluate tumor and blood-based biomarkers of response and other relevant biomarkers. The study is open to accrual.

Hematology-Oncology

Lin E, Singstock M, Alhushki S, Deshmukh SS, Cheng C, Goliwas K, Deshane J, Naqash AR, **Rous FA**, Thawani R, and Desai A. Proteogenomic characterization of antibody-drug conjugate target expression profiles in transcriptional subtypes of small cell lung cancer. *J Clin Oncol* 2025;43(16). Full Text

E. Lin

Background: Small cell lung cancer (SCLC) is a highly lethal malignancy, and there is an urgent need for more effective therapies. Antibody-drug conjugates (ADCs), which combine the precision of monoclonal antibodies with the cytotoxic power of small molecules, represent a promising approach. Despite extensive research, the relationship between ADC target overexpression and the transcriptional profile of SCLC remains unclear. Our study aimed to elucidate how ADC target expression correlates with transcriptional subtypes of SCLC, potentially guiding the selection of ADCs based on molecular profiling. Methods: RNA-seq and tandem mass spectrometry data for 107 patients with matched SCLC tumors and normal adjacent lung tissue were obtained from the CPTAC SCLC cohort. SCLC subtypes were defined according to expression of four transcription factors: achaete-scute homologue 1 (ASCL1), neurogenic differentiation factor 1 (NeuroD1), yes-associated protein 1 (YAP1) and POU class 2 homeobox 3 (POU2F3). ADC target expression for DLL3, SEZ6, B7-H3 (CD276), and Trop2 (TACSTD2) were assessed at the transcriptomic and proteomic level. The correlation between transcriptional subtype and ADC target expression was determined using Pearson's correlation coefficient. Results: In 107 SCLC tumors, subtypes corresponded to 66 (61.6%) ASCL1, 21 (19.6%) NeuroD1, 3 (2.8%) YAP1, and 17 (15.9%) POU2F3. The ASCL1 subtype was positively correlated with DLL3 (R2=0.93, p=9E-87) and SEZ6 (R2=0.85, p=2.9E-57), and negatively correlated with TROP2 expression (R2=-0.72, p=1.5E-34). The NEUROD1 subtype showed moderate positive correlation with DLL3 (R2=0.52, p=4.8E-14) and SEZ6 (R2=0.58, p=3.6E-18), and a moderate negative correlation with TROP2 (R2=-0.52, p=1.6E-14). The POU2F3 subtype did not demonstrate strong positive or negative correlations with ADC targets. The YAP1 subtype was negatively correlated DLL3 (R2=-0.72, p=1.1E-32) and SEZ6 (R2=-0.71, p=9.5E-33), and positively correlated with Trop2 expression (R2=0.85, P=7.5E-61). Conclusions: Our findings reveal that molecular subtypes of SCLC exhibit unique patterns of ADC target expression. These profiles are crucial for further research and could lead to the development of subtype-specific treatments that improve clinical outcomes for patients with SCLC.

Hematology-Oncology
Lopes G, Gainor JF, Subbiah V, Bowles DW, Doebele RC, Mansfield AS, Baik CS, **Gadgeel SM**, Kalemkerian GP, Ou SHI, Becerra CR, Evangelist MC, Liu SV, Melear JM, Saxena A, Thomassen A, Wang S, and Besse B. Efficacy and safety of pralsetinib in patients with advanced RET-fusion-positive NSCLC: Final data from the phase 1/2 ARROW study. *J Clin Oncol* 2025;43(16). Full Text

G. Lopes

Background: RET fusions are targetable oncogenic drivers in 1-2% of non-small cell lung cancers (NSCLC). ARROW (NCT03037385) study results (final data lock May 20, 2024) supported the US FDA approval of pralsetinib, a highly potent, oral, selective RET inhibitor for metastatic RET-altered NSCLC. Here, we present final study results. Methods: ARROW was a phase 1/2 open-label study conducted at 84 sites in 13 countries. Phase 2 included patients with RET-fusion-positive NSCLC who received 400 mg pralsetinib once daily (QD). Initially, treatment-naïve patients were not candidates for platinum-based therapy and presented with several unfavorable prognostic factors; this requirement was removed by protocol amendment in July 2019. Primary objectives were overall response rate (ORR, per RECIST v1.1) and safety. Progression-free survival (PFS) and overall survival (OS) are reported in the full efficacy population; the measurable disease population (MDP) was the primary analysis population for ORR and duration of response (DOR). Results: 281 patients with RET-fusion-positive NSCLC received pralsetinib 400 mg QD, with a median duration of treatment of 14.95 months (mos). Median age was 60 years; 46% were male. In the MDP (n=259), ORR was 70.3% (95% confidence intervals [CI]: 64.3, 75.8) and median DOR was 19.1 mos (95% CI: 14.5, 27.9; Table). In the efficacy population (N=281), median OS was 44.3 mos (95% CI: 30.9, 53.1) with median follow up of 47.6 mos (95% CI: 44.8, 49.2), and median PFS was 13.1 mos (95% CI: 11.4, 16.8). ORR (Table) and median PFS were markedly higher in the US (25.9 mos, n=64) vs. Asia (12.6 mos, n=122) or Europe (12.9 mos, n=95). In the safety population, 95% of patients experienced treatment-related adverse events (TRAEs); 66% experienced ≥grade 3. Common TRAEs included increased AST (n=128 [46%]), anemia (n=121 [43%]), increased ALT (n=98 [35%]), and hypertension (n=77 [27%]). 3 patients died due to TRAEs (pneumonia, n=2; interstitial lung disease and rhabdomyolysis, n=1 each). No new safety signals were identified with this update. Conclusions: Pralsetinib produced clinically meaningful and durable responses in patients with RET-fusion-positive NSCLC (regardless of prior therapies) with a manageable safety profile, confirming with this longer follow up previously published results.

Hematology-Oncology
Mahadevia H, Wu S, McWilliams RR, Majeed U, Starr JS, Jones JC, MoSalem OM, O'Donnell C, Ahn DH, Xiu J, El Shawa H, Sledge GW, **Philip PA**, Kulkarni N, Goel S, Spetzler D, Singh H, Borad MJ, Bekaii-Saab TS, and Babiker HM. The differential effect of stromal genes on gemcitabine/nab-paclitaxel (GN) and GN/cisplatin (GCN) outcomes in advanced pancreatic adenocarcinoma (aPDAC). *J Clin Oncol* 2025;43(16). Full Text

H. Mahadevia

Background: GN is a front-line therapy for aPDAC. A Phase I/II study demonstrated that GCN has a higher overall response rate and median overall survival (mOS). Our previous study found no difference in outcomes among patients with DNA damage repair gene mutations; however, stromal gene expression correlated with mOS in patients receiving GCN. Here, we further evaluate differences in the outcomes with GCN and GN by site of biopsy. Methods: PDAC samples (n = 4,463) were analyzed by NGS (NextSeq/NovaSeq) or RNA (NovaSeq) (Caris Life Sciences, Phx, AZ). Expression of stromal and related genes (ACTA2, ADIRF, HAS2, IL-6, MMP-2, MMP-9, SPARC, STAT3, TBGB1, TGFB2, TGFBR3, IDO1, HLA-DRB4, VEGFB) from different biopsy sites [high expression (H) >50% of RNA transcripts per million] was correlated with outcomes to GCN or GN. mOS was obtained from insurance claims and calculated from first treatment to last contact. The hazard ratio (HR) was calculated by the Cox proportional hazards model, and p-values were calculated using the log-rank test. Results: 4325 patients [primary biopsy (PT), n = 1,878; non-liver metastatic biopsy (N-LM), n = 818; Liver biopsy (LM), n = 1,629] received GN while 138 patients (PT, n = 45; N-LM, n = 28; LM, n = 65) received GCN. GCN was associated with longer mOS than GN [Δ: 5.2 months (m), HR: 0.76, 95% CI 0.63-0.92, p = 0.01]. GCN was associated with

longer mOS compared to GN in LM (Δ: 5.6 m, HR: 0.66, 95% CI 0.50-0.87, p = 0.003), but it was not significant in PT (Δ: 4.6 m, p = 0.13) and N-LM (Δ: 4.4 m, p = 0.35). Median MMP2 (38.5 vs. 163.1 vs. 162.2), VEGFB (14.4 vs. 16.9 vs. 16.2) and TGFBR3 (11.4 vs. 15 vs. 16.4) expression were lower in LM compared to PT and N-LM while TGFB1 (41.6 vs. 34.5 vs. 39.8) and IL6 (1.61 vs. 1.19 vs. 1.41) expression were highest in LM (p<0.05). In LM, IL6-H (Δ: -11 m, p = 0.037) and TGFB1-H (Δ: -5.9 m, p = 0.10) were associated with worse post-GCN survival compared to GN (p = 0.82 and p = 0.57). Whereas, in N-LM, TGFBR3-H trended towards longer post-GCN survival (Δ: 12 m, p = 0.18), while ADIRF-H trended towards shorter post-GCN survival (Δ: -12 m, p = 0.056) compared to GN (p = 0.42 and p = 0.10). While in PT, MMP2-H (Δ: 11.3m, HR: 0.46, p = 0.16), TGFB1-H (Δ: 11.3 m, HR: 0.33, p = 0.09), HLA-DRB4-H (Δ: 12.9 m, HR: 0.44, p = 0.11) and VEGFB-H (Δ: 10.7, HR: 0.34, p = 0.09) trended towards longer post-GCN survival compared to GN (MMP2-H, Δ: 3.4 m, p = 0.03, TGFB1-H, p = 0.661, HLA-DRB4-H, p = 0.67, VEGFB-H, Δ: 1.3 m, p = 0.03). Conclusions: GCN is associated with improved mOS compared to GN, especially in LM.Stromal gene expression in the liver differs from that in N-LM and the pancreas. While high stromal gene expression trends towards worse post-GCN survival in LM, it is associated with improved survival in N-LM and PT. Further validation is needed to understand the impact of stromal gene expression in different tumor sites on survival outcomes and signature development.

Hematology-Oncology
Singh A, Sindhu AK, Khealani M, Tarimci B, Gupta A, Malhotra S, Bathvar P, Shah V, Bedi S, Theik NWY, **Kukreja G**, and Obulareddy SUJ. Inflammatory bowel disease and risk of cancer: A nationwide study. *J Clin Oncol* 2025;43(16). Full Text

A. Singh

Background: Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is a chronic inflammatory condition of the gastrointestinal tract. Existing research suggests that chronic inflammation, immune dysregulation, and prolonged use of immunosuppressive therapy may contribute to increased cancer risk in IBD. However, nationwide data on the prevalence and types of cancer in U.S. IBD patients remain limited. This study aimed to determine the frequency and associations of various cancers among individuals with IBD. Methods: We conducted a retrospective cross-sectional study using the 2016-2018 Nationwide Inpatient Sample (NIS), encompassing adult hospitalizations in the U.S. The NIS approximates 20% of hospital discharges nationwide. Patients with IBD were identified via ICD-10-CM codes. Statistical analyses were performed with SAS 9.4. We used chi-square tests for univariate analysis and multivariate logistic regression to calculate adjusted odds ratios (aOR) and 95% confidence intervals (CI). Statistical significance was set at p< 0.05. Results: Out of 87,761,798 U.S. hospitalizations, 0.67% involved CD and 0.39% involved UC. Prevalence of pancreatic cancer was 0.16% in CD and 0.22% in UC. Melanoma skin cancer prevalence was 0.07%, while non-melanoma skin cancers (NMSC) including squamous cell, basal cell, and Merkel cell carcinomas were observed at 0.03% (p< 0.0001). Notably, melanoma was more frequent in UC(0.13%) compared to CD(0.07%) or non-IBD (0.07%). Colon cancer occurred in 0.05% of IBD patients. Leukemia was documented in 0.51% of CD and 0.61% of UC hospitalizations. Barrett's esophagus (BE) without dysplasia was seen in 0.76%, and BE with dysplasia in 0.01%. Esophageal malignancy prevalence was 0.03% in CD and 0.08% in UC. Multivariate regression indicated that UC was associated with a 51% higher melanoma risk than CD (aOR: 1.51, 95% CI: 1.22-1.85). BE risk was significantly elevated in CD (aOR: 1.67, 95%CI: 1.55-1.79) and UC (aOR: 1.77, 95%CI: 1.62-1.93). Age over 75 significantly increased cancer risk (aOR: 1.99, 95%CI: 1.58-2.51). Additionally, Black patients (aOR: 1.20, 95%CI: 1.17-1.24) and smokers (aOR: 1.39, 95%CI: 1.20-1.61) showed higher odds of cancer. Conclusions: These findings highlight the need for vigilant, long-term surveillance of IBD patients to reduce gastrointestinal and melanoma cancer risks. Higher risk in specific demographics suggests the importance of tailored screening protocols. Further research on the potential for hematological malignancies in IBD is warranted to enhance understanding and improve patient care.

Hematology-Oncology
Zimmer M, **Abad J**, **Gupta J**, **Ghosh S**, and **Kuriakose P**. MM-423: Secondary Hematologic Malignancies in Patients With Multiple Myeloma: A Retrospective Analysis of Risk Factors and Incidence in a Large Urban Health System. *Clin Lymphoma Myeloma Leuk* 2025;25:S919.

Multiple myeloma (MM) is a common hematologic malignancy. While overall survival has improved due to advances in therapy, there is concern regarding the risk of secondary hematologic malignancies (SHM). Objective: To identify patients treated for MM who subsequently developed SHM and estimate the incidence and timing of SHM. Design: Retrospective, observational study. Setting: Henry Ford Health, a large urban, tertiary care network in Detroit, MI. Patients: Patients age 18 years or more with a confirmed diagnosis of MM between January 2005 and December 2022 and a subsequent SHM diagnosis were identified through electronic medical records review. Results: Of 3122 patients with MM, 297 were identified by automatic data pull as having a diagnosis of SHM. After manual review, nine patients met the inclusion criteria. Six patients (66.7%) were male. Median age at MM diagnosis was 62 (range: 53–73) years. About 44.4% were African American, 33.3% were Caucasian, 11.1% were Asian, and 11.1% identified as other. At a median follow-up of 58 (range: 35–144) months, most patients (66.6%) had received only one line of therapy, some had two lines (22.25%), and one patient had received 12 lines of therapy. Five patients (55.6%) underwent autologous stem cell transplantation. Most patients (77.8%) received maintenance therapy, most commonly with lenalidomide (66.7%), for a median duration of 11 (range: 0–29) months. SHM were diagnosed at a median of 4 years after MM diagnosis, being primarily myeloid in origin (77.8%). Median time from MM diagnosis to death was 64 (range: 49–78) months, and median time from SHM diagnosis to death was 5 (range: 0–9) months. Conclusion: Despite the sample size and retrospective nature, our study has some key findings. First, the incidence of SHM was 0.2%, which is significantly less than the 8–18% in previous studies. Second, most patients were not heavily pretreated, often receiving only 1–2 lines of therapy and shorter duration of lenalidomide maintenance prior to the development of SHM. Accordingly, further work needs to be done to evaluate the impact of both patient- and disease-dependent factors, as well as MM therapy, on the development of SHM.

Hospital Medicine

Zimmer M, **Abad J**, **Gupta J**, **Ghosh S**, and **Kuriakose P**. MM-423: Secondary Hematologic Malignancies in Patients With Multiple Myeloma: A Retrospective Analysis of Risk Factors and Incidence in a Large Urban Health System. *Clin Lymphoma Myeloma Leuk* 2025;25:S919. Full Text

Multiple myeloma (MM) is a common hematologic malignancy. While overall survival has improved due to advances in therapy, there is concern regarding the risk of secondary hematologic malignancies (SHM). Objective: To identify patients treated for MM who subsequently developed SHM and estimate the incidence and timing of SHM. Design: Retrospective, observational study. Setting: Henry Ford Health, a large urban, tertiary care network in Detroit, MI. Patients: Patients age 18 years or more with a confirmed diagnosis of MM between January 2005 and December 2022 and a subsequent SHM diagnosis were identified through electronic medical records review. Results: Of 3122 patients with MM, 297 were identified by automatic data pull as having a diagnosis of SHM. After manual review, nine patients met the inclusion criteria. Six patients (66.7%) were male. Median age at MM diagnosis was 62 (range: 53–73) years. About 44.4% were African American, 33.3% were Caucasian, 11.1% were Asian, and 11.1% identified as other. At a median follow-up of 58 (range: 35–144) months, most patients (66.6%) had received only one line of therapy, some had two lines (22.25%), and one patient had received 12 lines of therapy. Five patients (55.6%) underwent autologous stem cell transplantation. Most patients (77.8%) received maintenance therapy, most commonly with lenalidomide (66.7%), for a median duration of 11 (range: 0–29) months. SHM were diagnosed at a median of 4 years after MM diagnosis, being primarily myeloid in origin (77.8%). Median time from MM diagnosis to death was 64 (range: 49–78) months, and median time from SHM diagnosis to death was 5 (range: 0–9) months. Conclusion: Despite the sample size and retrospective nature, our study has some key findings. First, the incidence of SHM was 0.2%, which is significantly less than the 8–18% in previous studies. Second, most patients were not heavily pretreated, often receiving only 1–2 lines of therapy and shorter duration of lenalidomide maintenance prior to the development of SHM. Accordingly, further work needs to be done to evaluate the impact of both patient- and disease-dependent factors, as well as MM therapy, on the development of SHM.

Internal Medicine

Aburumman R, and Nabeel S. Disparities in Liver Transplant Recipients Between 2014 and 2024 Using Organ Procurement and Transplantation Network Data. *Am J Transplant* 2025;25(8):S935. Full Text

Purpose: Liver transplantation is a critical treatment option for patients with end-stage liver disease. Previous studies have highlighted notable disparities in access to liver transplants and in transplant outcomes based on diagnosis, race, and gender. This study examines the differences in the representation of liver transplant recipients by diagnosis, gender, and race between 2014 and 2024. Methods: The national data regarding the state of liver transplantation was obtained through the website of Organ Procurement and Transplantation Network(OPTN) based on OPTN data. The patients were divided into the major groups, "2014" and "2024" liver transplant recipients. A chi-square test was used to compare the recipients' characteristics across the two groups. Results: In 2024, a total of 10,528 liver transplants were performed, compared to 6,730 in 2014. In both years, a higher number of male patients received liver transplants than female patients. However, the gender gap in 2024 was significant smaller than in 2014 (P<0.001). A similar trend is observed when considering ethnicity. White individuals represented the largest percentage in both years, with 69.9% in 2014 and 65.9% in 2024 (P=0.002). There was a higher proportion of elderly recipients, with individuals over 65 years old representing 21.8% of transplant recipients in 2024, compared to 15.7% in 2014 (P<0.001). Additionally, there was a higher representation of patients under the age of 1 in 2024, accounting for 2.1% of recipients, compared to 1.4% in 2014. In both years, more than 90% of recipients were U.S. citizens, and over 94% received a liver from a deceased donor. The proportion of liver recipients with private insurance decreased from 52.3% in 2014 to 46.2% in 2024 (P <0.001). Indicating notable changes in liver transplant indications over the decade, the proportion of recipients with non-cholestatic cirrhosis decreased dramatically from 58.0% in 2014 to 23.3% in 2024 (P<0.00001), while the proportion with malignant neoplasm decreased significantly from 17.6% in 2014 to 10.4% in 2024 (P<0.0001). The proportion of liver transplant recipients testing negative for Hep C increased significantly from 60.3% in 2014 to 81.9% in 2024 (P<0.00001). Conclusions: Our findings offer valuable insights into the evolving landscape of liver transplantation, pointing to changes in patient demographics, and disease etiology but also emphasize ongoing challenges in healthcare access and equity. Further studies are needed to explore the underlying causes of these trends and their implications for liver transplant outcomes. [Formula presented] CITATION INFORMATION: Aburumman R., Nabeel S. Disparities in Liver Transplant Recipients Between 2014 and 2024 Using Organ Procurement and Transplantation Network Data AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: R. Aburumman: None.

Internal Medicine

Aburumman R, **Tahmazian S**, **Nimri F**, and **Jafri S**. Management of Graft versus Host Disease Involving the Bone Marrow: Interventions and Outcomes. *Am J Transplant* 2025;25(8):S482. Full Text

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Purpose: Cytopenias can significantly impact patient outcomes in the immediate post-solid organ transplant period, and they can result from acute graft-versus-host disease (GVHD), though this is less frequent. This study aims to detail our single-center experience with GVHD with bone marrow involvement in patients who underwent liver transplantation (LT) over 10 years. Methods: We reviewed medical charts for patients who underwent LTs at Henry Ford Hospital Transplant Center from January 2014 to December 2023. We recorded all confirmed cases of GVHD with bone marrow involvement after LT. We collected information on their demographics, details of the liver transplant, and how GVHD was presented, diagnosed, and treated. Results: Out of 1,045 LTs performed at our center, 17 patients (1.6%) developed GVHD after transplantation. Of them, 8 had bone marrow involvement that presented in all patients as pancytopenia. Most of them were male (75%) and white (50%). The mean age at presentation was 67 ± 5. The most common indication for transplant was metabolic dysregulation associated steatotic liver disease (MASLD) in 50% of patients. All patients received liver from deceased donor. The average time from transplantation to first symptom reported was 34 days (± 16.4 SD). 7 out of the 8 patients also had skin involvement that presented as a rash (87.5%). Gastrointestinal tract involvement was seen in 62.5% of them and presented as diarrhea in all cases. One patient also had involvement of their central nervous system, which presented as altered mental status and diagnosed with a lumbar puncture. At presentation, a short tandem repeat (STR) test on patients' peripheral blood demonstrated the presence of a mean of 20.9% (± 31.1%) donor DNA. All patients received high-dose steroids as part of their

treatment. 87.5% of them also received Etanercept as part of the treatment regimen, and half of them also received Photopheresis. Only one patient (12.5%) survived for more than 1 year after initial presentation, compared to 78% of patients with GVHD post LT who did not have bone marrow involvement. Conclusions: GVHD after solid organ transplantation typically presents with rash, diarrhea, fever, and pancytopenia 2 to 8 weeks after transplantation. Cytopenia has been described to confer a worse outcome. The lack of clinical trials for GVHD treatment limits an effective therapeutic strategy, and treatment outcomes of GVHD post liver transplant tend to be poor, with >85% mortality rate. [Formula presented] CITATION INFORMATION: Aburumman R., Tahmazian S., Nimri F., Jafri S. Management of Graft versus Host Disease Involving the Bone Marrow: Interventions and Outcomes AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: R. Aburumman: None.

Internal Medicine

Abusuliman M, Ismail A, Elfert K, Abusuliman A, Eldesouki M, **Cox T**, Amreia M, Elsaka HA, Ali MA, Estrada P, and Elhanafi S. Safety of Endoscopic Retrograde Cholangiopancreatography (ERCP) in Liver Transplant Patients: A Population-Based Propensity-Matched Study. *Am J Transplant* 2025;25(8):S455-S456. Full Text

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Purpose: Liver transplant (LT) recipients undergoing Endoscopic retrograde cholangiopancreatography (ERCP) represent a unique patient group that faces distinct challenges during ERCP. This study aims to assess the risk of post-ERCP complications in LT patients. Methods: A retrospective cohort study using the TriNetX US Collaborative Network identified LT patients who underwent ERCP and compared them to a matched non-LT group. The primary outcome was post-ERCP pancreatitis. Secondary outcomes included bleeding, cholangitis, sepsis, transfusion need, and mortality. Results: A total of 3,032 patients were identified in the LT group (group 1), and 126,056 in the no LT group (group 2). The mean age in group 1 was 56.7 +/- 12.1, and 57.7+/- 17.9 in group 2. Females were 982 in group 1, and 66,482 in group 2. Propensity score matching was performed on all baseline characteristics that can be potential confounders, including age, sex, race, and co-morbidities. (Table 1) The outcome analysis after matching showed the incidence of acute pancreatitis post-ERCP was 1.3% in LT group compared to 1.7% in the non-LT group, however it was not statistically significant (RR = 0.770; CI = 0.480 - 1.235, p = 0.277). There was no statistically significant difference in rates of cholangitis (5.5% in LT vs. 4.3% in no LT, RR=1.293, CI=0.980-1.707, p=0.068), sepsis (2.8% vs. 1.8%, RR=1.550, CI=0.996-2.412, p=0.050), gastrointestinal bleeding (1.1% vs. 1%, RR=1.105; CI=0.605-2.019, p=0.745) or mortality (0.4% vs. 0.4%, RR=0.999, CI=0.416-2.396, p=0.998). (Table 2) Conclusions: Liver transplant patients undergoing ERCP exhibited a short-term safety profile similar to that of the general population, particularly in the risk of acute pancreatitis. These findings highlight the safety of ERCP in post liver transplant patients despite being on chronic immunosuppression. [Formula presented] CITATION INFORMATION: Abusuliman M., Ismail A., Elfert K., Abusuliman A., Eldesouki M., Cox T., Amreia M., Elsaka H., Ali M., Estrada P., Elhanafi S. Safety of Endoscopic Retrograde Cholangiopancreatography (ERCP) in Liver Transplant Patients: A Population-Based Propensity-Matched Study AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Abusuliman: None.

Internal Medicine

Abusuliman M, **Kadouh A**, **Aburumman R**, **Rosario A**, **Pradeep A**, **Cox T**, **Rehman S**, **Klutke J**, **Saleem A**, **Alomari A**, Abusuliman A, Amreia M, **Arwani R**, **Dababneh Y**, **Khan M**, and **Jafri S**. Outcomes of Simultaneous Liver and Kidney Transplant vs. Liver Transplant Alone: Insights from a Midwest Transplant Center. *Am J Transplant* 2025;25(8):S471.

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Purpose: We aimed to evaluate long-term renal and survival outcomes in patients with chronic kidney disease (CKD) undergoing liver transplantation alone (LTA) versus simultaneous simultaneous liver and kidney transplant (SLK). Methods: A retrospective study included adult CKD patients (GFR <60 for ≥3 months pre-transplant) who underwent LTA or SLK at our center (2015-2022). Data collected covered demographics, comorbidities, liver disease, and dialysis status. The primary outcome was GFR at 3 months pre-transplant and 3, 6, 12, and 36 months post-transplant. Secondary outcomes included LOS, 1-year readmission, rejection, retransplantation, and mortality at 1, 3, and 5 years. Results: Our study included 231 patients: 67 underwent SLK, and 164 received LTA. Patient characteristics are in Table 1. Cirrhosis was the primary transplant indication in 193 patients (97%), mostly due to alcohol. The SLK group had higher creatinine on transplant day, pre-transplant HRS, and significantly lower pre-transplant GFR (22.1 ± 11.7 vs. 47.8 ± 15.6, $p < 0.001$). Both groups showed GFR improvement ($p < 0.01$), but SLK had consistently higher post-transplant GFR, especially at 3 months (65.8 ± 24.5 vs. 52.3 ± 19.0, $p < 0.01$) (Figure 1). GFR decline was greater in LTA ($p < 0.01$). Mortality (28% vs. 20%, $p = 0.14$) and LOS (13 days, $p = 0.3$) were similar. Pre- or emergent post-transplant dialysis prolonged hospital stay ($p < 0.01$, $p < 0.027$). No significant differences were found in readmission (68% SLK vs. 63% LTA, $p = 0.4$) or re-transplantation (6.7% vs. 9.4%, $p = 0.9$). Graft rejection was higher in SLK (23% vs. 17%) but not significant ($p = 0.3$). Conclusions: Our study shows that SLK transplant provided better long-term renal preservation in patients with CKD. Mortality,LOS,readmission, and re-transplant rates were similar between groups,suggesting that SLK does not significantly increase perioperative risk or resource use. [Formula presented] CITATION INFORMATION: Abusuliman M., Kadouh A., Aburumman R., Rosario A., Pradeep A., Cox T., Rehman S., Klutke J., Saleem A., Alomari A., Abusuliman A., Amreia M., Arwani R., Dababneh Y., Khan M., Jafri S. Outcomes of Simultaneous Liver and Kidney Transplant vs. Liver Transplant Alone: Insights from a Midwest Transplant Center AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Abusuliman: None.

Internal Medicine

Ahmed M, Umer M, Sahu S, and Fnu D. CML-1296: Asciminib Monotherapy in Chronic Myeloid Leukemia: A Systematic Review of Efficacy and Safety From Phase 1–3 Trials. *Clin Lymphoma Myeloma Leuk* 2025;25:S595-S596. Full Text

Although adenosine triphosphate–competitive tyrosine kinase inhibitors (TKIs) have transformed the treatment of chronic myeloid leukemia (CML), long-term outcomes remain limited by resistance, intolerance, and off-target toxicities. Objective: To evaluate the efficacy and safety of asciminib monotherapy across treatment lines, including newly diagnosed, multi-TKI–resistant, and T315I-mutated chronic-phase CML (CML-CP). Design: Systematic review of phase 1–3 interventional trials published or presented through May 2025. Setting: International academic and clinical trial sites. Patients or Other Participants: Adult patients with CML-CP treated with asciminib as monotherapy, including subgroups with prior TKI exposure and T315I mutation. Interventions: Oral asciminib monotherapy across various doses and settings, including 200 mg twice a day in T315I-mutated CML. Main Outcome Measures: Major molecular response (MMR) rates, treatment discontinuation, grade ≥3 adverse events. Results: Ten studies met inclusion criteria. In heavily pretreated CML-CP, the ASCEMBL trial showed superior MMR at 96 weeks with asciminib versus bosutinib (37.6% vs 15.8%), along with lower discontinuation and toxicity rates. In newly diagnosed patients, the ASC4FIRST trial showedMMRof 67.7% vs 49.0% ($P < 0.001$) at 48 weeks with fewer severe adverse events compared with standard TKIs. For patients with the T315I mutation, asciminib 200 mg twice a day achieved nearly 49%MMRat 2 years, with higher rates in ponatinib-naive patients. A 4-year phase 1 update confirmed durable molecular responses and low vascular toxicity in those with ≥2 prior TKIs. Real-world data supported these findings. Grade ≥3 adverse events were uncommon and primarily included asymptomatic lipase elevation, cardiovascular events, and

thrombocytopenia. Conclusions: Asciminib achieves robust molecular responses and exhibits a favorable safety profile across diverse CML-CP populations. Its utility spans frontline use and resistant/mutated settings, supporting its integration into clinical practice. Ongoing trials are evaluating treatment sequencing and treatment-free remission strategies.

Internal Medicine
Aijaz A, Bibi A, Zaman U, Ashraf A, Bar J, Tanwir H, Rost M, Smith H, Machaalani M, Darwin A, So ACP, Kankaria RA, Von Eckstaedt HV, Baena J, Kataria N, Spagnolo F, Sobocki B, **Raslan S**, Pannu S, and Naqash AR. Non-infectious sarcoid-like inflammatory granulomatous conditions (NSIGC) associated with immune checkpoint inhibitors (ICIs) for cancer: Results from the International ICARUS (Immune Checkpoint Associated Rare and Unique Side effects) consortium. *J Clin Oncol* 2025;43(16). Full Text

A. Aijaz

Background: ICIs can be associated with a broad range of toxicities; however, limited data exists on NSIGC secondary to ICIs. Herein, we assembled the first international cohort of patients (pts) with cancer who received ICIs and subsequently developed NSIGC. Methods: We retrospectively collected data from 14 institutions globally on pts with cancer who received ICIs between 2015- 2025 and subsequently developed biopsy-confirmed NSIGC. Pts were eligible if they received anti-programmed cell death protein-1/programmed death-ligand 1 (anti-PD-1/PD-L1) alone or in combination with additional anti-cancer therapies such as chemotherapy, targeted agents or anti-CTLA-4, or if they were treated with other immunotherapies. The chi-squared goodness of fit test was used to analyze the distribution of different ICI regimens and their association with NSIGC, assuming a uniform distribution with an expected frequency of 25 for each of the 5 ICI regimens. Results: The study included 125 pts with biopsy-confirmed NSIGC post-ICI. Of these, 58.4% (n = 73) were male and 83.2% (n = 104) were Caucasians. Median age at cancer diagnosis was 62 years. The top three cancers in the cohort were melanoma (45.6%; n = 57) non-small cell lung cancer (16.8%; n = 21) and renal cell carcinoma (6.4%; n = 8). Out of 125 pts, 48.8% (n = 61) received anti-PD-1/PD-L1 monotherapy, 20% (n = 25) anti-PD-1/PD-L1 + anti-CTLA-4, 17.6% (n = 22) anti-PD-1/PD-L1 + chemotherapy, 8% (n = 10) anti-PD-1/PD-L1 + targeted agents, and 5.6% (n = 7) received other immunotherapies. Our result showed a significant difference between expected and observed NSIGC frequencies across different ICI regimens ($X2 = 74.2$, $df = 4$, $p < 0.01$) indicating a potential association between anti-PD-1/PD-L1 monotherapy and NSIGC. The median time to the diagnosis of NSIGC after ICI initiation was 7.1 months (range: 3.9-26.7 months). Of 125 pts, 55.2% (n = 69) were diagnosed after treatment completion. Among these 69 pts, 56.5% (n = 39) were diagnosed within 6 months, 14.5% (n = 10) between 6 months and 1 year, 10.1% (n = 7) between 1 and 2 years, and 18.8% (n = 13) were diagnosed after 2 years. The remaining 44.8% (n = 56) were diagnosed during treatment, out of which 48.2% (n = 27) required permanent treatment discontinuation due to NSIGC and 3.6% (n = 2) were re-challenged. 19.2% (n = 24) received steroid treatment for NSIGC. Conclusions: To our knowledge, this is the largest dataset to date demonstrating NSIGC as a rare side effect of ICIs. NSIGC frequently occurs after ICI therapy completion but can also result in ICI discontinuation. Biopsy confirmation is critical to prevent misdiagnosis, and further research is required to elucidate the biology, risk factors, and implications for ICI continuation or rechallenge to optimize patient outcomes.

Internal Medicine
Alberto M, Naveed F, Awan AR, Nadeem MA, Kakakhel MZJ, **Ismail M**, Chaudhary M, Raja AR, Ahmad A, Arshad MU, Ashfaq F, and Sohail A. Temporal and regional mortality trends due to pulmonary embolism in female patients with genital cancers in the United States from 1999 to 2020. *J Clin Oncol* 2025;43(16). Full Text

M. Alberto

Background: The involvement of pulmonary vessels by tumor emboli has been described from different primary sites of malignancy. Pulmonary embolism (PE) is a severe and potentially fatal complication in patients with female genital cancers, including ovarian, cervical, uterine, and vulvar malignancies. These cancers, along with associated treatments such as major abdominal surgery, chemotherapy, and hormone therapy, significantly increase the risk of venous thromboembolism (VTE), including PE. While

previous studies detail the advancements in cancer detection and treatment, temporal and regional trends of PE-related mortality among female genital cancer patients remain poorly characterized. Methods: This retrospective study analyzes national mortality data from the CDC WONDER database to assess mortality trends from 1999 to 2020 across different demographic subgroups in the United States. Patients with a known history of genital cancer were identified and PE related mortality data was retrieved. Age-adjusted mortality rates (AAMRs) per 100,000 individuals were calculated further stratified based on sex, age (15-64 years and.64 years), race and census region. Rstudio was used to perform t-test and Mann Kendall test. Results: From 1999 to 2020, a total of 13,692 deaths were reported in female genital cancer associated pulmonary embolism in the US (AAPC: 0.421 (95% CI: 0.414-0.428)). The AAMR has risen from 0.363 in 1999 to 0.590 in 2020, indicating a worsening trend over the study period (t: 0.680, p,0.001). AAMR varied greatly by region, with the Northeast having the highest AAMR (9.928). This was followed by the West (0.488), Midwest (0.43) and South (0.366). Black females had consistently higher AAMR than white females, with rates of 0.763 vs. 0.329 in 1999 and 0.976 vs. 0.523 in 2020, respectively. Females older than 65 years demonstrated a much higher total AAMR (1.506) compared to females between the ages of 15 and 65 (0.212) (p,0.001). Within the age group of 15-25 years, black females had higher AAMRs compared to white female (p,0.001). Black females of the age group .65 years demonstrated much higher mortality (total AAMR: 2.745) than white females of the same age group (1.419), and the highest AAMR overall (P,0.001). Conclusions: The analysis of AAMR for female genital cancer associated pulmonary embolism highlights a concerning disparity in this dangerous cancer related complication, particularly after 2015. This underscores the need for greater attention to be directed towards reproductive health and cancer related complications faced by black women and to address systematic inequalities in intervention and healthcare access. This can improve early detection and timely interventions in order to reduce mortality and improve outcomes for these patients.

Internal Medicine

Alomari A, Althunibat I, **Saleem A**, **Abusuliman M**, **Omari Y**, **Jomaa D**, **Dababneh Y**, and **Jafri S**.
Management of Patients with Vascular Reconstruction during Liver Transplantation. *Am J Transplant* 2025;25(8):S455. Full Text

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Purpose: Liver transplantation occasionally requires vascular reconstruction, such as arterial jump grafts or portal vein thrombectomy, to ensure adequate blood flow. Aspirin (ASA) and anticoagulation (AC) therapies are used to reduce thrombotic risk but may increase bleeding. Limited data exist on their impact in this context. This study evaluates the effect of ASA/AC use on survival, thrombotic events, bleeding, and retransplant rates, aiming to optimize care for this high-risk group. Methods: We performed a retrospective chart review of 400 patients who underwent liver transplant between 2019 and 2023. 66 patients received an arterial jump graft, a portal vein thrombectomy, or both. Demographic factors (age, gender, race), ASA/AC prescription at discharge, MELD scores at transplant, and clinical outcomes, including 1-year survival, ischemia/clots, bleeding events, and retransplant or death, were collected. Patients were stratified by ASA/AC prescription. Descriptive analysis was performed to identify trends in outcomes. Results: The study analyzed a cohort of 66 post-transplant patients with a median age of 62 years (range: 58-72). The majority were male (62%, n=41) and White (85%, n=56), with smaller proportions of Black (4%, n=3) and other racial backgrounds (11%, n=7). MELD scores at the time of transplant were higher in patients not on ASA/AC (median: 30, range: 23-40) compared to ASA/AC users (median: 24, range: 15-39). ASA/AC was prescribed at discharge to 87.87% of patients, while 12.12% did not receive ASA/AC. Clinical outcomes differed between groups: the 1-year survival rate was 96.5% in ASA/AC users compared to 75% in non-users. The incidence of ischemia/clots was comparable (27.6% vs. 25%), while bleeding events were more frequent in ASA/AC users (17.2% vs. 0%). Retransplant rates were 1.72% in ASA/AC users versus 12.5% in non-users. Among patients with clots, 16.7% experienced graft loss, with death occurring in 5.5% and retransplantation in 11.1% of these patients. In contrast,

patients without clots had a 4.3% graft loss (death) rate and 0% retransplantation. Conclusions: ASA/AC use post-transplant is associated with improved 1-year survival rates, lower retransplant and death rates, and minimal impact on ischemia/clot incidence. Among patients with clots, graft loss, death, and retransplantation rates were notably higher than in patients without clots. These findings suggest ASA/AC may confer protective benefits in the post-transplant population, warranting further research to optimize its role in this context. CITATION INFORMATION: Alomari A., Althunibat I., Saleem A., Abusuliman M., Omari Y., Jomaa D., Dababneh Y., Jafri S. Management of Patients with Vascular Reconstruction during Liver Transplantation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES:

Internal Medicine

Alomari A, **Saleem A**, Althunibat I, **Abusuliman M**, **Dababneh Y**, **Jomaa D**, Abdulraheem A, **Mo J**, **Chen K**, and **Jafri S**. Association of Mean Arterial Pressure (MAP) with Mortality in Patients with Liver Cirrhosis Awaiting Transplantation. *Am J Transplant* 2025;25(8):S477. Full Text

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Purpose: Patients with liver cirrhosis listed for liver transplantation often experience hemodynamic changes, including changes in mean arterial pressure (MAP). Identifying the prognostic impact of MAP on mortality in this population may guide clinical decision-making. This study evaluates the association between MAP and mortality in patients listed for liver transplant. Methods: We conducted a retrospective cohort study of adult patients with liver cirrhosis listed for liver transplantation at a quaternary care center. To ensure comparability, only patients with a Model for End-Stage Liver Disease (MELD) score of 20-24 at the time of listing were included, while those with hepatocellular carcinoma (HCC) were excluded. Data collected included demographic information, mean arterial pressure (MAP) at listing, and clinical factors such as the use of antihypertensive medications, beta-blockers, and midodrine, as well as complications like hepatorenal syndrome (HRS), hepatic encephalopathy (HE), ascites, and variceal bleeding. We used logistic regression models to analyze the relationship between MAP and mortality on the waiting list, adjusting for medications and complications to isolate the independent effect of MAP. Additionally, a two-sample t-test was performed to compare the mean MAP between patients who died and those who survived Results: A total of 103 patients were analyzed. Higher MAP was significantly associated with lower odds of mortality on the waiting list (OR = 0.94, 95% CI: 0.89-0.99, p = 0.041). Each unit increase in MAP was associated with a 6% reduction in mortality risk. The mean MAP was significantly lower in patients who died (76.9 mmHg) compared to those who survived (83.2 mmHg) (p = 0.043). Additionally, higher MAP was associated with a decreased risk of HRS (OR = 0.94, 95% CI: 0.89-0.98, p = 0.011), but no significant associations were found between MAP and HE (OR = 0.97, 95% CI: 0.93-1.02, p = 0.247), ascites (OR = 1.00, 95% CI: 0.95-1.05, p = 0.847), or variceal bleeding (OR = 1.02, 95% CI: 0.95-1.09, p = 0.567). Conclusions: Lower MAP at the time of listing is an independent predictor of mortality in cirrhotic patients awaiting liver transplantation. The association remains robust after controlling for disease severity (MELD score), medications, and common complications. Additionally, low MAP was associated with a higher risk of developing HRS but not with HE, ascites, or variceal bleeding. These findings highlight the potential importance of hemodynamic optimization in this population. CITATION INFORMATION: Alomari A., Saleem A., Althunibat I., Abusuliman M., Dababneh Y., Jomaa D., Abdulraheem A., Mo J., Chen K., Jafri S. Association of Mean Arterial Pressure (MAP) with Mortality in Patients with Liver Cirrhosis Awaiting Transplantation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES:

Internal Medicine

Anamika F, Chitkara A, **Bai S**, Vojjala N, Soni U, Adib A, and Patel R. Advancing pain and symptom management in cancer: A data-driven analysis of care delivery, psychosocial support, and communication strategies. *J Clin Oncol* 2025;43(16). Full Text

F. Anamika

Background: Effective pain and symptom management is critical in cancer care, yet gaps exist in addressing psychosocial needs and communication strategies. Non-pharmacological interventions, psychosocial support, and innovative care models have shown promise, but comprehensive, data-driven analysis is lacking, especially regarding underrepresented demographics. Methods: A systematic analysis was conducted using data from ClinicalTrials.gov and PubMed to identify studies published from 2020 to 2025 focused on pain management, psychosocial support, and communication strategies in cancer care. Outcomes analyzed include pain severity, emotional well-being, adherence, and patient satisfaction. The study also examined demographic representation, with a focus on age and ethnicity. Results: From 180 relevant studies, 40% incorporated non-pharmacological interventions (e.g., CBT, mindfulness). Psychosocial support (peer support, therapy) appeared in 30%, and 25% explored communication strategies (decision-making, symptom communication). Key findings include: Non-pharmacological interventions reduced pain severity by 35% ($p < 0.01$) and improved emotional well-being by 30% ($p<0.05$). Psychosocial support reduced perceived stress by40% ($p < 0.001$) and depressive symptoms by 25% ($p < 0.05$). Innovative care models, particularly telehealth, improved adherence by 50% ($p < 0.001$) and patient-care team communication by 45%($p<0.01$). Demographic analysis revealed underrepresentation: only 15% of trials included participants over 65 years, and 20% focused on racial/ethnic minorities. Conclusions: Psychosocial support, communication strategies, and non-pharmacological interventions enhance pain management and emotional well-being in cancer patients. Innovative care models like telehealth improve adherence and communication. However, underrepresentation of older adults and minorities in research limits the generalizability of these findings. Future research should prioritize inclusive recruitment strategies, explore the synergistic effects of combined interventions, and evaluate long-term outcomes to ensure equitable and effective care for all cancer patients.

Internal Medicine

Chitkara A, Anamika FNU, Vojjala N, **Bai S**, Soni U, and Patel R. CT-1272: Bridging to Allogeneic Hematopoietic Cell Transplantation Following CD19-Directed CAR-T Therapy in Relapsed/Refractory Large B-Cell Lymphoma: A Systematic Review of Outcomes and Prognostic Indicators. *Clin Lymphoma Myeloma Leuk* 2025;25:S1054. Full Text

Anti-CD19 chimeric antigen receptor T-cell (CAR-T) therapies have reshaped the therapeutic paradigm for relapsed/refractory large B-cell lymphoma (R/R LBCL). Yet, real-world durability remains limited, with up to 60% of patients progressing within 1 year. Allogeneic hematopoietic cell transplantation (allo-HCT) is increasingly considered as consolidative or salvage therapy, though its role after CAR-T therapy remains ill-defined. Objective: To systematically evaluate published outcomes of allo-HCT following CAR-T therapy in R/R LBCL and identify clinical or biological predictors of benefit. Design: A systematic review was conducted according to PRISMA guidelines. PubMed, Embase, and ClinicalTrials.gov were searched for studies published from 2017 to 2025. Inclusion criteria encompassed prospective or retrospective series reporting outcomes of adult patients with R/R LBCL undergoing allo-HCT following CAR-T therapy. Data on overall survival (OS), progression-free survival (PFS), nonrelapse mortality (NRM), and graft-vs-host disease (GVHD) were extracted. Setting and Patients: Seven studies comprising 142 patients were included. Median age ranged from 48 to 61 years. Most received axicabtagene ciloleucel or tisagenlecleucel. The interval between CAR-T infusion and allo-HCT ranged from 50 to 120 days. Approximately 60% to 75% of patients underwent transplant in complete response (CR), while others proceeded with partial response or stable disease. Intervention: Allo-HCT following CAR-T, using reduced-intensity or myeloablative conditioning. Donor sources included matched unrelated (44%–58%), matched sibling (18%–33%), and haploidentical (up to 15%) donors. GVHD prophylaxis regimens varied, with the most common post-transplant regimens based on cyclophosphamide and tacrolimus. Main Outcome Measures: Across studies, 1-year OS ranged from 36% to 59%, with PFS ranging from 30% to 45%. NRM ranged from 17% to 22%. Acute GVHD grade ≥2 occurred in 28% to 36%, and chronic GVHD in up to 40%. Durable remissions were predominantly observed in patients bridged in CR with minimal disease burden and fewer than two intervening salvage lines after CAR-T therapy. Conclusions: Allo-HCT remains a feasible and potentially curative option in select patients following CD19-directed CAR-T therapy failure. Optimal candidates are those with early response and minimal disease pre-HCT. The

heterogeneity of conditioning intensity, donor selection, and timing limits direct comparability. Prospective biomarker-guided trials are warranted to define transplant eligibility and improve sequencing after CAR-T therapy in R/R LBCL.

Internal Medicine
Dad A, Iftikhar A, **Tareen H**, Arham M, Zubair A, Khan MS, Khan SA, Bakht K, Nazir T, Jehangir H, Azeem M, and Ahmed H. AML-617: Longitudinal Trends (1999–2023) and Forecasted Mortality (2024–2050) in AML-Associated Sepsis Among US Older Adults. *Clin Lymphoma Myeloma Leuk* 2025;25:S444-S445. Full Text

Sepsis remains a major complication in acute myeloid leukemia (AML), conferring a 4-fold increased risk in adult patients with AML compared with adult patients without AML. Objective: This study analyzes sepsis-related mortality trends in US adults aged ≥65 years with AML (1999–2023), highlights socioeconomic disparities, and projects mean age-adjusted mortality rates (AAMR) through 2050 to guide targeted public health efforts. Methods: We conducted a retrospective analysis of CDC WONDER mortality data (1999–2023) using ICD-10 codes A41 (sepsis) and C92.0 (AML) from the Multiple Cause of Mortality dataset. We standardized AAMR to the 2000 U.S. population and calculated per million. We assessed trends using Joinpoint regression to estimate annual percentage change (APC) with a 95% confidence interval (CI). Future AAMR projections through 2050 were estimated using Holt's linear exponential smoothing model in R. Results: From 1999 to 2023, AML-associated sepsis resulted in 16,060 deaths in the US. The AAMR increased from 11.8 per million (95% CI, 10.7–12.9) in 1999 to 17.1 per million (95% CI, 16.0–18.2) in 2019, with an APC of 1.19% ($P < 0.000001$). Men exhibited higher mortality rates than did women, with AAMR of 20.52 per million (95% CI, 19.9–20.5) compared with 10.06 per million (95% CI, 9.7–10.1). Non-Hispanic White patients exhibited the highest change in APC of 1.2778% (95% CI, 0.9302–1.6778; $P < 0.00001$) from 1999 to 2023. The Northeast region had the highest AAMR at 20.3 per million (95% CI, 17.4–23.2) in 2018. Moreover, rural areas showed a rise in mortality rates, from 6.5 per million (95% CI, 4–10) to 16.1 per million (95% CI, 12.8–19). Arkansas had the highest AAMR among all states. Forecasting data indicate AAMR will increase to 20.53 per million (95% CI, 18.84–22.22) by 2050. Conclusion: This study highlights the growing burden of AML-associated sepsis mortality among older adults in the US. The disproportionate effect on men, non-Hispanic White patients, and residents of the Northeast and Arkansas—along with projections of continued overall increases in mortality—underscores the need for prevention strategies, improved access to care, and tailored public health interventions. Grant/Funding Acknowledgements: None.

Internal Medicine
Dad A, **Tareen H**, Arham M, Khan SA, Zubair A, Khan MS, Altaf MT, Jehangir H, Bakht K, Saleem F, and Ahmed H. AML-608: Acute Myeloid Leukemia-Associated Pneumonia Mortality Trends (1999–2023) and ARIMA-Based Projections Through 2050 in Geriatric US Adults. *Clin Lymphoma Myeloma Leuk* 2025;25:S443-S444. Full Text

Pneumonia is a prevalent and serious complication in acute myeloid leukemia (AML), affecting more than 25% of treated patients and substantially contributing to adverse clinical outcomes. The hypothesis posits that AML-associated pneumonia mortality demonstrates significant socioeconomic and regional disparities across the US population. Objective: To examine mortality trends in AML-associated pneumonia among US adults aged ≥65 years from 1999–2023 and project rates through 2050, focusing on socioeconomic disparities. Methods: Mortality data from the CDC WONDER Multiple Cause of Mortality dataset (1999–2023) were analyzed using ICD-10 codes for pneumonia (18) and AML (C92). Age-adjusted mortality rates (AAMR) per million were standardized to the 2000 US population. Joinpoint regression estimated annual percent change (APC) with 95% CI, using a significance threshold of $P < 0.05$. Trends were forecasted using an autoregressive integrated moving average (ARIMA) model after augmented Dickey–Fuller (ADF)-based stationarity testing. Results: A total of 12,447 AML-associated pneumonia deaths were recorded. AAMR rose to 13.7 per million (95% CI, 12.7–14.7) in 2020. The ARIMA model, with Akaike information criterion (AIC) of 33.41 and root mean square deviation (RMSE) of 1.05, projected AAMR of 11.6 in 2030 (95% CI, 8.73–14.47), 2040 (95% CI, 7.13–16.07), and 2050 (95% CI, 5.97–17.23). Males consistently exhibited higher AAMR, reaching 16.15 in 2050 (95% CI, 14.87–17.43), compared with females at 7.9 (95% CI, −0.69–16.49). Historically, males exhibited higher AAMR

(19.9; 95% CI, 18.1–21.7) than did females (9.6; 95% CI, 8.5–10.7). A significant increase was noted among non-Hispanic Whites (APC = 0.57%; 95% CI, 0.27–0.91; P < 0.001). The Western region reported the highest AAMR, maintaining 12.9 per million from 1999 to 2023. Large central metro areas peaked at 14.9 per million (95% CI, 12.9–17.0) in 2020. California had the highest state-level AAMR at 14.5 (95% CI, 13.7–15.2). Conclusion: Mortality from AML-associated pneumonia increased from 1999 to 2023, peaking post-COVID. Significant disparities were observed among males, non-Hispanic Whites, residents of the West, large metropolitan areas, and California, indicating the necessity for targeted interventions in response to projected rising trends. Grant/Funding Acknowledgements: None.

Internal Medicine
Deluca C, Stapp J, Kriz C, Massey J, **Loss T**, **Kafri Z**, Beyer M, Marshall J, Ying Y, Treisman J, and Ali Z. Fusing quality improvement and education frameworks to reduce delays in tumor genotyping at community cancer centers. *J Clin Oncol* 2025;43(16). Full Text

C. Deluca

Background: Delays in obtaining tumor genotyping results hinder the ability of communitybased oncologists to develop timely and effective treatment plans for patients with metastatic colorectal cancers (mCRC).Based on these identified challenges, a quality improvement educational intervention was developed to improve genotyping workflows and enhance clinicians' ability to incorporate timely biomarker testing results into treatment planning for patients with mCRC. Methods: Educational workshops were conducted at five US community cancer centers to address delays in tumor genotyping and their impact on treatment planning. These workshops aimed to enhance clinician knowledge and practice strategies for molecular testing protocols and treatment planning. Physician champions at each center facilitated learner engagement, encouraged multidisciplinary collaboration, and promoted institutional change by driving discussions tailored to their centers' specific challenges and baseline performance metrics. To date, pre- and post-intervention data have been collected from a mix of tumor board captured-metrics and case data compiled in spreadsheets. Baseline and follow-up analyses of patient cases (pre N = 96, post N = 62) evaluated changes in molecular testing rates enabling insights into the effectiveness of the intervention. Results: 90 clinicians participated in the educational workshops, collection of case data is ongoing. Results collected thus far show an overall average reduction of 20.6 days for tumor genotyping results being ready (51.7 days pre vs 31.1 days post). Physician champions report increased consistency in ordering molecular profiling earlier after the education. However, unresolved challenges remain, including insufficient tissue sampling that delay genotyping results as well as the initiation of chemotherapy while awaiting results, which may limit the immediate use of targeted therapies. Conclusions: Cases collected to date suggest that targeted educational workshops addressing genotyping delays formCRCat community cancer centers can drive measurable improvements in molecular testing workflows and reduce time to results. These changes highlight the potential of such interventions to enhance treatment planning timelines in order to optimize therapeutic decision-making. However, persistent barriers limiting further reductions in treatment initiation time underscore the need for continued efforts to address systemic challenges.

Internal Medicine
Di Federico A, Wang K, Chen MF, Barsouk A, Pagliaro A, Chen LN, Ogliari F, Stockhammer P, Thawani R, **Raslan S**, Gariazzo E, Fusco F, Hambelton G, Citarella F, Meyer D, Corassa M, Langer CJ, Offin M, Negrao MV, and Ricciuti B. First-line immunotherapy with or without chemotherapy versus BRAF plus MEK inhibitors for patients with BRAFV600E-mutated metastatic non-small cell lung cancer: The FRONT-BRAF study. *J Clin Oncol* 2025;43(16). Full Text

A. Di Federico

Background: Patients (pts) with BRAFV600E mutated non-small cell lung cancer (NSCLC) can be effectively treated with BRAF and MEK inhibitors (BRAFi+MEKi) or with immune checkpoint inhibitors ± chemotherapy (ICI±CT). Which one should be prioritized as initial systemic treatment in this population remains unclear. Methods: Clinicopathologic data were collected from pts with metastatic BRAFV600E mutated NSCLC treated with 1st line ICI6CT or BRAFi+MEKi between 2015 and 2024 at 17 centers

across the United States, Europe, and Brazil. Results: Of 284 patients, 88 received ICI6CT and 196 received BRAFi+MEKi. Compared to pts treated with BRAFi+MEKi, pts receiving ICI6CT were more likely to have a history of smoking (83% vs. 61%, P<0.001) and a higher median PD-L1 tumor proportion score (TPS) (68% vs 30%, P<0.001). ICI6CT, compared to BRAFi+MEKi, was associated with a lower objective response rate (ORR, 49% vs 63%, P=0.03), similar median progression-free survival [mPFS, 9.6 vs.12.2 months (mo.), HR 1.13, P=0.43], but significantly improved median overall survival (mOS, 40.9 vs 25.1 mo., HR 0.69, P=0.039), even after adjusting in a multivariable model (HR 0.66, P=0.02). Consistent results were observed in a propensity score-matched cohort (1:1 ratio, N=75 pts per treatment group), where ICI6CT, compared to BRAFi+MEKi, was associated with improved mOS (40.9 vs 22.7 mo., HR 0.63, P=0.04), but similar ORR and mPFS. In key subgroup analyses, ICI6CT, compared to BRAFi+MEKi, was associated with longer mOS in pts with a history of tobacco smoking (HR 0.60, P=0.01), PD-L1 TPS ≥1% (HR 0.66, P=0.039), and without brain metastases (HR 0.66, P=0.045). A shorter mPFS was noted in pts without tobacco smoking history (HR 1.94, P=0.03). In evaluating genomic correlates of treatment efficacy, pts with TP53 co-mutations (N=107) had worse outcomes compared to pts with wild-type TP53 (N=121) when treated with BRAFi+MEKi, including shorter mPFS (HR 1.67, P=0.01) andmOS(HR 1.77, P=0.01), but not with ICI6CT. Notably, pts with TP53 co-mutations had longer mOS with ICI6CT compared to BRAFi+MEKi (48.4 vs 18.8 mo., HR 0.46, P=0.005). In contrast, pts with IDH1 co-mutations (N=9) had worse outcomes compared to pts with wild-type IDH1(N=188) when treated with ICI6CT, including shorter mPFS (HR 4.04, P=0.03) and mOS (HR 6.12, P=0.007), as well as shorter mPFS with BRAFi+MEKi (HR 2.73, P=0.03). Safety of BRAFi+MEKi was comparable whether administered as 1st line or as 2nd line therapy following ICI±CT, with similar rates of adverse events of any grade (71% vs 76%, P=0.58) and grade ≥3 (22% vs 23%, P=0.92). Conclusions: Initial therapy with ICI±CT, compared to BRAFi+MEKi, showed a lower ORR, similar PFS, but superior OS, particularly among specific subgroups of pts. A prospective evaluation of the optimal 1st-line therapy for this population is warranted.

Internal Medicine

Dunn W, Alkhouri N, Yip TCF, Castera L, Takawy M, Adams L, Verma N, Arab JP, **Jafri SM**, Zhong B, Dubourg J, Chen V, Singal AK, Diaz LA, Dunn N, Nadeem R, Wong VWS, Abdelmalek MF, Wang Z, Duseja AK, Almahanna Y, Bajunayd A, **Omeish HA**, Ye J, Harrison SA, Wong GLH, Arrese M, Robert S, and Shao C. Enhancing prediction of moderate fibrosis in MASLD patients for Resmetirom treatment via machine learning. *J Hepatol* 2024;80:S84. Full Text

Background and aims: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) affects approximately 30% of the global adult population and poses significant risks of disease progression particularly in patients with moderate to advanced fibrosis (stages 2–3). Following the FDA's approval of Resmetirom for treating Metabolic Dysfunction-Associated Steatohepatitis (MASH) in these stages, there is a need for a surrogate marker to refine the selection of patients for liver biopsy. The ALADDIN study introduces a novel machine learning-based web calculator to estimate the probability of stage ≥2 fibrosis in MASLD using routine laboratory parameters, with and without Vibration Controlled Transient Elastography (VCTE). Method: A total of 3708 patients with biopsy-confirmed MASLD from six centers worldwide were divided into Derivation and Internal Validation cohorts on a 1:1 basis, supplemented by 1289 patients from nine centers for External Validation. ALADDIN models, employing Random Forest, Gradient Boosting Machines, and XGBoost enhanced by Bayesian updates, were developed to evaluate moderate fibrosis (stage ≥F2). Results: The VCTE model achieved an Area Under the Curve (AUC) of 0.800 (95% CI 0.773–0.827) in external validation, significantly outperforming the FAST (AUC: 0.707, 95% CI 0.674–0.739, p < 0.0001) and Agile-3 (AUC: 0.764, 95% CI 0.735–0.793, p = 0.001) models. The model using routine laboratory parameters without VCTE reached an AUC of 0.757 (95% CI 0.730–0.783), comparable to FASTand Agile-3. The VCTE model model also demonstrated superior decision curve analysis, calibration, and classification accuracy, using a dual cut-off approach, and outperformed existing models in predicting moderate fibrosis. Conclusion: The ALADDIN study, via an international consortium has successfully developed and externally validated machine learning models that predict moderate fibrosis with notable accuracy. Our VCTE model, available at https://aihepatology.shinyapps.io/ALADDIN1/, and our routine laboratory parameter model without VCTE, available at https://aihepatology.shinyapps.io/ALADDIN2/ demonstrate statistical superiority and comparable performance respectively, against traditional models including Agile-3 and FAST. These algorithms will facilitate targeted liver biopsy in line with the new FDA approval for Resmetirom treatment.

Internal Medicine

Faisal M, **Faisal M**, **Saleem A**, **Karmo B**, **Hasso M**, **Chaudhary A**, **Shahzil M**, **Jafri S**, and **Zuchelli T**. Strategies for Success in Endoscopic Retrograde Cholangiopancreatography (ERCP) Intervention in Liver Transplant Patients with Biliary Complications and Altered Intestinal Anatomy. *Am J Transplant* 2025;25(8):S464-S465. Full Text

Purpose: Surgically altered anatomy in patients who undergo Liver Transplant (LT) offers a unique challenge to endoscopists. There is limited data regarding the optimal endoscopic approach for the management of biliary complications in this population. We aim to assess the safety, efficacy and outcomes of various endoscopic approaches to managing patients with altered anatomy following LT. Methods: Retrospective data was collected after study approval from our IRB. Individuals who had a history of LT and surgically altered anatomy who subsequently underwent an ERCP from 2017-2024 were selected. Individual charts were reviewed to collect demographic and procedural data. Outcomes included post-procedure complications and technical success. Results: 61 patients were identified who had surgically altered anatomy with a history of LT. Of these, 13 underwent ERCP, for a total of 29 procedures. 24 ERCPs were done in patients with hepaticojejunostomy (HJ), and 5 in Roux-en-Y gastric bypass (RYGB). For patients with HJ, 6(25%) ERCPs were done within 6 months of LT, whereas 2(40%) were done in this timeframe for RYGB. Indications for both groups included jaundice(N=11, 38%), stent management(N=9, 31%), sepsis(N=6, 21%), and others. For the two patients who had RYGB, one had EDGE procedure with same day ERCP and three subsequent ERCPs through the gastrogastric fistula via the lumen apposing metal stent. The other patient had laparoscopy assisted ERCP. For patients with HJ anatomy, adult colonoscope was used in 15(26%) procedures, pediatric colonoscope for 4(17%) procedures, single balloon enteroscope for 4(17%) procedures and 1(4%) was done with a duodenoscope. Rigidizing overtube was used in 9(37.5%) of these procedures. Of these, 6(25%) were unsuccessful, with inability to reach HJ with colonoscope (N=3), excessive looping with single balloon enteroscope (N=1), and inability to locate HJ (N=2). Percutaneous Transhepatic Cholangiogram (PTC) drain placement was required in 3 of the unsuccessful procedures. Adverse events included esophageal mucosal breaks (N=2). Conclusions: We highlight the favorable success rate of endoscopic interventions in this population, with minimal adverse events. This suggest that ERCP can be a first step in managing biliary disease in post-LT patients with altered anatomy. Furthermore, successful interventions through ERCP can reduce the rate of PTC drain placement and the risk of infection related to PTC. Endoscopists should be aware of the various techniques and equipment available for technical success. Larger studies need to be done to establish guidelines for this indication. [Formula presented] CITATION INFORMATION: Faisal M., Faisal M., Saleem A., Karmo B., Hasso M., Chaudhary A., Shahzil M., Jafri S., Zuchelli T. Strategies for Success in Endoscopic Retrograde Cholangiopancreatography (ERCP) Intervention in Liver Transplant Patients with Biliary Complications and Altered Intestinal Anatomy AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Faisal: None.

Internal Medicine

Faisal M, **Garg N**, **Aburumman R**, **Saleem A**, Shahzil M, **Fatima M**, **Faisal M**, and **Jafri S**. Decreased Rate of Rejections Post Liver Transplant in Patients on a Glucagon-Like Peptide 1 (GLP-1) Analogue. *Am J Transplant* 2025;25(8):S487-S488. Full Text

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Purpose: Rejection is prevalent in patients undergoing liver transplant (LT), with studies showing a relation of Body Mass Index (BMI) to post transplant outcomes, including rates of rejection. Recently, Glucagon-like peptide-1(GLP-1) analogues are increasingly being used in post-transplant patients. We aimed to assess the association of semaglutide and tirzepatide with transplant rejection in patients with BMI > 30. Methods: Patients who underwent LTs at our institution were included from 1/2018-12/2023.

Inclusion criteria was BMI > 30. We did a retrospective cohort study to assess whether they received GLP-1 analogues, including semaglutide and tirzepatide, after the liver transplant. Data including patient demographics and comorbidities was collected. The primary outcome was transplant rejection at 1 and 2-3 years. The secondary outcome was 3-year mortality. Results: 137 patients were included who underwent liver transplant from 01/2018-12/2023 with a BMI > 30. Of these, 33(24.1%) were exposed to semaglutide or tirzepatide while 104 (75.9%) had no such exposure after transplant. The mean age of the population was 58.86 +/- 8.2 in the case group and 62.08 +/- 9.2 in the control group. 23 (69.7%) were male in the case group while 69 (66.3%) were male in the control group. Comorbidities, including HTN, stroke and ESRD were comparable in both groups. 27 (87.9%) in the case group had diabetes while 37(35.6%) in the control group had diabetes (p=0.001). Mean BMI for the case group was 36.34 ± 4.81 and mean BMI for the control group was 33.9 ± 3.82 (p=0.01). Underlying liver disease prior to transplant was similar between the 2 groups, with Metabolic Dysfunction-Associated Steatohepatitis (MASH) being the most prevalent. For outcomes, 2(6.1%) patients in the exposed group had rejection within 3 years, compared to 24(23.1%) in the control group (p=0.03). Of these, both the patients in the control group had rejection within 1 year compared to 20(19.4%) patients in the control group who had rejection within 1 year. At 3 years, there were 0 deaths in the case group compared to 4 (3.9%) deaths in the control group (P=1.0). Conclusions: In our cohort, the use of semaglutide and tirzepatide was associated with a decreased incidence of liver transplant rejections in patients with BMI > 30. We were limited by single center and smaller number of patients. Further large scale, multicenter studies are needed to confirm the efficacy of these medications, possibly suggesting a more significant role post liver transplant. [Formula presented] CITATION INFORMATION: Faisal M., Garg N., Aburumman R., Saleem A., Shahzil M., Fatima M., Faisal M., Jafri S. Decreased Rate of Rejections Post Liver Transplant in Patients on a Glucagon-Like Peptide 1 (GLP-1) Analogue AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Faisal: None.

Internal Medicine

Faisal M, **Saleem A**, **Fatima M**, **Chaudhary AJ**, **Shahzil M**, **Faisal M**, and **Jafri S**. Impact of Glucagon Like Peptide-1 (GLP-1) Analogue Medications on Liver Transplant Risk Factors. *Am J Transplant* 2025;25(8):S462. Full Text

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Purpose: Patients who undergo liver transplantation are at higher risk of complications from diabetes and obesity. Recently, GLP-1 analogues have revolutionized management of these conditions and are increasingly being used in post-transplant patients. However, the safety of these agents in this population, particularly their association with cancer risk, is controversial. We aimed to assess the association of semaglutide and tirzepatide with cancer in patients who undergo liver transplant. Methods: All patients who underwent liver transplant at our institution were included from 1/2018-12/2023. We did a retrospective cohort study to assess whether they received GLP-1 analogues, including semaglutide and tirzepatide, after the liver transplant. Primary outcome was development of malignancy. Secondary outcomes were 1-and 3-year mortality. Results: 366 patients were included who underwent liver transplant from 01/2018-12/2023. Of these, 42(13%) were exposed to semaglutide or tirzepatide while 324(88%) had no such exposure. The mean age of the population was 58.12 +/- 7.6 in the exposed group and 58.44 +/- 11.5 in the control group. Comorbidities, including HTN, stroke and ESRD were comparable in both groups. 37(88.1%) in the exposed group had diabetes while 111(34.2%) in the control group had diabetes(p<0.001). Similarly, 28(66.7%) patients in the exposed group had BMI>30 while 111(34.5%) patients in the control group had BMI>30(p<0.001). The follow up period was 3.74 +/-1.3 years for the exposed group and 4.01 +/-1.5 years in the control group. For outcomes, 2(4.8%) patients in the exposed group were diagnosed with cancer in the follow up period versus 26(8.1%) in the control group (p=0.76). There was no cancer related mortality at one year while at 3 years, it was similar in both groups. For malignancies, 1(50%) patient in the exposed group had HCC, while 5(18%) patients in the control group had either HCC or cholangiocarcinoma. No patients in the exposed group were diagnosed with skin

related malignancies including BCC, SCC and Malignant Melanoma, while 13(46%) patients in the control group were diagnosed with such malignancies. 1 patient in the exposed group was diagnosed with Post Transplant Lymphoproliferative Disorder. 11 patients in the control group were diagnosed with other malignancies including prostate cancer, lymphoma, follicular thyroid cancer, and leukemia. Conclusions: In our cohort, the use of GLP-1 analogues was not associated with cancer in patients who undergo liver transplantation. We were limited by single center and smaller number of patients. Further large scale, multicenter studies are needed to confirm the safety of these medications. [Formula presented] CITATION INFORMATION: Faisal M., Saleem A., Fatima M., Chaudhary A., Shahzil M., Faisal M., Jafri S. Impact of Glucagon Like Peptide-1 (GLP-1) Analogue Medications on Liver Transplant Risk Factors AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Faisal: None.

Internal Medicine

Gor D, **Rehman T**, **Pradeep A**, **Ghosh S**, and **Kuriakose P**. MM-259: Impact of the International Myeloma Working Group (IMWG) SLiM Criteria on Multiple Myeloma Management: A Tertiary Care Center Experience. *Clin Lymphoma Myeloma Leuk* 2025;25:S911. Full Text

Multiple myeloma (MM) is a hematologic malignancy characterized by the proliferation of plasma cells. IMWG's introduction of the SLiM criteria in 2014 expanded the diagnosis of MM. Our retrospective study evaluated the adoption and impact of these criteria at Henry Ford Cancer Institute (HFCI), focusing on patient demographics and outcomes of those diagnosed exclusively using the SLiM criteria. Methods: Electronic medical records at HFCI (January 2015–December 2023) were reviewed to identify MM patients meeting at least one SLiM criterion (≥60% plasma cells, free light chain (FLC) ratio >100, or MRI lesion), excluding those with CRAB features. Data on demographics, staging, treatment, and outcomes (through December 2024) were analyzed. Results: Between 2015 and 2023, 495MMpatients were diagnosed; 190 met at least one SLiM criterion. After excluding 177 with CRAB features, 13 patients remained who were diagnosed solely by SLiM criteria. Of these, 6 had plasma cells >60%, 11 had FLC ratio >100, and 3 met MRI criteria. The mean age was 63.6 years; 53.8% were female, 53.8% African American, and 38.4% Caucasian. High-risk cytogenetics were present in 53.8% patients. By Revised International Staging System (R-ISS) staging, 61.5% of patients had stage 1, 30.7% had stage 2, and 7.6% had stage 3 disease. Twelve patients received treatment with induction regimen, which included bortezomib, lenalidomide, dexamethasone (VRd) (n = 9), daratumumab-VRd (n = 1), carfilzomib, lenalidomide, dexamethasone (KRd) (n = 1), or bortezomib, dexamethasone (Vd) (n = 1), all starting treatment at diagnosis. Among them, there was one death (hospice, age/comorbidities), two relapses (both in remission after second-line therapy), and nine remained in remission. One patient, diagnosed in 2017, has not required treatment to date. Conclusion: Our study highlights real-world data on the impact of the IMWG SLiM criteria for MM diagnosis. Patients diagnosed solely based on SLiM criteria, who would previously have been classified as having smoldering myeloma, were treated at diagnosis, reflecting real-time adoption of the updated guidelines. This underscores the positive impact and practical applicability of the revised criteria. Interestingly, one untreated patient has not progressed, suggesting the need for appropriately powered randomized studies to better understand outcomes in this specific subset of patients.

Internal Medicine

Hicks PM, Dobson JN, Mitchell J, **Darnley-Fisch D**, Heisler M, Resnicow K, **Imami NR**, and Newman-Casey PA. Barriers and Facilitators of Glaucoma Medication Adherence by Patient and Neighborhood-level Factors in the Support, Educate, Empower Personalized Glaucoma Coaching Program Pilot Study. *Invest Ophthalmol Vis Sci* 2025;66(8). Full Text

P.M. Hicks, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, MI, United States

Purpose : To identify barriers and facilitators to glaucoma medication adherence for participants in the Support, Educate, Empower Personalized Glaucoma Coaching Program Pilot Study and assess any differences by age, sex, race, and Area Deprivation Index (ADI). Methods : This was a mixed-methods study of patients that reported glaucoma medication adherence of ≤80.00%. Patient (age, sex, and race) and neighborhood (ADI) factors were obtained, and patients completed an interview. To better understand the barriers and facilitators to glaucoma medication adherence, patient interviews were

transcribed and analyzed using the modified Penchansky and Thomas framework. This framework is instrumental in identifying and analyzing potential barriers to accessing healthcare services, and it helps in developing strategies to improve service delivery and patient outcomes. Results : Of the 44 patients, 52.27% were ≥65 years old, 45.45% female, 50% Black, and 34.09% lived in high ADI neighborhoods. Barriers and facilitators were reported across all domains except accommodation/adequacy. The most frequent barriers were patient-level factors (50%), and the most common facilitator were patient-level factors (45%). Difficulty with medication schedule was the top barrier for various demographics, including age groups, genders, races, and ADI levels. A daily routine around taking eye drops was the leading facilitator for 40-64-year-olds (19%). Location of eye drops was the leading facilitator for patients ≥65 years old (33%), females (25%), Black race (20%), White race (30%), low-ADI (36%) and mid-ADI (16%). Having an additional medication supply was the leading facilitator for males (25%) and social support for high-ADI (13%). Conclusions : Among glaucoma patients with poor adherence, difficulty with the medication schedule was the most frequent barrier to optimal adherence among all patients regardless of age, race, or ADI score, while having a daily routine around taking eye drops was reported as the most common facilitator to optimal medication adherence among patients of all ages and races, women, and those who lived in low and medium ADI areas. The issue of providing support to integrate glaucoma medication taking into the daily routine is a highly salient issue to address in coaching for glaucoma disease selfmanagement.

Internal Medicine
Ismail M, **Chopra N**, Ahmad H, Kakakhel MZJ, Arshad MU, Qadri M, **Klein J**, Iftikhar Y, Jawad H, Afridi MS, and **Barawi M**. Cardiovascular disease and gastrointestinal cancers: Mortality trends and persistent disparities in the U.S. *J Clin Oncol* 2025;43(16). Full Text

M. Ismail

Background: Cardiovascular disease (CVD) is a significant contributor to mortality among patients with gastrointestinal tract (GIT) cancers. This study analyses changes in age-adjusted mortality rates (AAMRs) for CVD in GIT cancer patients in the U.S. from 1999 to 2020, focusing on demographic and geographic disparities. Methods: CVD-related deaths in GIT cancer patients aged ≥25 years were examined using CDC WONDER data. AAMRs per 100,000 individuals were calculated, and trends were assessed via annual percentage changes (APCs) and average annual percentage changes (AAPCs). Results: Between 1999 and 2020, 921,107 CVD deaths occurred among GIT cancer patients. The overall AAMRdecreased from 230.0 in 1999 to 190.7 in 2020, with an AAPC of -0.97∗ (p< 0.000001). Men had higher AAMRs (255.3) than women (144.4), though women experienced a greater decline (AAPC: -1.44∗, p< 0.000001) compared to men (AAPC: -0.88∗, p< 0.000001). Black individuals exhibited the highest AAMR (273.03), followed by Hispanics (199.3), Asians/Pacific Islanders (190.0), American Indians (182.75), and Whites (180.87). Asians/Pacific Islanders showed the steepest decline (AAPC: -2.56∗, p< 0.000001). Geographically, New York had the highest AAMR (318.73), while Utah recorded the lowest (98.05). Nonmetropolitan areas showed higher AAMRs than metropolitan areas but smaller declines (AAPC: -0.15∗, p = 0.003 vs. -1.13∗, p<0.000001). Conclusions: Despite overall declines in CVD mortality among GIT cancer patients, significant disparities persist by gender, race, and geography. Targeted interventions are needed to address these inequalities and further reduce the burden of CVD among this vulnerable population.

Internal Medicine
Ismail M, **Sardarova N**, Kakakhel MZJ, Singh P, Zaied MA, Ahmad H, Alsaadi MH, Ikram M, Riffat G, and **Barawi M**. From liver to life: The overlooked impact of MASLD on digestive cancer outcomes. *J Clin Oncol* 2025;43(16). Full Text

M. Ismail

Background: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is an increasing public health concern with the potential to increase the development of malignancy of the digestive tract and beyond. We aim to explore mortality trends of digestive cancer (DC) among MASLD patients. Methods: The CDC WONDER database was examined to extract age-adjusted mortality rates (AAMR) regarding

DC among MASLD patients aged 25 years and older between 1999 and 2020. Data was stratified by age, gender, race, and U.S geographic regions. Results: 67616 deaths were documented from 1999 to 2020, with an overall AAPC of 2.8 (95% CI 1.99 to 3.62) and total AAMR of 13.6 (95%CI 13.5 to 13.7). Males showed higher mortality rates than females with an overall AAMR of 22.1 (95%CI 21.9 to 22.3). However, female gender showed higher AAPC with value of 3.6 (95%CI 2.88 to 4.32). Slight difference of AAPC between patients aged 55-64 and over 85 years as they showed the highest AAPC with value of 4.23 (95%CI 3.23 to 5.24) and 4.21 (95%CI 2.31 to 6.14) receptively. White race accounted for the highest AAPC followed by African American with 3.11 (95%CI 2.18 to 4.06) and 1.73 (95%CI 0.33 to 3.15) respectively. Conclusions: The highest AAPC was observed among Whites, older males, large central metropolitan residents and West residents. The observed disparities suggest the importance of improving outcomes for DC patients, particularly with MASLD. Keywords: Digestive cancer, MASLD, CDC WONDER, AAPC.

Internal Medicine
Kumar J, Garg A, **Khanna V**, Shakeel R, **Lavu VK**, Kancharla P, and **Kumar S**. A comprehensive five-year analysis of gastric cancer mortality disparities in the midwest region (2018-2023): Trends, factors, and implication. *J Clin Oncol* 2025;43(16). Full Text

J. Kumar

Background: Gastric cancer is a major public health issue, contributing to morbidity and mortality. In the U.S., disparities in gastric cancer mortality exist based on age, gender, race, ethnicity, and socioeconomic status. Despite a decline in overall mortality, some groups still face elevated risks. This study explores gastric cancer mortality trends in the Midwest (2018-2023). Methods: This retrospective study analyzed adults aged 25+ using CDC WONDER (2018-2023) and ICD-10 code C16. Mortality data were stratified by age, gender, race, and Hispanic status. Crude and age-adjusted mortality rates (AAMRs) per 100,000 were calculated, with 95% confidence intervals (CIs). Temporal trends and annual percentage changes (APCs) were assessed using Joinpoint regression. Results: A total of 12,047 deaths occurred in the Midwest, with an AAMR of 2.31 (APC -1.77, CI -2.78 to -0.76, $p < 0.001$) and a crude rate of 2.93 (CI: 2.88-2.98). Mortality increased with age, peaking at 85+ years (AAMR 21.48; crude 21.49), followed by 75-84 (AAMR 14.71; crude 14.75), 65-74 (7.77), 55-64 (4.34), 45-54 (2.05), 35-44 (0.77), and 25-34 (0.19). Males had a higher AAMR (3.13; APC -2.33, CI -4.43 to -0.30, $p = 0.025$) than females (1.66), with CR of 3.63 (CI: 3.55-3.71) vs. 2.24 (CI: 2.17-2.30). Black individuals had the highest crude (4.20, CI: 4.01-4.39) andAAMR (4.52), followed by Asians (3.17, CI: 2.88-3.46; AAMR 3.98) and Whites (2.83, CI: 2.77-2.88; AAMR 2.08). AI/AN crude was 1.91 (CI: 1.49-2.42), and multiracial, 0.65 (CI: 0.50-0.82). Hispanics had a higher AAMR (4.13; APC -4.71, CI -8.11 to -1.18, $p = 0.009$) than non-Hispanics (2.24; APC -1.66, CI -3.20 to -0.11, $p = 0.039$), although their CR (2.43, CI: 2.26-2.59) was lower than non-Hispanics (2.97, CI: 2.92-3.03). Conclusions: Mortality rates were highest among older adults, males, Black individuals, and Hispanics, reflecting ongoing disparities. Structural inequities, including socioeconomic barriers and limited healthcare access, significantly influence these trends. Addressing these requires better preventive care, addressing social determinants, and implementing culturally competent interventions. These findings highlight the need for equitable healthcare policies to reduce mortality and improve outcomes.

Internal Medicine
Makhkamov S, Aziz N, Nabi W, Khatun MK, Khan M, Rath S, Basharat A, Shahnawaz M, Bhat A, Chepkunov D, Chung D, Elsherif Y, Usama A, Mudassar M, Cheema A, **Tareen H**, Ahmad RU, Sahni S, and Fromer N. Prognostic significance of metaplasia in adenocarcinoma of the lung: A National Cancer Database analysis. *J Clin Oncol* 2025;43(16). Full Text

S. Makhkamov

Background: Pulmonary adenocarcinoma is a major subtype of non-small cell lung cancer (NSCLC), yet the impact of metaplasia within the tumor remains understudied. This study utilized the National Cancer Database (NCDB) to analyze the prognostic significance of metaplasia in pulmonary adenocarcinoma. Methods: Using the NCDB, we conducted a retrospective analysis on patients with lung adenocarcinoma

from 2010 to 2017 and followed STROBE guidelines. Kaplan-Meier survival analysis and Accelerated Failure Time (AFT) model were used for estimation of survival outcomes. Covariates included age, sex, race, tumor grade, TNM stage, Charlson Comorbidity Index, insurance status, year of diagnosis, facility type, and treatment modality. Statistically significant variables from AFT were subgroup analyzed with multivariate logistic regression to identify the relative representation of these variables in metaplastic and non-metaplastic arms. Results: A total of 16,330,918 patients were included, with 16,302,690 (99.83%) diagnosed with non-metaplastic adenocarcinoma (NMAC) and 28,228 (0.17%) with metaplastic adenocarcinoma (MAC). The unadjusted median overall survival (mOS) was significantly lower in MAC (12.25 months) compared to NMAC (24.48 months, $p < 0.05$). After covariate adjustment, MAC was associated with worse survival (HR 1.2, 95% CI: 1.12-1.28, $p<0.01$). Logistic multivariate regression analysis identified significant predictors of MAC. Grade 4 tumors had the highest odds (OR: 103.10; 95% CI: 51.45-206.61; $p<0.01$), followed by grade 3 tumors (OR: 20.05; 95% CI: 10.68-37.61; $p<0.01$). Patients with M1b stage disease (OR: 1.31;95%CI: 1.13-1.52; $p<0.01$) and those with a Charlson-Deyo Score of 1 (OR: 1.18; 95% CI: 1.03-1.35; $p<0.05$) were also more likely to have MAC. In contrast, female patients (OR: 0.79;95%CI: 0.70-0.90; $p<0.01$)TNMN3 stage patients (OR: 0.77;95%CI: 0.62-0.95; $p<0.05$) were less likely to have metaplastic adenocarcinoma. Conclusions: Metaplastic adenocarcinoma was associated with significantly worse outcomes compared to non-metaplastic adenocarcinoma. High grade, advanced M1b stage, and burden of comorbidities partially explains these poor outcomes, however, further studies are needed to explore and delineate the underlying mechanisms driving the worse outcomes seen by metaplasia in pulmonary adenocarcinoma.

Internal Medicine

Malick A, **Tepe G**, **Nagai S**, **Muszkat Y**, **Beltran N**, **Pietrowsky T**, and **Jafri S**. Outcomes of Intestinal Biopsies Which Are Indeterminate for Rejection Following Intestine Transplant. *Am J Transplant* 2025;25(8):S839-S840. Full Text

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Purpose: We evaluated the impact of “indeterminate for rejection” (IFR) biopsy results and subsequent clinical outcomes. We aim to evaluate whether changes in immunosuppressive medications and cytomegalovirus (CMV) status at the time of IFR biopsy influence the likelihood of a subsequent biopsy also being classified as IFR or showing a definitive rejection outcome. Methods: Retrospective analysis of adult patients who underwent intestinal transplantation, including those who received multi-organ transplants with intestine with at least one biopsy classified as IFR. Data collected includes immunosuppressive changes, subsequent biopsy results, and infection status. Results: We evaluated 31 patients with long term follow-up following IFR biopsy. 17 (55%) were female. Mean age at time of transplant was 48 years (22-68). 18 (57.9%) patients had intestine transplant only, 13 had multiorgan transplant. There were 84 recorded instances of IFR biopsy results. 54 instances (64%) led to immunosuppression changes, while 30 (36%) did not. 4% of patients in the immunosuppression change group (ICG) and 7% in the no-change group (NCG) had positive CMV PCR at the time of biopsy. In ICG, 69% of cases were negative for rejection on follow-up biopsy. In NCG, 60% were negative for rejection on follow-up biopsy. Persistent indeterminate classification was observed in 9.3% of ICG cases and 20% of NCG. Mild rejection occurred in 20% of ICG cases and 17% of NCG cases. Moderate rejection was seen in 1.9% of ICG cases and 0% of NCG cases. Severe rejection was seen in 0% of ICG cases and 3.3% of NCG cases. There were no statistically significant differences between the two groups (Odds Ratio [OR] = 1.27, 95% Confidence Interval [CI]: 0.47-3.38, $p = 0.6$). A secondary analysis focused on only the first instance of an IFR biopsy for each patient. 71% of these cases were ICG. 77% of these ICG cases showed subsequent results negative for rejection. 44% of NCG cases showed negative subsequent results for rejection. Persistent IFR occurred in 4.5% of ICG cases and 22% of NCG. Mild rejection occurred in 14% of ICG cases and 22% of NCG. Moderate rejection occurred in 4.5% of ICG and 0% of NCG. Severe rejection occurred in 0% of ICG and 11% of NCG. Conclusions: While medication adjustments were frequently implemented following IFR biopsy, their effect on subsequent biopsy results was not statistically significant. The majority of patients who underwent immunosuppression changes had negative subsequent biopsy outcomes, similar to those without immunosuppression changes. The study

highlights the complexity of managing IFR biopsy results in transplant recipients and underscores the need for further research to better understand the appropriate response to IFR biopsy. CITATION INFORMATION: Malick A., Tepe G., Nagai S., Muszkat Y., Beltran N., Pietrowsky T., Jafri S. Outcomes of Intestinal Biopsies Which Are Indeterminate for Rejection Following Intestine Transplant AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Malick: None.

Internal Medicine
Modi S, Bhimineni C, Kaur H, Mahadevia H, Shah A, **Ethakota J**, **Bai S**, Leighton JC, Morginstin M, and Dourado C. Incidence and survival trends in early-onset colorectal cancer. *J Clin Oncol* 2025;43(16). Full Text

S. Modi

Background: Early-onset colorectal cancer (EOCRC) is colorectal cancer that occurs in people under the age of 50 and represents an emerging public health concern with increasing incidence rates worldwide. The incidence of colorectal cancer in young adults has been rising globally over the past two decades. This study analyzes demographic patterns, risk factors, and survival trends in a cohort of 413 EOCRC patients. Methods: This study retrospectively analyzed 413 patients diagnosed with EOCRC from TriNetX database. Clinical data included disease stage, treatment modalities, and survival outcomes, with an event rate of 40% and a median followup time of approximately 26 months. Age-stratified survival analysis revealed distinct patterns across the three age groups examined. Statistical analyses were conducted using Kaplan-Meier methods for survival outcomes and multivariable Cox proportional hazards models to identify prognostic factors. All analyses complied with ethical guidelines and institutional review board requirements. Results: An analysis of 413 patients with early-onset colorectal cancer (EOCRC, ages 21-50, mean: 44 years, SD: 5) revealed distinct age-dependent patterns in incidence, molecular features, and survival. The cohort showed a male predominance (60.29%). HER2 testing was the most common molecular assessment (76%, with 75% undergoing ISH dual probe ratio testing), while KRAS mutation and hormone receptor/PDGFRA analyses were conducted in 4% and 2%, respectively. Testing rates were highest in the youngest (<35 years) and oldest (43-50 years) cohorts, suggesting potential age-specific molecular phenotypes. Survival analysis revealed an age-related gradient: younger patients (<35 years) had the highest survival rate (64.65%), followed by 57.58% in the middle age group (35-42 years) and 54.31% in the older group (43-50 years). A critical two-year post-diagnosis period showed an initial decline in survival, followed by stabilization. These findings highlight an age-dependent survival advantage in younger EOCRC patients, despite the aggressive nature of the disease. Conclusions: Key learning points include the age-dependent survival advantage observed in younger patients, the importance of comprehensive molecular profiling for personalized treatment, and identifying a critical two-year post-diagnosis period for intervention and monitoring. Future research should focus on elucidating the underlying biological mechanisms driving EOCRC in younger populations, developing targeted prevention strategies, and optimizing treatment protocols to improve long-term outcomes. Additionally, large-scale, multicenter studies are needed to validate these findings and explore the role of emerging therapies in this unique patient population.

Internal Medicine
Nabaty R, **Muszkat Y**, **Nagai S**, **Beltran N**, **Pietrowsky T**, and **Jafri S**. Intestinal Transplantation for Short Bowel Syndrome from Gun Shot Wounds: A Case Series. *Am J Transplant* 2025;25(8):S843-S844. Full Text

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Purpose: Short bowel syndrome (SBS) is a malabsorption disorder leading to nutritional deficiencies and high morbidity. Gunshot wounds (GSWs) and other abdominal traumas are known causes of SBS. Intestinal transplantation offers a unique therapeutic option for this patient population; however, outcomes are not well elucidated. We present two cases of patients who developed SBS secondary to GSWs,

underwent intestinal transplantation, and subsequently required transplant enterectomy. Methods: We evaluated patients with SBS due to GSW receiving an intestinal transplant at a single center for outcomes including rejection, infection, graft survival, and patient survival. Results: Two males sustained GSWs necessitating small bowel and colon resection, leading to SBS that became dependent on parenteral nutrition with multiple line-related complications. Both patients underwent isolated small bowel transplantation. Patient 1: A 21-year-old underwent transplant with post operative course remaining largely unremarkable for 102 months until he presented with abdominal pain and found to be in cellular and humoral rejection. He developed septic shock due to bacteremia and adenovirus enteritis and did not respond to medical management, necessitating eventual transplant enterectomy. Afterwards, he was managed with parenteral nutrition, however clinical course was complicated by multiple infections and opioid misuse. Patient ultimately expired 12 months post-transplant enterectomy. Patient 2: A 37-year-old underwent transplant and remained hospitalized for 41 days afterwards. Three weeks post-transplant he was noted to have cellular and humoral rejection requiring plasmapheresis and immunoglobulin. Approximately 12 months post-transplant, he presented with septic shock and multiorgan failure. Endoscopy revealed ulcerated and friable mucosa, leading to transplant enterectomy. Despite surgical intervention, his clinical status deteriorated, and he expired shortly thereafter. Conclusions: Patients undergoing intestinal transplantation for SBS secondary to GSW represent a unique and understudied population. These cases highlight the significant risks of rejection, transplant enterectomy, and morbidity. Despite these risks, outcomes are robust as illustrated with the first patient who had many years of normal bowel function, post-transplant. Further research is warranted to optimize management strategies and improve survival rates for this vulnerable population as advancements in transplantation continue. CITATION INFORMATION: Nabaty R., Muszkat Y., Nagai S., Beltran N., Pietrowsky T., Jafri S. Intestinal Transplantation for Short Bowel Syndrome from Gun Shot Wounds: A Case Series AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: R. Nabaty: None.

Internal Medicine

Ntukidem OL, Ogedegbe OJ, Olafimihan AG, **Bai S**, Gupta R, Mackenzie S, Lanka M, and Jackson I. Updated trends in second primary malignancy in patients with renal cell carcinoma: A retrospective population-based analysis. *J Clin Oncol* 2025;43(16). Full Text

O.L. Ntukidem

Background: Survival outcomes for patients with renal cell carcinoma (RCC) have improved in recent years. However, the risk of developing second primary malignancy (SPM) in RCC survivors remains underexplored. SPM pose significant challenges in cancer survivors, impacting long-term morbidity and mortality. Therefore, we aim to evaluate and discuss incidence and risk of SPM in RCC patients using a large population-based dataset. Methods: We analyzed the Surveillance, Epidemiology, and End Results (SEER) database, comparing secondary cancer rates among RCC cases diagnosed from 2000 to 2021. The histologic code for RCC in the SEER database is 8312/3. A second primary malignancy was defined as a malignancy developing at least six months after the initial RCC diagnosis. We used the SEER Multiple Primary Standardized Incidence Ratios (MP-SIR) session to obtain the p-value, observed/expected (O/E) ratios, absolute excess risk (AER) per 10,000. Results: 43,477 Renal Cell Carcinoma cases from 2000- 2021 met our inclusion criteria and were included in our study. Of these cases, 5,931 (13.6%) developed second primary malignancies. The mean age of SPM was 70.45 years. The risk of developing SPM was significantly higher than the general population, with an O/E ratio of 1.27 (CI 1.23-1.30, AER 42.67, $p < 0.05$). Most common SPM included Brain (O/E ratio 1.33 CI 1.02- 1.72, $p < 0.05$), Pancreas (O/E ratio 1.18 CI 1.01-1.36, $p < 0.05$), Liver (O/E ratio 1.67 CI 1.4-1.97, $p < 0.05$), Lung (O/E ratio 1.27 CI 1.18-1.36, $p < 0.05$), Prostate (O/E ratio 1.16 CI 1.09-1.23, $p < 0.05$, Thyroid (O/E ratio 2.7 CI 2.29-3.17, p,0.05), Multiple Myeloma (O/E ratio 1.42 CI 1.17-1.71, $p < 0.05$), AML (O/E ratio 1.6 CI 1.23-2.03, $p < 0.05$), CML (O/E ratio 1.77 CI 1.2-2.51, $p < 0.05$). Conclusions: Compared to the general population, there is a statistically significant increased risk of secondary primary malignancies in RCC patients. These findings highlight the importance of ongoing surveillance, risk stratification, and tailored follow-up strategies to improve early detection and intervention for SPM in RCC survivors.

Internal Medicine

Ntukidem OL, Ogedegbe OJ, Olafimihan AG, **Bai S**, Gupta R, Mackenzie S, Lanka M, Jackson I, and Winegarden JD. Sociodemographic disparities in survival outcomes among adolescent and young adult patients with pancreatic cancer: Insights from a SEER database analysis. *J Clin Oncol* 2025;43(16). Full Text

O.L. Ntukidem

Background: Pancreatic cancer in adolescent and young adult (AYA) patients is rare and understudied. Disparities in survival outcomes based on demographic and clinical factors in this population remain poorly understood. This study evaluates survival outcomes and their association with race, gender, stage at diagnosis, and geographic region within a cohort of AYA pancreatic cancer patients. Methods: A retrospective cohort of 2,260 AYA patients (ages 18-39) diagnosed with pancreatic cancer was analyzed. Survival outcomes were assessed using Kaplan-Meier survival analysis and Cox proportional hazards regression to examine the effects of race (American Indian, Asian, Black, White), gender, stage at diagnosis (localized, regional, distant), and geographic region (metropolitan vs. nonmetropolitan). Hazard ratios (HR) with 95% confidence intervals (CI) were calculated to evaluate the impact of these variables on survival, statistical significance was set at P , .05. The median follow-up time was 60 months. Results: The study population comprised of 1,218 females (53.9%) and 1,042 males (46.1%), with a racial distribution of 1,665 White (73.7%), 305 Black (13.5%), 601 Asian (11.8%), and 24 American Indian (1.0%) patients. Males had a higher risk of death compared to females (HR = 1.45;95%CI: 1.28-1.64; p,0.001). Patients in metropolitan areas (n = 2059) had longer median survival (60 months) compared to nonmetropolitan regions (n = 201, median survival = 24 months; p = 0.003). Those with metastatic disease had significantly poorer survival (HR: 17.86; 95% CI: 13.70-23.26, p < .001) compared to patients with localized disease. Racial differences in survival were modest (p = 0.014), with Asian patients showing the highest mean survival (38.4 months) and American Indian patients the lowest (29.9 months). Conclusions: This study demonstrates significant survival disparities among AYA pancreatic cancer patients, with outcomes influenced by stage at diagnosis, gender, race, and geographic region. The findings highlight the importance for targeted interventions to improve outcomes for at-risk groups, including male patients, those with late-stage disease, and individuals in nonmetropolitan regions.

Internal Medicine

Ogedegbe OJ, Ntukidem OL, Becerra H, Olafimihan AG, Nwachukwu CE, Gold-Olufadi S, Shrestha N, Saparov D, Cheema AY, **Bai S**, Ali H, Bajwa S, Ojo T, Winegarden JD, and Gupta R. Obesity paradox in non-small cell lung cancer (NSCLC) patients on immune checkpoint inhibitors: Real-world evidence using the global collaborative network database. *J Clin Oncol* 2025;43(16). Full Text

O.J. Ogedegbe

Background: Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for about 85% of all cases. Immune checkpoint inhibitors (ICIs) have recently transformed the landscape of cancer management. Recent studies suggest that obesity may improve survival outcomes in some cancer types; however, there remains a dearth of data on the effect of obesity in cancer patients on ICIs. We aim to analyse and evaluate this relationship. Methods: This retrospective cohort population-based real-world study was obtained by querying the TriNetX Global Collaborative Network database. We identified patients with NSCLC who received ICI. The ICIs included pembrolizumab, nivolumab, cemiplimab, iplimumab, atezolizumab, durvalumab and avelumab. The patient population was divided into two cohorts: patients with a BMI between 18.5-29.9kg/m2 and 30.0-39.9kg/m2. Racial and demographic information was obtained. Propensity score matching was carried out to remove confounders. Patients were matched for medical comorbidities, including tobacco use, emphysema, asthma, Type 2 diabetes mellitus and bronchiectasis. Survival analysis was conducted using Kaplan-Meier and log-rank test. The primary outcome was survival (OS) for 1 and 5 years. The secondary outcomes were complications of NSCLC, which included hemoptysis, malignant pleural effusion, SVC syndrome, dysphagia, and complications of ICI therapy, including hepatitis, colitis, thyroiditis, pneumonitis and rash. Results: Before propensity score matching (PSM), significant demographic and comorbid disparities existed between the obesity BMI group (N = 6,854) and the normal BMI group (N = 1,546). After PSM, both cohorts exhibited

strong similarities, with 1,545 patients in both cohorts. Mean age (69 years vs 64.7 years), male (56.6% vs 58.04%), white (55.75% vs 52.34%). The obesity BMI was associated with an improved OS at 1 year (hazard ratio [HR] 0.753 [95% CI, 0.671-0.844], p = 0.0295) and at 5 years (HR 0.687 [95% CI, 0.625-0.754], p = 0.0233) in patients treated with ICIs. Obesity BMI was also associated with a reduction in NSCLC complications, including dysphagia (odds ratio [OR] 0.711 [95% CI, 0.543-0.931], p = 0.013), SVC syndrome (OR 0.457 [95% CI, 0.230-0.909], p = 0.002). However, the differences in rates of other complications, including hemolysis and malignant pleural effusion, were insignificant. There was also no difference in the rates of immune-related adverse events (IRAEs) between both patient populations. Conclusions: Our retrospective population-based study found that obesity was associated with improved 1-year and 5-year OS compared to normal BMI. In addition, obesity was associated with reduced rates of complications such as dysphagia and SVC syndrome. It is pertinent to research these findings further to provide more holistic care for patients.

Internal Medicine
Olafimihan AG, Jackson I, Ntukidem OL, Ogedegbe OJ, George LJ, **Bai S**, Oh Y, Gold-Olufadi S, and Mullane MR. Trends and disparities in palliative care utilization in advanced head and neck cancer hospitalizations. *J Clin Oncol* 2025;43(16). Full Text

A.G. Olafimihan

Background: Greater than 60% of Head and neck cancer (HNC) patients have advanced cancer at the time of presentation. They have unique physical and psychological symptoms due to the cancer's anatomical location and multimodal treatment-related toxicities. Early integration of palliative care (PC) in their management can improve health-related quality of life. We examined the trends and predictors of PC utilization among hospitalized advanced HNC patients in the US. Methods: A retrospective longitudinal study was conducted using the NIS database (2008-2021). Using joinpoint regression and multivariable logistic regression, trends and factors associated with PC receipt were assessed. Results: The overall prevalence of palliative care utilization among 326,265 hospitalizations with advanced HNC was 11%. Over the period, palliative care utilizations increased from 3,651 to 16,982 per 100,000 advancedHNC admissions (p-trend,0.001) with an average annual percentage increase of 9.7%. Females with metastaticHNChad higher odds (Adjusted odds ratio (AOR): 1.11;95%CI: 1.04-1.19) of receiving palliative care compared to males. There was similar likelihood of utilizing palliative care across racial groups. Patients in teaching hospitals had 46% higher likelihood (AOR: 1.46; 95% CI: 1.33-1.60) of palliative care use in comparison to patients in non-teaching hospitals. Large hospitals had higher palliative care use compared to small hospitals (AOR: 1.12; 95% CI: 1.01- 1.25). Admissions in the south and west had higher likelihood of palliative care use relative to those in the North-east region. Patients covered by Medicaid had higher odds of palliative care receipt compared to those covered by Medicare. Relative to patients whohad a routine discharge home or with self-care, those discharged to facilities or with home health care were four-fold more likely (AOR: 4.35; 95% CI: 3.98-4.75) to receive palliative care. Those who died during hospitalization were also more likely to use palliative care (AOR: 21.4; 95% CI: 19.1-24.0). Nonelective admissions had higher likelihood of palliative care receipt relative to elective visits. Conclusions: Although palliative care utilization has improved over the years, it remains suboptimal. Tailored interventions addressing sociodemographic and hospital-level disparities will promote equitable access and meet the unique needs of this patient population.

Internal Medicine
Patel DM, Dharia A, Peshin S, Chaudhari J, Vojjala N, **Bai S**, Ser-Manukyan H, Kang G, Slade C, Patel S, and Muddassir S. Disparities in survival among younger breast cancer patients: A SEER database analysis (2000-2021). *J Clin Oncol* 2025;43(16):e13834-e13834. Full Text

D.M. Patel

Background: Breast cancer is a leading cause of cancer-related mortality, with survival influenced by stage at diagnosis. Early detection improves prognosis, yet ethnic and socioeconomic disparities persist, particularly among patients under 65. This study evaluates survival disparities stratified by stage, focusing on the impact of age, race, and income to inform targeted interventions and health policy reforms.

Methods: This retrospective cohort study analyzed 862,290 breast cancer cases in patients aged 20-65 years from the SEER database (2000-2021). Cases were stratified by stage (localized, regional, distant), and survival outcomes were assessed using Kaplan-Meier analysis for median survival and 5-year overall survival (OS). Log-rank tests evaluated subgroup differences. Multivariate Cox proportional hazards models assessed impact of age, race, and income. Disparities were identified by Stagestratified analyses. Results: The 5-year OS was 94.8% for localized, 85.1% for regional, and 34.6% for distant-stage disease ($p < 0.001$). Non-Hispanic (NH) Black patients had the worst distant-stage 5-year OS (23.0%), compared to NH White (37.5%) and NH Asian (39.6%) ($p < 0.001$). Among distant-stage patients, those aged,35 years had the highest 5-year OS (40.1%), and 50-64 years old had the lowest (31.2%). Also, lower-income patients (< $50,000) had the lowest 5-year OS (28.8%), while those earning .≥100,000 had the highest (38.4%) ($p<0.001$). Cox regression models demonstrated significant survival disparities across all stages. Black patients had higher mortality risk (HR: 1.40-1.54, $p < 0.001$). Older patients (50-64 years) had worse survival compared to younger (HR: 1.14-1.40, $p < 0.001$). Lower-income patients (, ≥50,000) faced worse survival (HR: 1.09-1.24, $p < 0.001$). Stage-stratified analysis confirmed that these disparities were most pronounced in distant-stage disease, in Black and lowerincome individuals. Conclusions: Racial and socioeconomic disparities persist in breast cancer survival among younger patients, particularly in advanced-stage disease. Black patients and lower-income individuals consistently face the worst outcomes. Expanding insurance coverage, improving access to early detection, increasing financial support for underserved populations, and ensuring equitable access to novel therapies are essential to reducing disparities. Systemic policy reforms and targeted interventions are needed to improve survival outcomes equitably.

Internal Medicine

Peshin S, Dharia A, Vojjala N, Cheema AY, Chaudhari J, Mahadevia H, Lal BM, **Bai S**, and Moka N. NSCLC in the immunotherapy era: Trends in survival and disparities across demographic and socioeconomic groups. *J Clin Oncol* 2025;43(16). Full Text

S. Peshin

Background: Advanced non-small cell lung cancer (NSCLC) has historically been associated with poor survival outcomes. The introduction of immune checkpoint inhibitors in 2015 revolutionized treatment by improving survival, yet access to these therapies remains inequitable. This study examines survival trends in NSCLC before and after 2015, focusing on racial and socioeconomic disparities in the immunotherapy era. Methods: This population-based study utilized SEER registry 22 to evaluate survival disparities in NSCLC cases diagnosed between 2004 and 2020. Patients were stratified by stage (regional and distant), age, race, income, and sex. Survival outcomes, including median survival (MS) and five-year overall survival (5-Year OS), were compared using Kaplan-Meier analysis and log-rank tests to assess disparities across demographic and socioeconomic subgroups. Results: Among 591,525 NSCLC cases were included, with 355,283 diagnosed pre-2015 and 236,242 post-2015. MS improved from 11 months pre-2015 to 13 months post-2015 ($p < 0.001$). Five-year overall survival increased from 16.8% pre-2015 to 19.6% post-2015, reflecting advancements in care over time. Racial disparities persisted across both periods. Non-Hispanic Black patients had the lowest survival rates, with five-year overall survival improving from 21.4% pre-2015 to 24.5% post-2015 in localized stages, compared to 25.7% and 29.2% for Non-Hispanic White patients. Among patients with distant-stage disease, survival improved marginally from 6.7% pre-2015 to 7.9% post-2015 for non-Hispanic Black patients, lagging behind non-Hispanic White patients, whose survival increased from 8.6% to 10.3%.Socioeconomic disparities were also evident. Patients earning less than ≥50,000 experienced a five-year overall survival increase from 28.2% pre-2015 to 30.4% post-2015 in regional stages, compared to 35.4% to 38.9% for those earning above ≥100,000. However, in distant stages, survival gains for low-income patients were less pronounced, rising only from 4.5% pre-2015 to 5.2% post-2015, compared to 7.8% to 9.3% for higher-income patients. Younger patients (<35 years) had consistently better outcomes across all stages and periods, with a five-year overall survival of 40.3% pre-2015 and 43.7% post-2015 in distant stages. Conversely, patients aged 50-64 years experienced the lowest survival gains, emphasizing the need for targeted interventions in this group. These findings underscore persistent disparities in NSCLC survival by race and income, despite overall improvements in outcomes over time. Conclusions: While survival improved modestly for NSCLC patients post-2015, significant disparities persist based on stage, race,

income, and age. Non-Hispanic Black patients and lower-income individuals face the greatest challenges, underscoring the need for targeted interventions to address these inequities.

Internal Medicine
Rajarajan S, Babu K, Bhanushali C, Jayakumar J, Shah RN, Maryam B, Dhamija K, Dileo R, Khan E, Chattaraj A, Ramesh N, **Ramanan S**, and Correa A. Impact of graft-versus-host disease on mortality, length of stay, and hospitalization costs in bone marrow transplant patients: A retrospective analysis using the 2021 NIS database. *J Clin Oncol* 2025;43(16). Full Text

S. Rajarajan

Background: Graft-versus-host disease (GVHD) is a significant complication of bone marrow transplantation (BMT), influencing patient outcomes, length of stay (LOS), and hospitalization costs. This study evaluates the prevalence of GVHD in hospitalized BMT patients and its impact on outcomes using the 2021 National Inpatient Sample (NIS) database. Methods: We conducted a retrospective analysis of the NIS 2021 dataset. Patients who underwent BMT and patient's who developed GVHD were identified using the appropriate ICD-10 codes. Survey-weighted descriptive statistics were used to analyze patient demographics, mortality rates, LOS, and total hospitalization charges (TOTCHG). Multivariable logistic and linear regression models evaluated GVHD's impact on outcomes, adjusting for age, sex, race, income quartiles, Charlson comorbidity index (CCI), hospital region, teaching status, and bed size. The top principal diagnoses were ranked by weighted counts. Results: A total of 20,165 weighted BMT hospitalizations were analyzed, of which 10.9% (95% CI: 9.8%-12.1%) were associated with GVHD. GVHD patients had a significantly higher mortality rate compared to non-GVHD patients (6.4% vs. 4.5%, p=0.04), longer LOS (10.7 vs. 7.2 days, p,0.001) and GVHDpatients had significantly higher mean hospitalization charges (≥235,485 vs. ≥113,706). Adjusted regression showedGVHDwas associated with a50%higher odds of mortality (aOR: 1.50,95%CI: 1.03-2.31, p=0.031), 3.3 additional hospitalization days (95% CI: 1.70-4.87, p,0.001), and ≥112,376 higher total charges (95% CI: ≥54,212-≥170,539, p,0.001). Significant adjusted predictors of mortality included age (OR = 1.01, p = 0.009) and Charlson Comorbidity Index (OR = 1.47, p < 0.001). Length of stay was significantly influenced by CCI (0.51 days, p = 0.022), and teaching hospital status (1.76 days, p < 0.001). Hospital charges were significantly higher with CCI (≥13,646.94, p = 0.023), and at teaching hospitals (≥45,054.57, p < 0.001). The most common primary diagnoses among BMT patients with GVHD included septicemia (650 cases), pneumonia (202 cases), acute kidney failure (320 patients) and COVID-19 (130 cases). Conclusions: GVHD significantly exacerbates the clinical and economic burden of BMT, leading to increased mortality, LOS, and healthcare costs. Age, Charlson Comorbidity Index, and teaching hospital status were also significant predictors of mortality, length of stay, and hospital charges. The most common primary diagnoses among GVHD patients included septicemia, pneumonia, acute kidney failure, and COVID-19, underscoring the complexity and resource-intensive care required for this population. These findings emphasize the need to focus on early detection strategies and innovative treatment modalities to mitigate the impact ofGVHDinBMTpatients.

Internal Medicine
Rajarajan S, Babu K, Maryam B, Shah RN, Jayakumar J, Bhanushali C, Dileo R, Dhamija K, Khan E, **Ramanan S**, Ramesh N, Chattaraj A, and Correa A. The paradoxical impact of depression on mortality, length of stay, and hospitalization charges in patients with prostate and bladder cancer: Using the 2021 NIS database. *J Clin Oncol* 2025;43(16). Full Text

S. Rajarajan

Background: Depression is a prevalent comorbidity in patients with cancer, potentially influencing treatment outcomes. This study evaluates the association of depression with mortality, length of stay (LOS), and hospitalisation charges (TOTCHG) among patients with prostate cancer and bladder cancer. Methods: We conducted a retrospective analysis of the NIS 2021 database. Hospitalised patients with prostate cancer, bladder cancer and depression were identified using the appropriate ICD-10 codes. Survey-weighted descriptive statistics were utilized to analyze patient demographics, mortality rates, LOS, and TOTCHG. Multivariable logistic and linear regression models evaluated the impact of depression on

outcomes, adjusting for age, sex, race, income quartiles, Charlson comorbidity index, hospital region, teaching status, and bed size. Results: In this study, 182,280 hospitalised prostate cancer patients and 40,855 hospitalised bladder cancer patients were analyzed. Among prostate cancer patients, 9.3% (16,785 patients) were depressed, with depressed individuals slightly younger (adjusted coefficient -0.42 years, p=0.036), predominantly White (76.2%, p,0.001), privately insured (76.1%, p,0.001), with higher comorbidity (85.9%, p,0.001), & in the Midwest region (25.9%, p,0.001). Among bladder cancer patients, 11.4% (4,645 patients) were depressed, with depression more common in younger individuals (adjusted coefficient -1.07 years, p=0.004), women (31.4%, p,0.001), White patients (86.9%, p,0.001), those with higher comorbidity (85.8%, p,0.001), Northeast (29.1%, p=0.019) and privately insured (63.2%). Depressed prostate cancer patients had lower mortality rates (3.75% vs. 4.67%, adjusted OR 0.76, p=0.004), shorter hospital stays (5.33 vs 6.13 days, adjusted - 0.72 days, p,0.001), & lower hospitalization charges (≥73,977 vs. ≥85,966, adjusted reduction -≥11,699, p,0.001). Depressed bladder cancer patients had lower mortality rates (6.45% vs. 9.53%, adjusted OR 0.63, p=0.001), slightly shorter hospital stays (7.25 vs. 7.66 days, adjusted - 0.42 days, p=0.032), and reduced hospitalization charges (≥92,321 vs. ≥104,156, adjusted reduction -≥10,327, p=0.023). Conclusions: This study reveals that depression was more prevalent in younger, White, privately insured patients with higher comorbidities. Interestingly, depressed patients in both cohorts had lower mortality rates, shorter hospital stays, and reduced hospitalisation charges despite their higher comorbidity burdens, suggesting potential differences in healthcare utilisation, disease management, or psychosocial factors. These findings underscore the importance of recognising and addressing depression, as it may not only affect patient quality of life but also play a significant role in shaping clinical and economic outcomes.

Internal Medicine

Rehman S, Garg N, **Rahman T**, **Abusuliman M**, **Saleem A**, and **Jafri S**. Everolimus Does Not Alter Non-Hepatic Malignancy Following Liver Transplant. *Am J Transplant* 2025;25(8):S709. Full Text

Purpose: Malignancy after solid organ transplant especially skin cancers is common phenomenon and remains a major etiology of post-transplant mortality. Some case reports and small single center studies highlight various antioncogenic effects of mammalian target of rapamycin (mTOR) inhibitor class of immunosuppressants especially everolimus. This study aims to assess the effect of everolimus on the incidence of post-transplant skin malignancy and outcomes among liver transplant recipients. Methods: A retrospective chart review of post liver transplant patients at a large tertiary center in the midwest who received a liver transplant between 1/2015-12/2019 was conducted. Patients were split into 3 groups: not on everolimus post-transplant (group 1), started on everolimus within 1 year of transplant and discontinued before 3 years (group 2) and on everolimus for at least 3 consecutive years post-transplant (group 3). Demographic data including age, gender and etiology of cirrhosis was collected with primary outcomes assessing incidence of skin cancer. Secondary outcomes included other malignancy, transplant rejection, and death. Linear regression model used to compare these groups (group 1 vs. 3 and 2 vs. 3). Results: Among 381 liver transplant recipients, 59 patients were started on everolimus within 1 year of transplant and discontinued before 3 years (15.4%, group 2) and 65 patients were on everolimus for 3 consecutive years (17.1%, group 3). 25 patients in group 1 (9.7%), 6 in group 2 (6.8%) and 6 (9.2%) developed some skin malignancy with squamous cell carcinoma the most common among all three groups. 26 patients in group 1 (10.1%), 6 in group 2 (6.8%) and 5 (7.7%) developed some other type of malignancy with hematologic (23%) most common in group 1 and GI (67%) in group 2 and 3 (80%). There was no significant difference in incidence of skin malignancy (group 1 vs 3, p = 0.835; group 2 vs 3, p =0.513) or other malignancy across the groups. Similarly no significant difference in death (group 1 vs 3, p = 0.502; group 2 vs 3, p =0.611) or transplant rejection (group 1 vs 3, p = 0.30; group 2 vs 3, p =0.066). Conclusions: Our data demonstrates everolimus did not have a protective effect against skin malignancy, other malignancy, rejection or death among liver transplant patients. Whether these findings were related to a small sample size or time frame is unclear. Further investigations are warranted with a larger sample size and over a longer period to evaluate the long term benefit this immunosuppressant may have. CITATION INFORMATION: Rehman S., Garg N., Rahman T., Abusuliman M., Saleem A., Jafri S. Everolimus Does Not Alter Non-Hepatic Malignancy Following Liver Transplant AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Abusuliman: None.

Internal Medicine

Roy DL, **Ismail M**, Kakakhel MZJ, **Rudy R**, Ahmad H, Rath S, Arshad F, Asghar T, Tahir MF, and Noor R. Obesity and cancer in america: From declining mortality to emerging challenges. *J Clin Oncol* 2025;43(16). Full Text

D.L. Roy

Background: Obesity is a global epidemic linked to various health issues, including cancer. This study investigates temporal trends in cancer burden among obese individuals in the U.S., emphasizing its long-term public health impact. Understanding these trends is crucial for informing effective public health strategies and resource allocation. Methods: Using the Multiple-Causes of Death database from the CDC WONDER, we retrospectively analyzed annual age-adjusted mortality rates (AAMR) per 100,000 population from 1999 to 2020 in cancer patients with obesity. Joinpoint v5.3 was utilized to assess average annual percent change (AAPC) and annual percent change (APC) across significant trends. Results: Between 1999 and 2020, 14,937,519 deaths were recorded among adults aged 25 and older due to obesity and cancer. The overall AAMR for cancer and obesity-related deaths decreased from 1999 to 2020 with an AAPC of -1.13 (95% CI: -1.27 to -1.06, p < 0.0001). The overall AAMR significantly declined from 1999 to 2018, followed by a non-significant increase until 2020 (APC:1.25, 95% CI: -0.63 to 1.97, p = 0.1332). Across ethnicities, AAMR rose from 2018 to 2020, with the steepest incline among the non-Hispanic (NH) American group or Alaskan native group (APC: 6.10; 95% CI: 0.27 to 10.20, p = 0.040), followed by Hispanics andNHBlack. Cancer and obesity death rates were stable between all U.S. Census Regions. Midwest showed a decline from 1999 to 2018 (APC = -1.0; 95% CI: -1.4 to-0.7, p = 0.004) followed by a steep increase till 2020 (APC = 6.6; 95% CI: 1.3 to 9.4, p = 0.013). Similarly, for the West, a decline till 2018 (APC = -1.0; 95% CI: -1.2 to -1.0, p < 0.0001) followed by a steep increase to 268.5 in 2020 (APC = 5.4; 95% CI: 3.1 to 6.6, p < 0.0001) was recorded. States in the 90th percentile of Cancer and Obesity mortality included West Virginia, Kentucky, Mississippi, Oklahoma, and the District of Columbia, while those in the 10th percentile included Colorado, North Mexico, Arizona, Hawaii, and Utah. Conclusions: This study reveals a complex relationship between obesity and cancer mortality over time, highlighting disparities across demographics and regions. While AAMRs decreased until 2018, the subsequent increase warrants further investigation, especially in light of the COVID-19 pandemic. Further studies are needed to assess the cause-and-effect relationship between obesity and cancer, as well subgroup analysis regarding specific cancer types.

Internal Medicine

Roy DL, **Ismail M**, Kakakhel MZJ, Singh P, **Rudy R**, Ali MF, Noor R, Alsaadi MH, Ahmad H, and Jawad H. Genital cancer mortality in comorbid vs. non-comorbid populations: A nationwide trend analysis. *J Clin Oncol* 2025;43(16). Full Text

D.L. Roy

Background: Genital cancers (GCs) remain a critical public health issue, with comorbidities such as hypertension (HTN) and diabetes significantly impacting outcomes. This study investigates comparative mortality trends in GCs with and without comorbid HTN and diabetes in U.S. adults aged 35 years and older. Methods: Data from 1999-2022 was extracted from the CDC WONDERdatabase. Age-adjusted mortality rates (AAMR) and annual percentage changes (APC) were calculated using Joinpoint regression. Results: Between 1999 and 2022, 277,938 GC deaths occurred with comorbid HTN and diabetes compared to 1,817,017 without these comorbidities. AAMRs for GCs with comorbidities increased significantly from 39.23 in 1999 to 68.34 in 2022, while AAMRs for GCs without comorbidities declined from 424.63 to 319.56. Men consistently had higher AAMRs thanwomen in both groups (Men: 96.01 vs Women: 25.57 and Men: 513.59 vs Women: 264.00). NH Blacks had the highest average APC for GCs both with (7.12) and without (-0.94) comorbidities, though the burden of GCs-related mortality was significantly lower without comorbidities. Mortality rates were highest in the 85+ age group in both cohorts. Geographical analysis revealed the highest overall AAMR in the Midwest, with 53.77 for GCs with comorbidities and 352.6 for those without. Non-metropolitan areas accounted for 20.4% of deaths (AAMR: 43.82 to 75.45; APC: 2.37) in GCs with comorbidities, while metropolitan areas accounted for 79.6% (AAMR: 38.18 to 62.25; APC: 2.08), both demonstrating increasing mortality. For GCs without

comorbidities, non-metropolitan areas had 18.4% of deaths (AAMR: 444.8 to 346.76; APC: -1.36), and metropolitan areas had 81.6% (AAMR: 419.96 to 315.75; APC: -1.47), both showing a decline over time. Conclusions: Mortality trends for GCs with comorbid HTN and diabetes are rising, in stark contrast to declining trends for GCs without these comorbidities. Disparities by sex, race, age, and geography highlight the need for targeted interventions and equitable access to care, particularly for high-risk populations.

Internal Medicine
Rudy R, **Ismail M**, Kakakhel MZJ, Ahmad H, Singh P, Ikram M, Keen MA, Maryem F, and Zaied MA. Where you live and who you are: The unequal face of cancer and diabetes mortality in the United States. *J Clin Oncol* 2025;43(16). Full Text

R. Rudy

Background: Cancer and diabetes represent leading causes of mortality in the United States, with considerable disparities in rates across demographic and geographic factors. Despite advancements in medical research and healthcare interventions, mortality rates for both conditions remain persistently high, particularly among certain populations. These variations are influenced by multiple factors, including gender, race, socioeconomic status, and geographic location. The findings aim to inform public health strategies to address these disparities and improve health outcomes. Methods: Mortality data from the CDC WONDER database were retrospectively analyzed for adults aged 25 years and older who died with cancer and diabetes between 1999 and 2020. Temporal and demographic trends were assessed using the Joinpoint Regression Program (Version 5.3.0.0), providing insights into changes over time by age, gender, race, and geographic location. Results: From 1999-2020, the age-adjusted mortality rate (AAMR) rose from 157.3 to 189.4, with a significant surge from 2015-2020. Males consistently exhibited higher AAMRs than females, with both genders experiencing notable increases in recent years. Racial disparities were stark, as non-Hispanic Black populations had the highest AAMRs, followed by non-Hispanic American Indian/Alaskan Natives and Hispanics, with substantial increases from 2018-2020. Non-metropolitan areas displayed persistently higher mortality rates than metropolitan regions, with a marked surge between 2016-2020. Across all age groups, the 25-44 year old cohort showed the steepest AAMR increase, particularly from 2018-2020. Conclusions: This study highlights the growing burden of cancer and diabetes mortality in the U.S. and underscores widening demographic and geographic disparities. Addressing these inequities requires targeted public health strategies, improved healthcare access, and resource prioritization to support high-risk populations and underserved regions. Efforts should focus on health equity and reducing disparities to mitigate the rising mortality trends effectively.

Internal Medicine
Rudy R, **Ismail M**, Kakakhel MZJ, Rath S, Ahmad H, Mansoor A, Hemida MF, Javaid H, and Singh P. 21 years of tonsillar cancer mortality: Trends, disparities, and public health challenges. *J Clin Oncol* 2025;43(16). Full Text

R. Rudy

Background: Tonsillar squamous cell carcinoma (SCC), the most common oropharyngeal cancer, has shown increasing mortality trends despite declining traditional risk factors like tobacco use. Using CDC WONDER data from 1999 to 2020, this study examined demographic and geographic disparities in age-adjusted mortality rates (AAMRs) for individuals aged ≥25 years. Methods: Data was extracted from the CDC-WONDER database using ICD-code C09, specific to age-adjusted mortality rates (AAMR) due to tonsillar cancer per 100,000 population. Analysis was conducted using Joinpoint v5.3 to calculate average annual percent change (AAPC) and annual percent change (APC). Results: A total of 21,665 deaths were analyzed, revealing an overall AAMR increase from 0.42 in 1999 to 0.50 in 2020, with an AAPC of 1.16% (p,0.000001). The overall AAMR declined from 1999 to 2005 insignificantly, which was followed by an increase in AAMR with an APC of 1.84 (95% CI -0.60 to 4.77, p=0.05). Male mortality was significantly higher (AAMR: 0.75) than female (AAMR: 0.17) with a 2.78% annual increase (p=0.02). African Americans initially had the highest mortality, but rates declined (-1.96% AAPC, p=0.0004), while White populations experienced a significant rise (2.42% AAPC, p,0.000001). Mortality rates were highest

among individuals aged 65-84 years and disproportionately affected rural areas (AAMR: 0.49) compared to urban areas (AAMR: 0.46). Geographic variability was notable, with rural and southern regions showing higher mortality. Maine had the highest AAMR of 0.67 (95% CI 0.57 to 0.78), while lowest AAMR was recorded in Utah (0.15 (95% CI 0.11 to 0.20)) from 1999 to 2020. Other states in the upper 90th percentile of tonsillar cancer related mortality included District of Columbia, Kentucky, Tennessee, Vermont and Washington whereas states in the lower 10th percentile included Alaska, Hawaii, New Jersey, New York and Rhode Island. The highest AAMR for tonsillar cancer was recorded in the Midwest (0.48, 95% CI 0.47 to 0.50), followed by the South (0.47,95% CI 0.46 to 0.48) and West regions (0.40 95% CI 0.39 to 0.41) with lowest in Northeast region (0.36, 95% CI 0.35 to 0.38). Conclusions: These findings highlight increasing tonsillar cancer mortality among males and Whites and persistent rural disparities. Public health interventions focusing on HPV vaccination, early detection, and addressing healthcare inequities are critical for mitigating these trends.

Internal Medicine
Sahu S, **Ahmed M**, Dixit A, and Marlecha P. AML-1263: Transcriptomic Profiling of Acute Myeloid Leukemia Before and After Induction Therapy: A Public Data-Based Analysis. *Clin Lymphoma Myeloma Leuk* 2025;25:S495-S496. Full Text

Acute myeloid leukemia (AML) presents a variable response to induction therapy, necessitating the identification of early transcriptomic biomarkers that reflect treatment effectiveness. Publicly available gene expression data offer a noninvasive approach to study such shifts. Objective: To identify differentially expressed genes (DEGs) in patients with AML before and after induction chemotherapy, and to elucidate biological pathways associated with treatment response. Design: A secondary analysis of publicly available microarray data (GSE10358) using GEO2R. Samples included paired bone marrow aspirates from patients collected pre- and postchemotherapy. DEGs were filtered by adjusted $P < 0.05$ and $|\log2FC| > 1$. Functional enrichment was performed using Enrichr. Setting: Data were collected from an academic oncology research center, archived on the NCBI Gene Expression Omnibus platform. Patients or Other Participants: Ten adult patients with AML with paired samples (n = 20 total). Inclusion was based on dataset availability and treatment label metadata. No additional selection criteria were applied beyond dataset-defined identifiers. Interventions: All patients received standard induction chemotherapy (details not disclosed in dataset). The analysis was observational and did not involve clinical interventions by the investigators. Main Outcome Measures: Differential gene expression levels pre- and posttreatment; significantly enriched pathways relevant to AML biology. Results: A total of 324 DEGs were identified posttreatment, including 145 upregulated and 179 downregulated genes. Post-treatment upregulation was noted for genes such as CDKN1A, GADD45B, and BCL2A1, implicated in DNA damage response and apoptosis. Downregulated genes included MYC, CDC20, and CCNA2, consistent with suppression of proliferation. Enrichment analysis revealed significant activation of p53 signaling and apoptotic pathways, alongside repression of cell cycle and mitotic progression. Conclusions: Transcriptomic changes in AML following chemotherapy demonstrate a shift from proliferative signaling toward cellular stress and apoptotic regulation. Public data mining can reveal candidate biomarkers of early treatment response. Further validation in prospective studies is warranted before clinical implementation.

Internal Medicine
Sahu S, **Ahmed M**, Younas S, Nattala AG, Sai APS, Patel T, and Marlecha P. AML-1276: CRISPR-Cas9 Therapies in Hematologic Malignancies: A Meta-Analysis of Clinical Outcomes, Safety, and Translational Implications. *Clin Lymphoma Myeloma Leuk* 2025;25:S497. Full Text

CRISPR-based gene editing has introduced transformative possibilities in hematologic oncology, offering precise and durable immunologic interventions. With increasing adoption in early-phase trials, an integrated understanding of its efficacy and safety is essential. Objective: To evaluate the efficacy, safety, and translational potential of CRISPR-Cas9-based therapies in hematologic malignancies through a structured meta-analysis of early-phase clinical trials. Design: Systematic review and meta-analysis of CRISPR-based hematologic cancer trials published between 2019 and 2024. Random-effects modeling was used due to inter-trial heterogeneity. Setting: Academic hospitals and early-phase clinical centers conducting gene-modified cellular therapy trials. Patients or Other Participants: Nine clinical trials

encompassing 80 patients with relapsed or refractory hematologic malignancies, including Tcell acute lymphoblastic leukemia (T-ALL), aggressive B-cell lymphomas, and multiple myeloma. Inclusion criteria varied by trial; most patients had exhausted standard therapies. Interventions: All studies employed ex vivo CRISPR editing of immune cells. Interventions included TRAC- and PD-1-knockout chimeric antigen receptor (CAR) T cells, universal CD7-targeted base-edited T cells, and suicide-gene modified donor lymphocytes. Products were administered as single infusions following lymphodepletion. Main Outcome Measures: Overall response rate (ORR), complete response (CR) rate, incidence of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), and detection of off-target edits. Results: The pooled ORR was 62.3% (95% CI, 50.1%–73.2%), with a CR rate of 34.6%. Base-edited CAR7 T cells achieved CR in five of nine pediatric T-ALL patients. CRS occurred in 48% of patients (mostly grade 1–2) and ICANS in ~17%, with no grade ≥3 events. No treatment-related deaths or clinically significant off-target events were reported. Deep sequencing confirmed primarily on-target edits with rare, non-propagating chromosomal changes. Follow-up ranged from 6 to 12 months. Conclusions: CRISPR-Cas9-based therapies exhibit promising antitumor activity and a manageable safety profile in hematologic cancers. These findings support the clinical viability of gene-edited cellular therapy, especially in relapsed settings. However, larger trials and long-term data are essential to validate the durability, genomic stability, and scalability of these platforms.

Internal Medicine

Saleem A, **Al-Juburi S**, **Alomari A**, **Faisal M**, **Abusuliman M**, **Omeish H**, **Dababneh Y**, and **Jafri S**.
Management in the Era Before Biomarkers: Long-Term Outcomes and Immunosuppression Strategies Following Liver Transplantation. *Am J Transplant* 2025;25(8):S488. Full Text

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Purpose: Post-liver transplantation survival has substantially improved over the last few decades. However, post-transplant management remains challenging due to the intricate balance between immunosuppression and its adverse effects. Excess immunosuppression is associated with metabolic disease, infection, readmission, and malignancy, whereas insufficient immunosuppression increases the risk of rejection. Our study aims to delineate this balance to guide clinicians in safely minimizing immunosuppression without predisposing to rejection. Methods: Our study included patients who have had a 10-year liver transplant course starting in 2013 and were on tacrolimus immunosuppression. Patients who expired between 2018-2023 or lacked adequate clinical data were excluded. Mean 5-year tacrolimus troughs 5 years after transplant (2018 - 2023) were calculated. A mean trough level of 4 was used as a cutoff to subcategorize our patients into those with a 5 year mean trough of ≤4 or >4.We compared the incidence of rejection, infection, malignancies, hyperkalemia, nephrotoxicity, and hospital admissions between these groups during this time period. Results: Seventy-nine patients underwent liver transplantation at our center in 2013. Thirty-three patients expired or lacked sufficient data, leaving 44 for analysis, 17 females (39%) and 27 males (61%). The mean age was 54.6 with a standard deviation of 8.9 years. Etiologies of cirrhosis were Hepatitis C (45.45%), Alcohol (18.18%), Nonalcoholic Steatohepatitis (18.8%), Cryptogenic (9.09%), Primary Biliary Cirrhosis (4.55%), Primary Sclerosing Cholangitis (2.27%), and Cystic Fibrosis (2.27%). Tacrolimus troughs were >4 in 23 (52%) and ≤4 in 21 (48%). Rejection occurred in 6 patients in the >4 group and 3 in the ≤4 group. Hospitalization for infection occurred in 2 patients per group. Malignancy was identified in 2 patients in the >4 group and 3 in the ≤4 group. Nephrotoxicity was noted in 2 patients in the ≤4 group and 1 in the >4 group. The median overall hospital admission rate was 1 for both groups, with no statistically significant difference observed (p=0.667, Mann-Whitney test). No significant relationship between the mean 5-year trough and incidence of rejection, hyperkalemia, infection, cancer, overall hospital admission, and nephrotoxicity was found in our analysis (p>0.05). Conclusions: Our findings suggest that clinicians can safely down-titrate tacrolimus without an increased risk of rejection, infection, malignancy, nephrotoxicity, or readmission. Higher tacrolimus levels were also not associated with increased complications. These findings highlight the potential for individualized immunosuppression strategies to balance rejection risk and adverse effects. Larger studies

are needed to improve generalizability. CITATION INFORMATION: Saleem A., Al-Juburi S., Alomari A., Faisal M., Abusuliman M., Omeish H., Dababneh Y., Jafri S. Management in the Era Before Biomarkers: Long-Term Outcomes and Immunosuppression Strategies Following Liver Transplantation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Saleem: None.

Internal Medicine

Saleem A, **Alomari A**, **Samad M**, **Ilyas O**, **Khaliq I**, **Abusuliman M**, **Chaudhary A**, **Omeish H**, **Faisal M**, **Dababneh Y**, **Affas S**, and **Jafri S**. Orthopedic Surgery in Liver Transplant Recipients: Does Surgical Urgency Influence Post Operative Morbidity. *Am J Transplant* 2025;25(8):S489. Full Text

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Purpose: Despite chronic immunosuppression, liver transplant recipients often require surgical interventions, with a growing demand for orthopedic procedures in this population. These surgeries present significant perioperative challenges, requiring a balance between maintaining immunosuppression and minimizing post-operative complications. However, the impact of surgical urgency on post-operative outcomes remains unclear. This study evaluates post-operative complications in liver transplant recipients undergoing elective versus emergent orthopedic surgeries and examines whether immunosuppressive regimens influence outcomes. Methods: A retrospective cohort study was conducted using SlicerDicer to identify liver transplant recipients who underwent orthopedic surgeries between 2013 and 2022. Patients were categorized based on surgical urgency as either elective or emergent. Collected data included demographics, type of surgery, and immunosuppressive regimen. Outcomes assessed included infection, transaminitis, acute kidney injury (AKI), and hospital readmission within one year post-operatively. Differences in outcomes among various immunosuppressive regimens were also examined. A descriptive analysis was performed to identify trends in post-operative complications based on surgical urgency and immunosuppressive regimen. Results: A total of 87 patients were included, with a mean age of 67.5 years and a mean transplant-to-surgery interval of 87 months. The majority were male (59%, n=51) and White (82%, n=71), with smaller proportions of African American (16%, n=14) and other racial backgrounds (2%, n=2). Of these, 69 patients (79.3%) underwent elective orthopedic procedures, while 18 patients (20.7%) underwent emergent surgeries. Post-operatively, infection occurred in 7.2% of elective cases and 16.7% of emergent cases, transaminitis in 7.2% of elective cases and 11.1% of emergent cases, and AKI in 17.4% of elective cases and 16.7% of emergent cases. Hospital readmission within one year was observed in 36.2% of elective cases and 50.0% of emergent cases. These findings suggest a trend toward increased post-operative complications in patients undergoing emergent orthopedic surgery, particularly infections and transaminitis. Additionally, no significant differences in complication trends were observed among different immunosuppressive regimens. Conclusions: Orthopedic surgery in liver transplant recipients carries a risk of post-operative complications, with emergent procedures showing a trend toward systemic complications. While no differences were observed between immunosuppressive regimens, these findings highlight the need for careful perioperative management, particularly in emergent cases. Further studies with larger sample sizes are warranted to better define perioperative risks and guide clinical decision-making in this patient population. CITATION INFORMATION: Saleem A., Alomari A., Samad M., Ilyas O., Khaliq I., Abusuliman M., Chaudhary A., Omeish H., Faisal M., Dababneh Y., Affas S., Jafri S. Orthopedic Surgery in Liver Transplant Recipients: Does Surgical Urgency Influence Post Operative Morbidity AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Saleem: None.

Internal Medicine

Saleem A, **Obri M**, **Ilyas O**, **Alomari A**, **Faisal M**, **Abusuliman M**, **Chaudhary A**, **Rehman S**, **Franco-Palacios D**, **Nagai S**, **Venkat D**, and **Jafri S**. Outcomes and Risk Factors for Post-Operative Rejection and Transaminitis Following Dual Liver-Lung Transplantation: A Retrospective Cohort Study. *Am J Transplant* 2025;25(8):S468-S469. Full Text

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Purpose: Dual liver-lung transplantation (DLLT) is a rare and complex procedure, with limited data on post-operative rejection and liver function abnormalities. Understanding risk factors for acute cellular rejection and transaminitis is critical for optimizing immunosuppressive management. This study evaluates post-transplant outcomes in DLLT recipients and explores associations with recipient demographics, transplant indication, and underlying liver/lung disease etiology. Methods: A retrospective analysis was conducted on patients at our center who underwent DLLT between 2013 and 2024. Data collected included demographics, transplant indications, length of stay, incidence of acute rejection, and subsequent infections. Post-operative liver function tests (LFTs) beyond one month post-transplant were analyzed, and their relationship with age at transplant, liver disease etiology, and lung disease etiology was assessed. Results: A total of 10 patients (5 males, 5 females, mean age 53.7 years) underwent DLLT between 2013 and 2024. Liver disease etiologies were ethanol-related cirrhosis (n=2), hepatitis C (n=1), cryptogenic cirrhosis (n=1), autoimmune hepatitis (n=1), cystic fibrosis (n=1), and other unspecified causes (n=4). Lung transplant indications included idiopathic pulmonary fibrosis (n=5), pulmonary hypertension (n=2), other forms of interstitial lung disease (n=2), and cystic fibrosis (n=1).Post-operatively, 4 of 10 patients developed transaminitis beyond one month post-transplant, with liver biopsy confirming acute cellular rejection. Three patients received IV solumedrol, while one was managed with an oral steroid taper. Transaminitis resolved in all four cases after steroid treatment. Within three months, two patients treated with IV solumedrol developed infections from Candida and Aspergillus, though none developed CMV viremia. Two deaths occurred in the cohort. One patient passed away four years after transplant due to multifocal pneumonia, while the second patient passed away nine years post-transplant due to septic shock secondary to pneumonia in the setting of a new diagnosis of angiosarcoma. Neither patient had experienced rejection. Rejection and transaminitis were not significantly associated with age at transplant, liver disease etiology, or lung disease etiology. Conclusions: This study provides one of the first detailed assessments of rejection and liver function abnormalities following DLLT. While transaminitis and acute cellular rejection occurred in 40% of patients, no clear predisposing factors were identified. IV solumedrol use for rejection was associated with increased infection risk, emphasizing the need for careful immunosuppressive management in this population. Further research with larger cohorts is essential to improve risk stratification and post-transplant care in DLLT recipients. CITATION INFORMATION: Saleem A., Obri M., Ilyas O., Alomari A., Faisal M., Abusuliman M., Chaudhary A., Rehman S., Franco-Palacios D., Nagai S., Venkat D., Jafri S. Outcomes and Risk Factors for Post-Operative Rejection and Transaminitis Following Dual Liver-Lung Transplantation: A Retrospective Cohort Study AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Saleem: None.

Internal Medicine

Saleem A, **Obri M**, **Ilyas O**, **Alomari A**, **Faisal M**, **Omeish H**, **Chaudhary A**, **Nagai S**, **Franco-Palacios D**, **Venkat D**, and **Jafri S**. Characterization and Risk Factors for Readmission and Emergency Department Presentations in Dual Liver-Lung Transplantation Patients. *Am J Transplant* 2025;25(8):S468. Full Text

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Purpose: Dual liver-lung transplantation (DLLT) is a rare procedure, with limited data characterizing patient demographics, risk factors, and post-transplant outcomes, particularly regarding hospital readmissions and emergency department (ED) presentations. This study aims to assess the rates of hospital readmission, ED presentations, and associated risk factors in DLLT recipients. Methods: A retrospective analysis was conducted on patients at our center who underwent DLLT between 2013 and 2024. Demographics, transplant indications, length of stay, acute rejection, causes of readmission, and ED presentations were analyzed. Readmission rates were categorized as occurring within 0-3 months and between 3 months and 1 year post-transplant. Mortality outcomes were also assessed. Results: Ten patients (5 male, 5 female) with a mean age of 53.7 years underwent DLLT. Liver disease etiologies were ethanol-related cirrhosis (n=2), hepatitis C (n=1), cryptogenic cirrhosis (n=1), autoimmune hepatitis (n=1), cystic fibrosis (n=1), and other unspecified causes (n=4). Lung transplant indications included idiopathic pulmonary fibrosis (n=5), pulmonary hypertension (n=2), interstitial lung disease (n=2), and cystic fibrosis (n=1). All patients (100%) were readmitted within 3 months, and 40% experienced additional readmissions within the first year. The most common causes of early readmissions (0-3 months) included infections (40%), diarrhea (20%), critical illness myopathy (20%), rejection (10%), and biliary stricture (10%). ED presentations within 1 year occurred in 50% of patients, with leading causes including melena (n=2), tachycardia (n=1), fever (n=1), and gastrostomy tube dysfunction (n=1). Initial length of stay, lung transplant etiology, liver disease etiology, and age at transplantation were not associated with readmission or ED presentation rates ($p>0.05$). Two patients (20%) died within 10 years post-transplant, one at 4 years and one at 8 years. Readmission within 1 year was not significantly associated with mortality at 5 or 10 years. Conclusions: DLLT recipients experience high rates of early readmission, with infections being the leading cause. ED presentations are common, with gastrointestinal and infectious concerns predominating. No significant associations were found between transplant etiology, initial hospital stay, or age at transplantation and readmission or ED presentation rates. Long-term mortality was not associated with early readmission. These findings underscore the need for enhanced post-transplant surveillance and targeted interventions to mitigate early complications. CITATION INFORMATION: Saleem A., Obri M., Ilyas O., Alomari A., Faisal M., Omeish H., Chaudhary A., Nagai S., Franco-Palacios D., Venkat D., Jafri S. Characterization and Risk Factors for Readmission and Emergency Department Presentations in Dual Liver-Lung Transplantation Patients AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Saleem: None.

Internal Medicine

Saleem A, **Samad M**, **Khaliq I**, **Ilyas O**, **Farah B**, **Alomari A**, **Faisal M**, **Abusuliman M**, **Omeish H**, and **Jafri S**. Infectious Morbidity and Mortality in Small Intestine Transplantation: A Decade of Experience. *Am J Transplant* 2025;25(8):S845. Full Text

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Purpose: Small intestine transplant (SIT) is a life-saving procedure for patients with intestinal failure; however, long-term success is challenged by post-transplant infections due to immunosuppressive therapy. Despite advancements in transplantation, SIT recipients remain at high risk for infectious complications significantly impacting morbidity and mortality. Identifying patterns of infection and survival outcomes in these patients is critical for optimizing post-transplant care and developing targeted preventive strategies. This study aims to evaluate the incidence, timing, and mortality associated with

infectious complications in SIT recipients, providing insight into the most vulnerable periods and the need for enhanced surveillance and intervention. Methods: A retrospective cohort study was conducted at a single urban quaternary care center in the Midwestern United States, analyzing 27 SIT recipients from 2012 to 2022. Data collected included age at transplant, sex, and causal organisms of infection. Patients were stratified into three groups based on the onset of infection: within six months, 6-12 months, and beyond 12 months post-transplant. Primary outcomes included one- and three-year survival rates. Results: The cohort included 27 patients (62% female, mean age 49 years). Intra-abdominal infections were the most common (29.6%, n=8), with 88% occurring within six months, yielding an 86% one- and three-year survival. CMV viremia (19%) occurred mostly beyond 12 months (80%), with a 100% three-year survival; however, cases arising within 6-12 months had 0% survival at three years. Pneumonia (15%) primarily developed within six months, with 100% three-year survival, except for one case (6-12 months) with no survival at three years. Upper respiratory and skin infections accounted for 7.4% and 11.1% of cases, respectively, both demonstrating favorable three-year survival except for late-onset skin infections (6-12 months), which had 0% survival at three years. Conclusions: Intra-abdominal infections were the most frequent and occurred predominantly within six months post-SIT. CMV viremia, while the second most common, showed variable outcomes based on timing. Larger multicenter studies are needed to better characterize infectious risks and optimize post-SIT management. CITATION INFORMATION: Saleem A., Samad M., Khaliq I., Ilyas O., Farah B., Alomari A., Faisal M., Abusuliman M., Omeish H., Jafri S. Infectious Morbidity and Mortality in Small Intestine Transplantation: A Decade of Experience AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Saleem: None.

Internal Medicine

Saleem M, **Qureshi MA**, and **Ananthasubramaniam K**. FDG-PET For Myocardial Viability Assessment: Does it Guide Decision Making For Revascularization In Real World Practice? A Single Center Experience. *J Nucl Cardiol* 2025;50. Full Text

Introduction: The incidence of heart failure driven by ischemic heart disease is increasing. Intuitively it makes sense that identification of ischemic viable myocardium could drive revascularization decisions and survival, but recent study evidence has not favored it. We sought to evaluate if FDG PET guides real world decision making for revascularization in ischemic cardiomyopathy and if it makes a difference Methods: This is a retrospective chart review study of PET ischemia and viability testing performed between 2020-2024 at our institution; Patients' baseline characteristics including comorbidities, ejection fraction and PET study results were evaluated. We compared baseline characteristics between positive viability and negative viability groups. Revascularization and changes in ejection fraction outcomes were assessed Results: Data of 111 patients who underwent PET ischemia and viability testing were analyzed; mean patients age is 69 yr old, M:F ratio 4:1, 64% white and 29% African American, all patients had HTN and HLD, 51 % diabetics and 53% were smoker. 78% of patients had a history of MI and 95% of patients have ischemic cardiomyopathy with a mean EF of 34%. The average SRS, SSS, SDS were 14, 13, 7 respectively. 99 patients received FDG for viability assessment. We found the following; First; 65 patients (67%) were positive for ischemic viable myocardium and 31 patients (31%) with non-viable myocardium. Second, there was no statistically significant difference in baseline characteristics of patients with positive viability and negative viability groups. Third, in the positive viability group (n=65); 37 patients (56%) had revascularization with PCI/CABG and 31 patients (43%) were treated medically and in the negative viability group, 19 patients (61%) were treated medically and only 11 patients (35%) received revascularization. Fourth, there is a significant improvement of the ejection fraction in the positive viability patients who underwent revascularization (mean baseline EF of 32%, mean post revascularization EF of 38% with P value =0.0004) and significant improvement in EF in the positive viability patient who were treated medically (mean baseline EF of 34%, mean EF post 3 months of medical therapy 37% with P value =0.005). Fifth, there is no significant improvement in the ejection fraction in the negative viability patients who underwent revascularization (mean baseline EF of 32%, mean post revascularization EF of 23% with P value =0.39). Finally, symptoms were reported to be improved in 36 patients (52%) in the viability positive group. Conclusion: - Our single center experience shows that clinicians continue to believe in viability assessment and refer patients for FDG-PET testing.-FDG-PET viability studies can be utilized to guide management and decision making of revascularization which can predict functional recovery and symptoms improvement

Internal Medicine
She Ng L, Jan Kakakhel MZ, Ahmad H, Ur Rafe SA, Ali MF, **Ismail M**, Chaudhary M, Jawad H, Ikram J, and Ahmed F. Global trends in disability adjusted life years (DALYs) and mortality rates in gastric cancer among elderly (70+ Years) from 1990-2021: A Global Burden of Disease study. *J Clin Oncol* 2025;43(16). Full Text

L. She Ng

Background: Although the incidence and mortality of gastric cancer have decreased over the past decades due to the progress in diagnostic methods, treatment approaches and preventive measures, it still poses serious global health challenges particularly in the elderly population with significant disparities in the overall Disability-Adjusted Life Years (DALYs) and mortality. This study evaluates gastric cancer related overall DALYs and mortality from 1990-2021 using the Global Burden of Disease (GBD) database. Methods: GBD data for 2021 were studied to evaluate overall DALYs and mortality rate per 100,000 population among 70 and above aged individuals. The Annual Average Percentage Change (AAPC) was calculated to assess trends from 1990 to 2021, and statistical significance assessed through p-values. Results: From 1990 to 2021, the overall DALYs rate for gastric cancer demonstrated a gradual decline. The DALYs rate per 100,000 decreased from 2656.08 in 1990 to 1511.71 in 2021. Similarly, the mortality rate declined from 166.11 per 100,000 in 1990 to 100.06 per 100,000 in 2021. The steepest declines in both DALYs and mortality rates occurred between 2004 and 2007, with annual percentage changes (APC) of -3.81% (95% CI: -4.023 to -3.531; $p < 0.000001$) and -3.41% (95% CI: -3.632 to -3.155; $p = 0.0004$), respectively. Across the entire study period (1990-2021), the average annual percentage change (AAPC) for DALYs was -1.80% (95% CI: -1.809 to -1.784; $p < 0.000001$), while for mortality rates, it was -1.63% (95% CI: -1.655 to -1.605; $p < 0.000001$). Conclusions: From 1990 to 2021, the burden of gastric cancer among individuals aged 70+ significantly declined, with a 43% reduction in DALYs and a 40% reduction in mortality rates. The sharpest declines occurred from 2004 to 2007. These trends highlight advancements in prevention and treatment but emphasize the need for continued efforts to address the burden in aging populations.

Internal Medicine
She Ng L, Kakakhel MZJ, Ahmad H, Khan I, **Ismail M**, Chaudhary M, Jawad H, Mansoor A, Mansoor A, Khan AZ, and Haider MU. Sex-stratified mortality and disability-adjusted life years (DALYs) due to gastric cancer among older adults (70+) from 1990 to 2021: A global burden of disease study. *J Clin Oncol* 2025;43(16). Full Text

L. She Ng

Background: Gastric cancer is a malignant disease characterized by the uncontrolled growth of cells in the stomach lining and is a global health concern. It is a significant health burden in older adults, with long-term complications affecting quality of life and survival. We aim to explore sex-stratified trends in mortality and disability-adjusted life years (DALYs) due to Gastric Cancer from 1990 to 2021. Methods: We obtained sex-stratified data for older adults aged 70 years and above with Gastric Cancer from the Global Burden of Disease (GBD) from 1990 to 2021. The mortality rates were age-standardized and expressed per 100,000 deaths. Trends were analyzed as annual percentage change (APC) and average APC (AAPC) using Joinpoint Regression. Results: From 1990 to 2021, deaths due to Gastric Cancer in older adult males increased globally from 187,690 to 305,807 per annum, with age-standardized mortality rates (ASMRs) decreasing from 227 to 140 and standardized DALYs decreasing from 3734 to 2189. In females, deaths rose from 147,867 to 188,861, with ASMRs declining from 124 to 68 and DALYs declining from 1908 to 979. Despite the apparent rise in deaths, ASMRs exhibited a significant decline in both sexes, with an AAPC of -1.53% (95% CI: -1.56 to -1.49) in males and -1.91% (-1.94 to -1.88) in females. The DALYs showed a significant decline in females with an AAPC of -2.13% (-2.16 to -2.1) but a significant increase in males with an AAPC of -1.72% (-1.75 to -1.69). Males experienced the greatest APC decline in deaths of -3.33% from 2004 to 2007, while females showed their steepest decline of -3.50% during the same period. Prior to this, males exhibited a decline of -1.59% from 1990 to 1998, followed by a non-significant increase of 0.06% from 1998 to 2004. For females, the decline was more pronounced from 1990 to 1998 at -2.13%. After 2007, males experienced declines of -1.24% from 2007 to

2010 and -1.24% from 2018 to 2021. In contrast, females saw declines of -2.29% from 2007 to 2014, followed by a smaller decline of -1.36% till 2021. DALYs in females showed the greatest decline of -4.01% from 2004 to 2007, after decreases of -2.19% (1990-1998) and -1.21% (1998-2004). This was followed by declines of -2.73% till 2015 and -1.22% till 2021. Males saw the steepest decline of -3.74% from 2004 to 2007, with earlier reductions of -1.56% (1990-1998) and -0.07% (1998-2004), followed by -2.85% till 2015 and -1.68% till 2021. Conclusions: Although ASMRs declined, the recent decline in ASMRs in females is becoming less pronounced highlighting the importance of ongoing monitoring and improvement strategies. The disparity in DALYs between males and females also demands the need for targeted interventions addressing malespecific challenges to reduce the burden of Gastric Cancer.

Internal Medicine

Singh D, and **Mroke P**. ABCL-089: Masquerading as Breast Cancer: Rare Metastatic Peripheral T-Cell Lymphoma. *Clin Lymphoma Myeloma Leuk* 2025;25:S721-S722. Full Text

Peripheral T-cell lymphoma (PTCL) is a rare subtype of non-Hodgkin lymphoma that typically originates in the lymph nodes and rarely involves the breast. Here, we present a case in which PTCL not only originated in the breast but also mimicked an aggressive primary breast cancer—an exceptionally rare diagnosis, with only 18 documented cases in the literature. Patient: A 76-year-old debilitated female with diabetes, hypertension, and blindness from glaucoma presented after a mechanical fall. During evaluation, she reported a 3-week history of left breast pain with intermittent malodorous discharge. Years prior, a similar episode had resolved after incision and drainage and antibiotics for a presumed abscess. Results and Interventions: On examination, the breast was indurated without active discharge, although purulent and bloody drainage was observed in the emergency department. There was no lymphadenopathy or hepatosplenomegaly. Surgery attempted drainage unsuccessfully, prompting biopsy and oncology evaluation. Imaging added to the diagnostic dilemma. A recent mammogram was unremarkable. Noncontrast head computed tomography showed unchanged skull lucencies. However, brain MRI revealed new lytic calvarial lesions without brain involvement. Labs showed pancytopenia. Workup ruled out primary breast malignancy and multiple myeloma. Ultimately, immunohistochemistry showed a distinct but non-specific T-cell marker profile (BETAF1, CD8, TIA1, CD3, CD43, CD56, CD15, BCL2, GATA3, CD79a, c-MYC), leading to the diagnosis of PTCL-not otherwise specified (PTCL-NOS) with skull metastases and bone marrow infiltration. Outcome: Given the aggressive disease course, lack of defined treatment protocols, and poor prognosis, the patient opted for hospice care. Conclusions: This case illustrates several key challenges: • rare extranodal breast presentation. • clinical mimicry of primary breast carcinoma. • diagnostic confusion from lytic skull lesions and pancytopenia. • delayed diagnosis due to non-specific immunohistochemistry. • lack of data to guide management—only 4 of 18 known PTCLbreast cases involved metastasis. This case underscores the need for heightened suspicion in atypical breast lesions and highlights the diagnostic complexity and treatment uncertainty of rare extranodal lymphomas like PTCL.

Internal Medicine

Tareen H, Aziz N, Nabi W, Khan M, Ganiyani MA, Rohita D, Garje R, Basharat A, Usama A, Cheema A, Rath S, Majeed MW, Bhat A, Elsherif Y, Makhkamov S, Ali A, Babak JM, Fuentes-Rosales JC, Gulas J, and Fromer N. Predictors of survival in advanced-stage, high grade primary peritoneal serous cystadenocarcinoma: An NCDB based analysis. *J Clin Oncol* 2025;43(16). Full Text

H. Tareen

Background: High-grade primary peritoneal cystadenocarcinoma (HPPC) is a rare and aggressive malignancy originating from the peritoneal lining, frequently diagnosed at advanced stages with a poor prognosis. Despite its severity, data on clinical behavior, prognostic factors, and survival outcomes remain limited, particularly in advanced disease. This study utilizes the National Cancer Database (NCDB) to identify key predictors of survival to enhance clinical understanding and inform treatment strategies. Methods: Using the NCDB, we conducted a retrospective analysis of patients diagnosed with HPPC from 2010 to 2017. The primary cohort included AJCC stage III-IV, high grade pathologies. Immunotherapy and chemotherapy were combined into a single variable, systemic therapy (ST) as certain drugs were reclassified in the NCDB during the study period. Treatment modalities included

systemic therapy alone (ST), surgery alone (S), and surgery with systemic therapy (S+ST). Kaplan-Meier survival analysis and Accelerated Failure Time (AFT) model were used for estimation of survival outcomes. STROBE guidelines were followed for reporting. Results: A total of 1,539 patients were included. Of these, 935 (60.8%) were aged≥65 years, 1,430 (92.9%) were White, 872 (57%) had Medicare insurance, and 593 (38.57%) received care in Comprehensive Community Cancer Programs. 225 patients (14.6%) received ST, 84 (5.5%) received S, 1,095 (71.1%) received S+ST, and 135 (8.8%) received unspecified regimen combinations. mOS, however, varied by stage and treatment. In stage III,mOSwas 28.02 months with ST, 30.23 months with S, and 51.15 months with S+ST (p, 0.05). In stage IV, mOS was 20.47 months with ST, 4.47 months with S, and 41.17 months with S+ST ($p < 0.05$). Collectively, covariate adjustment using AFT showed that S+ST significantly improved survival over ST alone (HR 0.63, $p < 0.01$), while S alone showed no statistically significant benefit (HR 0.93, $p = 0.64$). Older patients (≥65 years), with Charlson-Deyo Score (CDS) of 1 (vs 0; HR 1.17, $p < 0.05$), and those with oligometastatic disease M1 (vs M0; HR 1.24, $p < 0.01$) exhibited worse survival outcomes. Race, gender, insurance, and facility type did not significantly impact mortality, but patients treated in the East South Central (HR 1.82, $p < 0.001$) and the West South Central (HR 1.42, $p = 0.038$) had worse survival compared to the Northeast. Conclusions: Older age, burden of comorbidities, presence of metastasis, and treatment in certain geographic regions appear to be associated with worse outcome. Surgery combined with systemic therapy significantly improves survival outcomes, highlighting the importance of a multimodal approach in advanced stage HPPC.

Internal Medicine

Toiv A, **Justus H**, Lee V, Altamura-Murgia G, Horslen S, Weiner J, Schiano T, Segovia M, and **Jafri S**.
Glucagon-Like Peptide-2 Therapy Outcomes Following Intestinal and Multivisceral Transplantation: A Multicenter Experience. *Am J Transplant* 2025;25(8):S844. Full Text

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Purpose: Glucagon-like peptide-2 (GLP-2) plays a critical role in intestinal adaptation, mucosal growth, and nutrient absorption. While GLP-2 therapy has shown benefits in patients with short bowel syndrome, its effects following intestinal transplantation (IT) and multivisceral transplantation (MVT) remain unknown. This study aims to describe the clinical outcomes of patients who received GLP-2 therapy after IT or MVT, providing insights into its potential role in post-transplant recovery and long-term outcomes. Methods: A retrospective analysis was conducted on sev7en patients who received GLP-2 therapy following IT or MVT across four transplant centers between 2014 and 2024. Results: Among the 7 transplant recipients, there were 2 men and 5 women. 5 patients underwent IT alone, while 2 underwent MVT. The median age at transplantation was 46 years (mean 45, range 19-62), with a median transplant waitlist time of 71±109 days. 71% of recipients developed short bowel syndrome due to bowel resection, while 29% had dysmotility as the underlying cause. All patients received teduglutide, with 57% starting treatment prior to undergoing IT. At GLP-2 initiation, 71% of patients were dependent on total parenteral nutrition (TPN), and with treatment, 67% successfully transitioned off TPN. GLP-2 therapy was eventually discontinued in 71% of patients, with bowel obstruction being the most common reason (67%). Notably, all patients retained their colons post-transplant. No patients had a history of colon polyps or colon cancer, and no polyps were detected during follow-up colonoscopies. Only one patient died 66 days post-transplant due to septic shock from a leg abscess, which occurred 10 days after discontinuing GLP-2 treatment. The remaining patients surpassed the 1- and 3-year survival milestones and did not have any infectious complications on treatment. Conclusions: GLP-2 therapy may play a beneficial role in intestinal adaptation and post-transplant recovery, potentially facilitating independence from TPN in IT and MVT

recipients. Bowel obstruction appears to be the main complication leading to therapy discontinuation and occurred in the majority of patients undergoing GLP-2 therapy. Despite these challenges, survival outcomes were generally favorable, warranting further investigation into the long-term benefits and risks of GLP-2 therapy in transplant recipients. CITATION INFORMATION: Toiv A., Justus H., Lee V., Altamura-Murgia G., Horslen S., Weiner J., Schiano T., Segovia M., Jafri S. Glucagon-Like Peptide-2 Therapy Outcomes Following Intestinal and Multivisceral Transplantation: A Multicenter Experience AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Toiv: None.

Internal Medicine
Toiv A, **Justus H**, Sarowar A, Lee V, Marquez J, Altamura-Murgia G, Horslen S, Weiner J, Schiano T, Segovia M, and **Jafri S**. Outcomes Following Graft Enterectomy After Intestinal and Multivisceral Transplantation: A Multicenter Analysis. *Am J Transplant* 2025;25(8):S843. Full Text

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Purpose: Graft enterectomy following intestinal transplantation (IT) or multivisceral transplantation (MVT) is a critical event that significantly impacts patient morbidity, survival, and long-term nutritional dependence. Data on IT failure requiring enterectomy and outcomes following enterectomy remain poorly defined. This study aims to describe the clinical outcomes of patients who underwent enterectomy after IT or MVT, providing insights into the post-enterectomy course. Methods: Retrospective analysis of 20 patients who underwent IT or MVT and subsequently required graft enterectomy from four transplant centers between 2012 and 2024. The primary outcome was patient survival analyzed by Kaplan-Meijer analysis. Secondary outcomes included retransplantation and infection within 3 months. Results: Among the 20 patients who underwent graft enterectomy following IT or MVT, there were 10 men and 10 women, with 55% receiving their transplants before the age of 18. The average age of the cohort at the time of enterectomy was 21 years, with a median age of 7 years. The average age of the pediatric patients was 4, and adult patients was 45. IT alone accounted for 75% of transplants, while 25% were MVT. Rejection was the primary indication for enterectomy in 100% of cases. MVT recipients were significantly more likely to undergo re-transplantation compared to IT recipients (p=0.01) and showed a trend toward improved survival (p=0.40). At 6 months and 1-year post-enterectomy, survival rates were 73% and 67% for IT recipients and 80% and 80% for MVT recipients, respectively. The pediatric transplant recipients had significantly increased survival compared to the adults (p=<0.01). There was no significant difference between IT and MVT recipients in their development of PTLD or infection within 3 months of enterectomy. Conclusions: Graft enterectomy remains a significant event following IT and MVT, with rejection being its most common indication. MVT demonstrated a trend of higher survival and significantly higher re-transplantation rates compared to IT alone after enterectomy. Pediatric transplant recipients had higher survival rates than adult transplant recipients. Our findings highlight the need for improved immunosuppressive protocols and post-transplant monitoring to mitigate the risk of graft failure. Further research is warranted to enhance long-term survival and quality of life in this complex population. CITATION INFORMATION: Toiv A., Justus H., Sarowar A., Lee V., Marquez J., Altamura-Murgia G., Horslen S., Weiner J., Schiano T., Segovia M., Jafri S. Outcomes Following Graft Enterectomy After Intestinal and Multivisceral Transplantation: A Multicenter Analysis AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Toiv: None.

Internal Medicine
Toiv A, **O'Brien HB**, **Andrews T**, and **Jafri S**. The Effects of Demographic Factors Upon Intestinal Transplant Outcomes. *Am J Transplant* 2025;25(8):S840-S841. Full Text

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Purpose: Demographic factors are increasingly recognized as potential influences on transplant outcomes. Limited data exist on the impact of demographic factors on intestinal transplantation (IT) and multivisceral transplantation (MVT) outcomes. This study aims to evaluate the impact of both sex and age on IT and MVT post-transplant outcomes. Methods: Retrospective chart review of all patients who underwent IT or MVT at an academic transplant center from 2010 to 2023. Patients were stratified by sex (male vs. female) and age (<50 vs. ≥50 years). The primary outcome was patient survival, analyzed using Kaplan-Meier analysis. Secondary outcomes included graft failure (GF), reoperation rates, moderate-to-severe rejection, and the development of chronic kidney disease (CKD). Results: Among 50 IT recipients, there were 20 men and 30 women. When stratified by age, 21 were <50 years old, while 29 were ≥50 years old. IT alone accounted for 58% of transplants, while 42% were MVT. Survival analysis revealed no significant mortality difference between the groups when analyzed by sex (p=0.28) or when comparing IT alone to MVT (p=>0.05 in all subgroups). Male IT recipients showed a higher need for reoperation within 1 month (p=0.01), though this difference did not persist at 3 months (p=0.44). No significant differences were observed between the sexes for GF, rejection rates, or CKD. In contrast, age was a significant predictor of survival, with recipients ≥50 years old demonstrating significantly lower survival rates than younger recipients (p<0.01). Older recipients had a trend towards higher incidence of reoperation within 3 months and an increased risk of developing CKD. No significant differences were found between age groups in terms of GF or rejection rate. Conclusions: While transplant recipient sex did not significantly impact survival or transplant-related outcomes, age ≥50 years was associated with significantly lower survival rates following IT. Further studies are needed to explore immunosuppression modifications and infectious surveillance strategies that may help reduce the incidence of CKD and improve mortality outcomes in these populations. CITATION INFORMATION: Toiv A., O'Brien H., Andrews T., Jafri S. The Effects of Demographic Factors Upon Intestinal Transplant Outcomes AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Toiv: None.

Internal Medicine

Toiv A, **O'Brien HB**, **Sarowar A**, **Andrews T**, and **Jafri S**. Liver Transplant Outcomes and Complications for Metabolic- Dysfunction Associated Alcohol Related Liver Disease (MetALD). *Am J Transplant* 2025;25(8):S493. Full Text

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Purpose: Metabolic alcohol-associated liver disease (MetALD) describes the coexistence of alcohol-associated liver disease (ALD) and metabolic dysfunction-associated steatotic liver disease (MASLD), two leading indications for liver transplantation (LT). However, the impact of this increasingly recognized dual pathology on LT recipient outcomes has not been thoroughly investigated. Our aim was to determine whether LT recipients with MetALD had less favorable postoperative outcomes than those with isolated ALD. Methods: A retrospective cross-sectional study of all patients who underwent LT for the primary indication of ALD at a high-volume academic transplant center between January 1, 2014, and September 26, 2023. Patients were stratified into 2 groups: LT recipients with isolated ALD and those with MetALD based on the presence of metabolic comorbidities. Kaplan-Meier analysis was used to compare mortality and graft survival rates between groups. Results: Of 381 LT recipients with ALD, 159 (42%) had isolated ALD, and 222 (58%) had MetALD. The MetALD group had a significantly higher median age (58 vs 50 years; p<0.001) and was predominantly female (77% vs. 45%). Comorbidities in the MetALD group included diabetes (37% vs. 0%), hyperlipidemia (23% vs 0%), hypertension (77% vs. 0%), and coronary artery disease (27% vs. 0%) (all p<0.001). Despite the greater prevalence of baseline metabolic comorbidities in the MetALD group, no significant differences in postoperative mortality was observed

between groups at 1 (94% vs 96%), 3 (91% vs. 90%), or 5 years (90% vs. 88%) after LT. Furthermore, no significant differences in graft failure were observed between groups at 1 (91% vs 95%), 3 (88% vs 89%), or 5 years (99% vs 87%) after LT. Rejection rates and surgical complications were also comparable between groups. Conclusions: Despite being older and having a significantly higher prevalence of metabolic and cardiovascular comorbidities including diabetes, hyperlipidemia, hypertension, and coronary artery disease, LT recipients with MetALD demonstrated positive patient and graft survival outcomes comparable to those in patients with isolated ALD. These results highlight the value of LT as a treatment option in this complex patient population and suggest that the presence of MetALD should not preclude consideration for LT. CITATION INFORMATION: Toiv A., O'Brien H., Sarowar A., Andrews T., Jafri S. Liver Transplant Outcomes and Complications for Metabolic- Dysfunction Associated Alcohol Related Liver Disease (MetALD) AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Toiv: None.

Internal Medicine

Toiv A, **Yoshida A**, **Roberman J**, **Doshi N**, **Poisson L**, **Abouljoud M**, **Moonka D**, and **Jesse M**. Listed or Left Behind: The Impact of Social Support on Liver Transplant Access. *Am J Transplant* 2025;25(8):S493. Full Text

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Purpose: Liver transplantation (LT) is the only curative therapy for patients with decompensated liver disease, but the complex evaluation process for selecting LT recipients limits access for many. “Social support” is a subjective and controversial criterion often used for determining LT eligibility. However, transplant centers inconsistently apply this criterion, and using social support to determine LT eligibility contributes to racial, ethnic, and socioeconomic inequities in transplant listing. Here we investigated the impact of using social support as a criterion for LT listing. Methods: We conducted a retrospective analysis of all patients evaluated for LT between January 1, 2019, and December 31, 2021 at an academic liver center with a clearly defined objective social support evaluation criterion. Logistic regression analysis was used to determine the association between social support inadequacy (unable to report ≥2 support people and/or other significant concerns) and LT listing status. Kaplan-Meier analysis was used to examine the relationship between social support and time-to-decision. Results: Of 711 LT candidates who had social support information available, 498 (70%) were not listed for LT, of whom 13 (2.6%) were not listed for LT solely due to having inadequate social support. After controlling for several variables, having inadequate social support was significantly associated with decreased odds of being listed for LT (odds ratio 0.38; 95% CI, 0.13-0.93). Other predictors of non-listing included female sex and having recommendations for substance use treatment. Conversely, being married/partnered and higher education levels were positively associated with listing. Kaplan-Meier analysis did not show significant differences in time-to-decision based on social support status; however, patients with inadequate social support exhibited a steeper decline in evaluation completion during the initial 125 days. Conclusions: At our transplant center, <3% of patients who were excluded from LT listing were not listed solely due to having inadequate social support, and inadequate social support was significantly associated with a lower likelihood of listing. Social support remains a critical and controversial criterion for determining LT eligibility, and the subjective nature of social support evaluations can perpetuate disparities in access to life-saving transplantation. Standardizing assessments and implementing interventions to strengthen social support systems could reduce inequities and ensure more equitable access to transplantation. CITATION INFORMATION: Toiv A., Yoshida A., Roberman J., Doshi N., Poisson L., Abouljoud M., Moonka D., Jesse M. Listed or Left Behind: The Impact of Social Support on Liver Transplant Access AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Toiv: None.

Internal Medicine

Zimmer M, **Abad J**, **Gupta J**, **Ghosh S**, and **Kuriakose P**. MM-423: Secondary Hematologic Malignancies in Patients With Multiple Myeloma: A Retrospective Analysis of Risk Factors and Incidence in a Large Urban Health System. *Clin Lymphoma Myeloma Leuk* 2025;25:S919. Full Text

Multiple myeloma (MM) is a common hematologic malignancy. While overall survival has improved due to advances in therapy, there is concern regarding the risk of secondary hematologic malignancies (SHM). Objective: To identify patients treated for MM who subsequently developed SHM and estimate the incidence and timing of SHM. Design: Retrospective, observational study. Setting: Henry Ford Health, a large urban, tertiary care network in Detroit, MI. Patients: Patients age 18 years or more with a confirmed diagnosis of MM between January 2005 and December 2022 and a subsequent SHM diagnosis were identified through electronic medical records review. Results: Of 3122 patients with MM, 297 were identified by automatic data pull as having a diagnosis of SHM. After manual review, nine patients met the inclusion criteria. Six patients (66.7%) were male. Median age at MM diagnosis was 62 (range: 53–73) years. About 44.4% were African American, 33.3% were Caucasian, 11.1% were Asian, and 11.1% identified as other. At a median follow-up of 58 (range: 35–144) months, most patients (66.6%) had received only one line of therapy, some had two lines (22.25%), and one patient had received 12 lines of therapy. Five patients (55.6%) underwent autologous stem cell transplantation. Most patients (77.8%) received maintenance therapy, most commonly with lenalidomide (66.7%), for a median duration of 11 (range: 0–29) months. SHM were diagnosed at a median of 4 years after MM diagnosis, being primarily myeloid in origin (77.8%). Median time from MM diagnosis to death was 64 (range: 49–78) months, and median time from SHM diagnosis to death was 5 (range: 0–9) months. Conclusion: Despite the sample size and retrospective nature, our study has some key findings. First, the incidence of SHM was 0.2%, which is significantly less than the 8–18% in previous studies. Second, most patients were not heavily pretreated, often receiving only 1–2 lines of therapy and shorter duration of lenalidomide maintenance prior to the development of SHM. Accordingly, further work needs to be done to evaluate the impact of both patient- and disease-dependent factors, as well as MM therapy, on the development of SHM.

Internal Medicine

Zubair A, Arham M, Khan SA, **Tareen H**, Dad A, Siddiqui E, Altaf MT, Bakht K, Jehangir H, Saleem F, Iqbal K, and Ahmed H. MM-581: Tracking Mortality in Multiple Myeloma-Associated Acute Kidney Injury: U.S. Trends (1999–2023) and ARIMA-Based Projections Through 2050. *Clin Lymphoma Myeloma Leuk* 2025;25:S928. Full Text

Acute kidney injury (AKI) affects up to 20% of patients with multiple myeloma (MM), rendering it a significant contributor to the mortality burden of the disease. Our hypothesis posits that MM-associated AKI mortality demonstrates significant socioeconomic and regional disparities. Objectives: This study aims to assess MM-associated AKI mortality trends in U.S. adults (≥65 years) from 1999 to 2023 and project overall trends through 2050 using the CDC WONDER database, focusing on socioeconomic disparities. Methods: Mortality data were obtained from the CDC WONDER database (1999–2023) using ICD-10 codes C90 (MM) and N17 (AKI). Age-adjusted mortality rates (AAMR) were calculated per million and standardized to the 2000 U.S. population. Joinpoint regression analysis estimated annual percent change (APC) and AAMR with 95% confidence intervals (CIs). Stratifications included sex, race, state, region, and urbanization zone. Future AAMR trends were forecasted using ARIMA after ADF-based stationarity testing. Results: From 1999 to 2023, 11,414 deaths occurred due to AKI-associated MM. AAMR increased from 7.7 (95% CI: 6.8–8.7) to 14.1 (95% CI: 13.1–15.1) per million. The ARIMA model fit well (AIC 50.28, RMSE 3.19) and forecasted AAMR values of 10.32 in 2030 (CI: 7.12–13.52), 2040 (CI: 5.49–15.15), and 2050 (CI: 4.29–16.35). In 2050, the projected AAMR for males was 13.56 (95% CI: 5.11–22.02), compared with 8.12 (95% CI: 4.12–12.13) for females. Historically, males had higher AAMR (18.4 per million, 95% CI: 16.7–20.1) than females (11 per million, 95% CI: 9.8–12.1). Non-Hispanic Whites saw a consistent increase in mortality (APC 2.83%, 95% CI 1.92–5.70, P = 0.002), particularly in the South (APC 2.55%, 95% CI 1.77–3.57, P < 0.001), where AAMR rose from 7.3 (95% CI: 5.8–9) to 14 (95% CI: 12.5–15.6). Rural non-core areas had the highest AAMR (13.8 per million, 95% CI 10.2–18.3). South Dakota had the highest state-specific AAMR (16.2 per million, 95% CI: 11.8–21.9). Conclusion: MM-associated AKI mortality among older U.S. adults has increased significantly, particularly affecting males, non-Hispanic Whites, and residents of the southern U.S. and South Dakota. Given the disparities, targeted public health interventions are required to mitigate these inequalities. Grant/Funding Acknowledgements: Nil.

Nephrology

Kreitler K, **Fitzmaurice M**, **Wright S**, **Khoury N**, **Shrivastava P**, **Patel A**, and **Prashar R**. Safety of Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2is) in Kidney Transplant Recipients. *Am J Transplant* 2025;25(8):S413. Full Text

Purpose: SGLT2is have the potential to improve kidney function in kidney transplant recipients (KTRs) by reducing proteinuria and preserving eGFR, but safety concerns exist due to increased risk of urinary tract infections (UTI), volume depletion and genital infections in immunocompromised patients. We present a single center retrospective study assessing the safety of SGLT2i in KTRs. Methods: Data from 130 KTRs who were started on SGLT2i following KT were retrospectively collected from a single academic center. Data at drug initiation, and 12 months were assessed. T-test was performed to assess statistical significance in difference in clinical characteristics of KTRs at baseline and at 1 year post SGLT2i initiation. Results: Baseline characteristics are summarized in Table 1. Empagliflozin was the most prescribed SGLT2i and median time from transplant to drug initiation was 731 days. 45% of patients had diabetes pre-transplant, 37% had new onset diabetes post-transplant, and 18% were non-diabetics. Mean baseline estimated eGFR was 55.2 mL/min/1.73 m2. Mean HgbA1c at initiation was 6.9%, and urine albumin creatinine ratio (UACR) was 262 mg/g. 26% of patients had glycosuria at baseline. At 12 months, 88% patients developed glycosuria, 13 (10 %) had UTIs, and but only 16 (12.3%) patients had discontinued the needed to discontinue the SGLT2i. The reasons for drug discontinuation were recurrent UTIs (7), AKI acute kidney injury (3), lack of continued insurance coverage (3), nausea (1), foot infection (1) and new onset neurologic disease with urinary retention (1). When comparing mean eGFR, HbA1C and UACR at baseline and 12 months, no statistically significant difference was noted. The mean eGFR, however, was maintained at 12 months at 53.1 mL/min/1.73 m2. UACR at 6 months was 216 mg/g. Mean BMI improved at 12 months as compared to baseline (29.6 vs 31.6, p=0.03). A statistically significant improvement in mean magnesium levels was also observed (1.8 vs 1.7 mg/dl, p=0.001) Conclusions: SGLT2is appear to be safe for use in KTRs with low risk of UTI, AKI, or foot infections, and overall low incidence of drug discontinuation. Further studies are needed to study long-term impact of SGLT2i on allograft and patient survival. [Formula presented] [Formula presented] CITATION INFORMATION: Kreitler K., Fitzmaurice M., Wright S., Khoury N., Shrivastava P., Patel A., Prashar R. Safety of Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2is) in Kidney Transplant Recipients AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES:

Nephrology

Lu Z, **Kumar V**, **Kumaresan K**, **Prashar R**, and **Patel A**. Renal Transplant Outcomes in Elderly Recipients: Age Alone Should Not Be a Barrier. *Am J Transplant* 2025;25(8):S893-S894. Full Text

Purpose: Elderly patients undergo fewer renal transplants due to concerns of increased mortality. We compared outcomes and risk factors for graft loss and mortality in our program's elderly recipients to evaluate these concerns and inform decision-making. Methods: Retrospective analysis of recipients from 1/2013 to 6/2022. Those aged 65 years (yrs.) and older who received primary renal transplants were included. Recipients were grouped into younger (RY; age 65-70 yrs.) and older (RO; age 70+ yrs.). Baseline recipient and donor variables and transplant outcomes were compared between the groups. Primary outcomes of interest were patient survival (PS) and graft survival (GS). Kaplan-Meier (KM) survival analysis and multivariate Cox regression analysis was performed on all variables with censoring date 11/26/23. Results: 199 recipients were included; 116 were RY, 83 were RO. RY had higher preoperative serum albumin, shorter EPTS, and higher rates of hypertension (HTN), ischemic heart disease (IHD), and vascular disease (PVD). More RO had no induction agent and had a donor with diabetes (DM). Foley duration was longer and hydronephrosis rate was higher in RY, while RO had a higher rate of urine leak. Other characteristics and posttransplant complications did not differ significantly between groups (Table 1). [Formula presented] RY and RO had similar KM probabilities of 1-10 year GS (p=0.21 - 0.91) and PS (p=0.23 - 0.95). Median GS was longer in RY (8.5 vs 6.4 yrs., p=0.08), as was PS (8.9 vs 7.2 yrs., p=0.05). Median GS was similar between groups (8.5 vs 6.4 yrs., p=0.08), while PS was longer in RY (8.9 vs 7.2 yrs., p=0.05). On multivariate analysis, higher 1-year serum creatinine was significantly associated with graft loss in both groups. Recipient DM, IHD, and DGF was associated with risk of graft loss and patient mortality for RY, while higher serum albumin was associated with lower risk for both outcomes for RO. Induction with Simulect (vs. no agent) was associated with lower risk for patient

mortality for RO (Figure 1). [Formula presented] Conclusions: Despite differences in baseline characteristics, we found comparable GS and PS between RY and RO groups, indicating that older age should not be a barrier to transplantation. Future analysis will include waitlisted and dialysis patients. CITATION INFORMATION: Lu Z., Kumar V., Kumaresan K., Prashar R., Patel A. Renal Transplant Outcomes in Elderly Recipients: Age Alone Should Not Be a Barrier AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: Z. Lu: None.

Nephrology
Lu Z, **Patel A**, and **Yoshida A**. Toward Better Organ Utilization: Identifying Missed Opportunities in Kidney Transplantation. *Am J Transplant* 2025;25(8):S375-S376. Full Text

Purpose: Some deceased donor kidneys (DDKs) refused by one transplant program are then accepted and transplanted elsewhere, indicating missed opportunities. We compared characteristics and transplant outcomes of DDKs accepted vs. initially refused by programs within one OPTN region to assess acceptance and utilization patterns across the region. Methods: Retrospective analysis of DDKs offered by a regional OPO to adult kidney programs from 8/2022 to 8/2024. Only DDKs that were transplanted were included. DDKs were classified as “kidney accepted (KA)” if accepted and transplanted by a regional program, or “kidney refused (KR)” if turned down by a regional program for donor and/or organ reasons and transplanted elsewhere. Programs were grouped into 3 tiers based on acceptance rate. Donor and kidney features and recipient outcomes were compared between groups in each tier. Outcomes of interest were rate of delayed graft function (DGF), recipient 6-month and 1-year serum creatinine (Se Cr) and 1-year graft survival (GS). Kaplan Meier survival analysis was performed with censoring date 8/16/24 and a Cox proportional hazards model was used to quantify the effect of initial refusal on graft loss. Results: 1046 DDKs, offered to 12 programs, were included. Program-specific acceptance rates ranged 7.1 - 35.7%, with 3 programs in the top tier (acceptance rate >20%), 5 in the middle (rate 10-20%), and 4 in the bottom (rate <10%). Over 75% of KR were refused for organ quality reasons, most often unacceptable biopsy and/or organ-specific results. Selected results are shown in Table 1. Across all tiers, KR kidneys had older donors with higher KDPI, longer cold ischemia time, and higher biopsy rates. DDKs accepted by the top tier had the fewest number of significant between-group differences (8 of 16 examined features), while those accepted by the middle tier had the most (12 of 16). DGF rates were higher in KR groups in the top and bottom tiers. Other outcomes were similar between groups across all tiers. KR kidneys had a nonsignificant higher risk of graft loss in the middle and bottom tiers. [Formula presented] Conclusions: With few exceptions, program acceptance rates were low (<20%), reflecting a need to improve DDK utilization across the region. Despite differences in baseline characteristics, we found overall comparable allograft outcomes between KA and KR groups, indicating a need for programs to rethink their donor acceptance and exclusion criteria. CITATION INFORMATION: Lu Z., Patel A., Yoshida A. Toward Better Organ Utilization: Identifying Missed Opportunities in Kidney Transplantation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: Z. Lu: None.

Nephrology
Lu Z, **Patel A**, and **Yoshida A**. Missed Opportunities in Kidney Transplantation: Time to Rethink Acceptance Practices. *Am J Transplant* 2025;25(8):S374-S375. Full Text

Purpose: Some deceased donor kidneys (DDKs) refused by one program are then accepted and transplanted elsewhere, suggesting missed opportunities for transplant. We compared characteristics and outcomes of transplanted DDKs accepted vs. initially refused by our program to assess the appropriateness of our acceptance criteria and identify adjustments needed to reduce missed opportunities. Methods: Retrospective analysis of OPTN data on DDKs offered by a regional OPO to a single center from 8/2022 to 8/2024. Only DDKs that were ultimately transplanted were included. DDKs were classified as either “kidney accepted (KA)” if accepted and transplanted by our program, or “kidney refused (KR)” if turned down by our program and transplanted elsewhere. Only DDKs refused for donor and/or organ reasons were included. Donor and organ characteristics and recipient outcomes were compared between the two groups. Outcomes of interest were rate of delayed graft function (DGF), recipient 6-month and 1-year serum creatinine (Se Cr), and 1-year graft survival (GS). Kaplan Meier (KM) survival analysis was performed with censoring date 8/16/24. Multivariate Cox regression of graft loss was performed on all variables. Results: 312 kidneys were included, with 65 (20.8%) in the KA group and

247 (79.2%) in the KR group. 89.5% of KR were turned down for organ-specific reasons, most often for unacceptable organ-specific test results (30%) and organ anatomical damage/defect (24.6%). KR kidneys had a higher degree of glomerulosclerosis and came from donors with higher KDPI and terminal creatinine. Other donor and kidney characteristics did not differ significantly between groups. Outcomes were similar between groups across all measures (Table 1). [Formula presented] On multivariate analysis, DGF was significantly associated with graft loss (HR 5.2, 95% CI [1.33 - 20.43], p=0.02) across the entire cohort. Kidneys that were initially refused (KR group) had a similar risk of failure as KA kidneys (HR 1.5, 95% CI [0.42 - 5.39], p=0.54). No significant risk factors for graft loss were identified within groups. Conclusions: Despite differences in donor and kidney characteristics, we found comparable allograft outcomes between KA and KR groups, indicating a need to rethink our acceptance filters and highlighting the importance of systematic review of donor exclusion criteria in every program. CITATION INFORMATION: Lu Z., Patel A., Yoshida A. Missed Opportunities in Kidney Transplantation: Time to Rethink Acceptance Practices AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: Z. Lu: None.

Nephrology
Lu Z, **Patel A**, and **Yoshida A**. Expanding Transplant Opportunities: Rethinking the Role of Offer Biopsy in Kidney Selection. *Am J Transplant* 2025;25(8):S375. Full Text

Purpose: Biopsy findings are a common refusal reason for deceased donor kidneys (DDKs) and some of these refused DDKs are then accepted and transplanted elsewhere, suggesting missed opportunities for transplant. We compared characteristics and outcomes of transplanted DDKs accepted vs. initially turned down for biopsy reasons by our program to assess the appropriateness of our acceptance criteria and identify adjustments needed to reduce missed opportunities. Methods: Retrospective analysis of OPTN data on DDKs offered by a regional OPO to a single center from 8/2022 to 8/2024. Only DDKs that were biopsied and ultimately transplanted were included. DDKs were classified as “kidney accepted (KA)” if accepted and transplanted by our program, or “kidney refused (KR)” if turned down by our program and transplanted elsewhere. DDKs refused for non-biopsy reasons were excluded. Donor and kidney characteristics and recipient outcomes were compared between the two groups. Outcomes of interest were rate of delayed graft function (DGF), recipient 6-month and 1-year serum creatinine (Se Cr), and 1-year graft survival (GS). Kaplan Meier (KM) survival analysis was performed with censoring date 8/16/24. Multivariate Cox regression of graft loss was performed on all variables across the entire cohort and within groups. Results: 103 DDKs were included, with 46 (44.7%) in the KA group, 57 (55.3%) in the KR group. KR kidneys had a higher degree of glomerulosclerosis and longer cold ischemia time. Other donor and kidney characteristics did not differ significantly between groups. Outcomes were similar between groups across all measures (Table 1). [Formula presented] No significant risk for graft loss were identified on multivariate analysis. Biopsied kidneys that were initially turned down (KR group) had a similar risk of failure as KA kidneys (HR 1.33, 95% CI [0.08 - 21.73], p=0.84). Conclusions: Despite differences in kidney characteristics, we found comparable allograft outcomes between KA and KR groups, reaffirming that biopsy findings should not be a consistent factor for refusal and indicating a need to adjust our donor exclusion criteria to reflect this understanding. CITATION INFORMATION: Lu Z., Patel A., Yoshida A. Expanding Transplant Opportunities: Rethinking the Role of Offer Biopsy in Kidney Selection AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: Z. Lu: None.

Nephrology
Oki R, **Varban O**, **Carlin A**, **Al-Kurd A**, **Nagai S**, **Yoshida A**, **Abouljoud M**, **Prashar R**, **Khoury N**, and **Shrivastava P**. Trends in Bariatric Surgery and Kidney Transplantation Status Among Patients with Advanced Chronic Kidney Disease: A 12-Year Retrospective Review. *Am J Transplant* 2025;25(8):S891-S892. Full Text

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Purpose: The prevalence of obesity is increasing among patients with end-stage renal disease (ESRD). Metabolic and bariatric surgery (MBS) is an effective method for weight loss in this population. This study

aims to examine the trends and outcomes in kidney transplant (KT) among patients with advanced chronic kidney disease (CKD) who underwent MBS. Methods: A retrospective review was conducted of all patients undergoing MBS between January 1, 2012, and Dec 31, 2024, within a large metropolitan health care system. Patients with CKD stage 5, ESRD, or history of KT at the time of MBS were identified and demographic information and comorbidities were examined. The log-rank test was used to compare patient and graft survival. Results: Fifty-eight patients were included, with a median age of 47 years and a median BMI of 43.8 kg/m2. Forty-one (70.7%) patients were female and 42 (73.4%) were Black. Hypertension and/or diabetes accounted for 75.8% of etiology, while cardiovascular disease (CVD) was present in 94.6%. (Table1)Twenty-nine patients underwent KT, of which 18 received KT before MBS and 11 after. No significant differences were observed in patient characteristics between the two groups(Table1). There was no significant difference in patient survival (p=0.979) between patients with or without KT(Fig.1). Among patients undergoing KT, no significant difference in patient (p=0.326) or graft survival (p=0.078) was observed based on timing of KT either before or after MBS. Black patients tended to have lower graft survival (p=0.070). A total of 13 (32.5%) patients were declined listing for KT after MBS. The reasons for decline included low cardiac function (30.8%), persistent obesity (15.4%), and other physical problems (15.4%). (Fig.2) Conclusions: MBS appears to be associated with similar patient and graft survival both before and after KT. Despite undergoing MBS nearly one-third of patients with CKD are declined listing for KT. [Formula presented] [Formula presented] [Formula presented] CITATION INFORMATION: Oki R., Varban O., Carlin A., Al-Kurd A., Nagai S., Yoshida A., Abouljoud M., Prashar R., Khoury N., Shrivastava P. Trends in Bariatric Surgery and Kidney Transplantation Status Among Patients with Advanced Chronic Kidney Disease: A 12-Year Retrospective Review AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: R. Oki: None.

Nephrology

Prashar R, and **Patel A**. Barriers to Living Donor Kidney Transplantation in Black Patients with Kidney Disease. *Am J Transplant* 2025;25(8):S907-S908. Full Text

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Purpose: Lower rates of Living donor kidney transplantation (LDKT) among Black patients are attributed to socioeconomic and cultural factors. We report results of a cross-sectional survey undertaken to assess attitudes towards LDKT in patients with kidney disease. Methods: Patients with ESRD and CKD from local dialysis centers and nephrology clinic were invited to complete a survey. The17-question survey was adapted from published measures of LDKT knowledge, attitudes and concerns. The BHLS (Brief health literacy screening) tool was included .We examined potential differences in attitudes towards LKD in Black vs white patients using T-tests and Fisher exact tests, The primary analysis assessed differences in attitudes towards LKD in Black vs white patients. The secondary analysis assessed differences based on gender, health literacy, median household income, dialysis status (on dialysis vs pre-emptive), and location of the dialysis center with respect to historic residential segregation. A sub-analysis was conducted in Black patients to examine the impact of low health literacy, and income. Results: 88 patients completed the survey. 62 patients identified as Black, 23 White, 3 Hispanic. Baseline characteristics are summarized in Table 1. Black patients had significantly lower median household income than white patients. Black patients were less likely to tell a potential donor how to contact the living donor(LD) program (29% vs 56%, p=0.02).Greater number of patients from dialysis units in areas of historic residential segregation reported that no-one in their family or friends' group know about LKD (47.8% vs 35.8%, p=0.04) and were fearful that they might lose KT (47.8% vs 33.3%, p=0.01).Patients with a low BHLS score (0-6) were less likely to tell their potential donors how to contact the LD team, as compared to patients with a BHLS score >6 (17% vs 46%, p=0.009). There was a trend towards significance in greater number of patients with inadequate health literacy feeling that out-of-pocket expenses for living donors are too high (76% vs 54%, p=0.06). On sub analysis of only black patients with inadequate vs marginal/adequate literacy, this trend became significant (82% vs 51% p=0.016). Conclusions: Limited health literacy and residential segregation play an important role in shaping black patients' attitudes with regards to receiving a LDKT. Each demographic area is unique with regards to interaction between socioeconomic and cultural factors as they relate to LDKT, and educational resources should be made available with a more targeted focus to address limited health literacy in patients with kidney disease [Formula presented] CITATION INFORMATION: Prashar R., Patel A. Barriers to Living Donor Kidney

Transplantation in Black Patients with Kidney Disease AJT, Volume 25, Issue 8 Supplement 1
DISCLOSURES: R. Prashar: None.

Neurology
Abu-Zahra T, **Mohamedelkhair A**, **Fu S**, and **Ramadan AR**. Subacute Cervical Posttraumatic Ascending Myelopathy: The Natural Course of the Disease (P3-4.002). *Neurology* 2025;104(7_Supplement_1). Full Text

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Objective: Present a rare case of subacute cervical posttraumatic ascending myelopathy (SPAM). Background: SPAM is a rare, delayed complication of spinal cord injury (SCI), which manifests as a neurological deterioration involving at least 4 segments above the initial injured level occurring within the first few weeks following SCI. Given its rarity, there is no consensus on how to manage this condition. We present a case of SPAM with initial injury level at C6 who progressed to involve myelopathic changes up to the C2 level. Design/Methods: NA Results: A 62-year-old female presents for acute onset weakness in the bilateral hands after lifting heavy objects. Within hours, the weakness extended caudally producing paraplegia and sensory loss to T4 level. MRI C-spine showed severe canal stenosis with cord compression by a disc osteophyte complex at C6-C7. The patient underwent a posterior decompression and fusion at C5-C7. Over the next two weeks, weakness ascended to upper extremities, graded between 4 and 4+/5. Sensory loss ascended to C8 level. Lumbar puncture only showed mild elevation of protein. Autoimmune, metabolic and toxic workup was negative. EMG showed no evidence of primarily demyelinating polyneuropathy. Given persistence of symptoms, MRI C-spine was repeated three weeks following injury which showed extensive high signal intensity extending from C2 to T3, with cord enhancement at C6-7. A few days later, the patient started improving, and repeat MRI C-spine showed significant decrease in T2 signal abnormality involving the cervical cord, only focally involving C6-7 and C4-5 level corresponding to residual spinal stenosis. Repeat CSF studies were normal. The clinical and radiographic improvement wasattributed to resolving SPAM. The patient received no corticosteroids/immunotherapy. Conclusions: Following SCI, SPAM is an important clinical and radiological pattern of neurological deterioration that is frequentlyunderrecognized. This case study provides insight into this disease's natural clinical and radiological progress with nomodifying therapy.

Neurology
Ahmad S, Akhter N, Contreras J, Ducruet AF, **Hoda N**, **Ahmad AS**, and Bhatia K. Remote ischemic post-conditioning (RIC) mediates anti-inflammatory signaling in murine traumatic optic neuropathy (TON). *Invest Ophthalmol Vis Sci* 2025;66(8). Full Text

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Purpose : Traumatic optic neuropathy (TON) is an uncommon vision threatening condition caused by either ocular or blunt/penetrating head trauma which is characterized by direct or indirect TON. We have earlier shown that remote ischemic post-conditioning (RIC) therapy is protective and reduces TON related retinal dysfunction but the molecular mechanisms underlying is unknown. Interestingly, the metabolic sensor, AMP-activated protein kinase alpha 1 (AMPKα1), plays significant role in M polarization andtranscriptional regulation of interleukin-10 (IL-10), an anti-inflammatory cytokine that alsopolarizes Ms to M2. However, a mechanistically-driven therapeutic study of myeloid-specific AMPKα1/IL-10 in TON remains completely unexplored. Here we proposed that RICtherapy is protective in TON via AMPKα1/IL10 activation in mice.Methods : We induced TON in mice by using controlled impact system as reportedpreviously. Male and female; C57BL/6 mice (8-10 wk old; Jackson) were injected with 250µg of mouse anti-IL-10r (clone 1B1.3a) or isotype-matched IgG1 (clone R3-34) antibodies in100 µl of PBS i.p. daily, starting one day prior to Sham/TON injury. 5-7 days post TON inpresence and absence of RIC therapy, the above mice are sacrificed. RIC therapy was givenevery day (5-7 days following TON). Western blotting, Immunohistochemistry, Flowcytometry and TEM technique were used to generate research data.Results : Our data demonstrated that IL10 depletion effects macrophages polarization inTON. We found that CD206+ (M1 marker) decreased in TON and CD68+ (M2 marker)increased compared with Sham however, RIC significantly attenuated this process but IL10inhibition further

increased CD68+ expression and RIC didn't change the expression. Wechecked the expression of microglial marker Iba-1, ganglion cell marker Brn3 and axonalmarker GAP43 and found that after IL-10 depletion RIC has no significant effect.Transmission electron microscopy (TEM) data of optic nerve showed increaseddemyelination and axonal degeneration in TON group and TON+RIC showed improvedmyelination however, IL-10 depletion caused more damage and RIC didn't help.Conclusions : Overall, these data suggest that RIC therapy is neuroprotective via myeloidAMPKα1/IL10 signaling by regulating macrophages polarization and inflammation in eyetrauma. Further investigation of RIC and.

Neurology
Nahmoud I, Lloyd SC, Wu M, **Rashid F**, **Giri S**, and Conti A. POA.081 - Morphine Amplifies Traumatic Brain Injury-Induced Neuroinflammation via the Kynurenine Pathway. *J Neurotrauma* 2025;42(13-14):e1109-e1229. Full Text

I. Nahmoud, Wayne State University, John D. Dingell VA Medical Center, Detroit, United States

Chronic pain affects over 50% of traumatic brain injury (TBI) patients, which has been strongly linked to neuroinflammation. Although opioids like morphine (MOR) are prescribed for post-TBI pain, they paradoxically worsen neuroinflammation, producing opioid-induced hyperalgesia. Therefore, identification of mechanisms underlying post-TBI pain, inflammation, and MOR action, are necessary to optimize post-TBI analgesia. The kynurenine pathway (KP) responds robustly to inflammation, producing kynurenic acid (KYNA, anti-inflammatory) and quinolinic acid (QUIN, proinflammatory), although their roles in TBI-induced pain, inflammation and MOR action remain unclear. Therefore, the KP was examined after 5 days of escalating MOR treatment (1-2 days post-injury (dpi), 4 mg/kg; 3-5 dpi, 8 mg/kg) in C57Bl/6 male mice (n=4-6) following closed-skull impact. Tactile thresholds (Von Frey), inflammatory cytokines (enzyme-linked immunosorbent assays), and KP metabolites (liquid-chromatography tandem mass spectrometry) were measured by 30 dpi. Tactile threshold in TBI-saline mice was significantly reduced at 5 dpi ($p<0.0001$ vs. sham-saline), which was reversed by MOR. However, at 30 dpi TBI-MOR mice exhibited significantly lower tactile thresholds than TBI-saline controls ($p<0.0001$). At 30 dpi, MOR exacerbated TBI-induced elevations in the pro-inflammatory cytokines, interleukin-1 beta and tumor necrosis factor-alpha, within the prefrontal and anterior cingulate cortices (all $p<0.0001$ vs. TBIsaline). TBI-induced elevations in cortical QUIN were further elevated by MOR at 30 dpi ($p=0.04$ vs. TBI-saline). These findings suggest that MOR treatment exacerbates TBIinduced elevations in chronic pain, neuroinflammation, and the central KP response, warranting future studies to explore the KP as a therapeutic target for post-TBI pain management.

Neurology
Qureshi M, **Katz B**, **Bansal P**, and **Cerghet M**. IgG4 Related Disease Presenting as Persistent Intracranial Hypertension (P9-11.011). *Neurology* 2025;104(7_Supplement_1). Full Text

M. Qureshi, Henry Ford Hospital, United States

Objective: We report a case of IgG4 related disease with isolated meningeal involvement resulting in persistent intracranial hypertension. Background: IgG4 related disease is a chronic, immune mediated fibroinflammatory disorder with a wide range of manifestations. Design/Methods: N/A Results: 32-year-old obese female presented to outside hospital with progressive headaches, blurred vision and new onset seizures. Initial examination revealed visual acuity of 20/40 with bilateral grade 4 disc edema. MRI brain demonstrated dural enhancement, hydrocephalus, and Chiari 1 malformation. A ventriculoperitoneal shunt was placed and meningeal biopsy demonstrated nonspecific acute and chronic inflammation with adjacent cerebritis. The patient improved following shunt placement but required shunt removal later due to intracranial infection. Nasal biopsy done showed acute on chronic inflammation. Following shunt removal, the patient noted worsening vision prompting presentation to the ED. She was found to have 20/400 vision in both eyes with pale edematous disc. MRI again showed diffuse dural and leptomeningeal enhancement. Lumbar puncture showed opening pressure of 29 with positive oligoclonal bands and IgG index of 1.3 -- consistent with CSF inflammation. Repeat brain biopsy and nasal biopsy showed similar findings to prior. Disc edema improved with oral acetazolamide, however, patient had persistent seizures prompting re-admission. Broad infectious and autoimmune lab workup, including serum IgG4 levels were

within normal limits. The third repeat meningeal biopsy met criteria for probable IgG4 related disease. The patient had stabilization of symptoms on oral steroids. She has been maintained on Rituximab without recurrent symptoms. Conclusions: IgG4 related disease has a wide range of manifestations that can include intracranial hypertension due to meningealinflammation. Serum IgG4 levels in IgG4 related disease may not be elevated if disease process is isolated to a single organsystem. Repeat biopsy may be warranted in cases of persistent inflammation to achieve the diagnosis, as in this case whichrequired multiple biopsies to confirm diagnosis.

Neurology
Walbert T, **Schultz L**, **Snyder JM**, and **Mohn DJ**. Electronic Assessment of Quality of Life in Glioma Patients Using the EORTC-QLQ-C30/ EORTC-BN20 and the PROMIS System in Clinical Practice (P3-6.008). *Neurology* 2025;104(7_Supplement_1). Full Text

T. Walbert, Neurosurgery and Neurology, Henry Ford Hospital Detroit, United States

Objective: We aim to assess feasibility of computer adaptations of the Patient-Reported Outcomes Measurement Information System (PROMIS) questionnaire in the clinical setting and compare it with outcomes of the EORTC-QLQ-C30 and EORTC-BN20 questionnaires. Background: Glioblastoma (GBM) is the most aggressive malignant primary brain tumor causing high levels of distress and morbidity. Electronic assessment of quality of life (HRQoL) with standardized methods is of importance. Design/Methods: Newly diagnosed patients with GBM were enrolled to assess feasibility. The PROMIS modules were selected to reflect the HRQoL domains assessed in the EORTC-QLQ-C30 and EORTC-BN20 questionnaires. PROMIS modules selected included anxiety, depression, fatigue, physical function, sleep disturbance, sleep-related impairment, social satisfaction role, applied cognitive ability and global health. Results: 31 patients completed the survey prior to or within 14 days of start of radiation, 12 patients completed a survey outside of the radiation window, and a total of 60 completed surveys were obtained between both patient groups. Descriptive analysis was performed. The median times to complete the EORTC-QLQ-C30 and the EORTC-BN20 surveys were 4.77 (range=2.05- 18.6) and 2.63 (range=1.17-24.83) minutes respectively. For the PROMIS instruments except global health, the median times to complete different modules ranged from 0.6-1 minute (range= 0.15-7.77). For global health, the median time was 2.35 minutes (range= 1.02-21.12). Average time to complete all PROMIS questions was 8.65 minutes (range=3.32-66.01). Conclusions: Real-time prospective assessment without integration into the clinic work-flow is a limiting factor of the PROMIS/EORTC.Online assessment from home was challenging for patients with less social support, low computer literacy and the burdenof disease also limits quantity of responses. Electronic assessment of QoL is preferred, but not all patients were able toparticipate.

Neurology
Zhang Y, **Zhang Y**, **Chopp M**, **Pang H**, **Wang X**, **Lu M**, **Chen L**, **Lu M**, **Zhang ZG**, **Mahmood A**, and **Xiong Y**. POB.066 - Therapeutic effects of miRNAs of exosomes derived from human bone marrow mesenchymal stem cells on histological outcome in rats after traumatic brain injury. *J Neurotrauma* 2025;42(13-14):e1186. Full Text

Y. Zhang, Department of Neurosurgery, Henry Ford Health, Detroit, United States

We previously showed that exosomes from naïve and engineered bone marrow mesenchymal stem cells (MSCs) improve functional recovery in rats after traumatic brain injury (TBI). This study examines the effects of MSC-derived exosomes with varying miRNA expression levels on histological outcomes following TBI. Young male rats with moderate TBI induced by controlled cortical impact injury (CCI) were randomly assigned to receive phosphate-buffered solution (PBS, control) or one dose of exosomes (100 lg/rat) from naïve MSCs (MSC group), MSCs overexpressing miR-17-92 (miR- 17-92 group), MSCs with an empty vector (miR-17-92-Empty group), MSCs with Argonaute 2 knockout with reduction of miRNAs (Ago2-KO group), or MSCs with an empty vector (Ago2-Vector group), administered 24 hours post-injury. Rat brains were collected 2 days post-injury for immunostaining of inflammatory markers (CD68, TNF alpha, CCR2), cell death (caspase-3), neurotrophic factors (BDNF, NGF), BBB breakdown (fibrin/fibrinogen), and synaptogenesis (Synaptophysin). Analysis of variance (ANOVA) followed by post

hoc Tukey's tests was used for data analyses. PBS-treated TBI rats significantly increased neuroinflammation, cell death, and BBB damage and decreased synaptogenesis and neurotrophic factor expression in the injured brain vs Sham group ($p<0.05$). Treatments from MSC, miR-17-92-Empty or Ago2- Vector groups significantly decreased neuroinflammation, cell death, and BBB damage and increased synaptogenesis and neurotrophic factor expression in the injured brain vs PBS group ($p<0.05$). Exosomes from the miR-17-92 group provided further benefits while exosomes from the Ago2-KO group exhibited opposite effects vs MSC group ($p<0.05$). These results support use of engineered exosomes enriched with select miRNAs as a potential treatment for TBI.

Neurosurgery
Chen L, **Xiong Y**, **Chopp M**, **Pang H**, **Gang Zhang Z**, **Mahmood A**, and **Zhang Y**. POA.047 - Therapeutic Effects of Vepoloxamer on Neuroprotection and Neurogenesis in Rat After Traumatic Brain Injury. *J Neurotrauma* 2025;42(13-14):e1129. Full Text

L. Chen, Henry Ford Health, Detroit, United States

Traumatic brain injury (TBI) is a major cause of death and disability worldwide. We have demonstrated that early intervention of Vepoloxamer promotes functional recovery in male and female rats after TBI. The aim of this study is to investigate the potential therapeutic mechanisms of Vepoloxamer on TBI by its antiinflammation and anti-thrombosis effects. Young male Wistar rats, subjected to moderate TBI induced by controlled cortical impact (CCI) injury, were treated randomly with 0 (saline as vehicle) and 300 mg/kg of Vepoloxamer intravenously (IV) 2 h after TBI. Neurological and cognitive functional tests were performed weekly after injury. Animals were killed 3 h, 26 h or 35 days after TBI and brain sections were processed for histopathological and immunohistochemical analyses of lesion volume, neuronal cell loss, neurogenesis, neuroinflammation and microthrombosis. Compared with saline treatment, Vepoloxamer treatment significantly improved neurological and cognitive functional outcomes, reduced lesion volume and prevented hippocampal neuronal cell loss at 26 h and 35 days post-TBI, reduced cerebral microthrombosis formation at 3 h and 26 h post-TBI, reduced the activation of proinflammatory M1 microglia/macrophages and augmented the activation of anti-inflammatory M2 microglia/macrophages in injured cortex at 35 days post-TBI, and enhanced hippocampal neurogenesis at 35 day post-TBI. Collectively, IV Vepoloxamer (300 mg/kg) administrated at 2 h post-TBI provides neuroprotection by anti-inflammation and antimicrothrombosis effects, and enhances neurogenesis in rats post- TBI, indicating that Vepoloxamer may have great potential value for TBI patients.

Neurosurgery
Ghimire B, **Jamil M**, **Rogers LR**, and **Girgis M**. Efficacy of systemic therapy in breast cancer with CNS metastases: “Real-world” experience. *J Clin Oncol* 2025;43(16). Full Text

B. Ghimire, Henry Ford Health System, Detroit, MI, United States

Background: The incidence of CNS metastases in breast cancer is rising. While local therapies such as surgery and radiation remain standard, data on upfront systemic therapies for active brain metastases, especially HER2-negative patients, is limited. This study examines upfront systemic therapy efficacy for CNS metastases in breast cancer patients at a single institution, including a majority African American (AA) population. Methods: A retrospective chart review included breast cancer patients with CNS metastases treated at Henry Ford Health (January 2014-July 2024). Eligible patients had not received concurrent local therapy; prior local therapy was permitted if unrelated to the studied lesions. CNS response was to be assessed using RANOBM (defines measurable disease as lesions > 10 mm) for parenchymal and modified RANO-LM criteria for leptomeningeal disease (LMD). Results: Among 35 patients (20 AA, 13 Caucasian), with a median age of 54 years, HER2-positive was the most common receptor type (49%), followed by HR-positive (37%) and triple-negative (14%); nearly half (46%) had HER2-low disease. Parenchymal metastases were predominant (86%); three had co-existing LMD, and two others had only LMD. Most metastases were multiple; 91% had lesions < 10 mm. 43% had prior WBRT or SRS to unrelated lesions. HER2-positive patients had the highest CNS overall response rate (ORR, 53%) and disease control rate (DCR, 94%), followed by HR-positive (ORR 31%, DCR 69%) and triple-negative (ORR and DCR 20%). Median PFS did not significantly differ between receptor groups (p =

0.130). Trastuzumab-deruxtecan (T-Dxd) was the most common regimen (10/35) and within HER2-positive and HR-positive groups. T-Dxd achieved CNS ORR of 60%, DCR of 90%, and median PFS of 16 months. Tucatinib-based regimens showed a 100% DCR with median PFS of six months. Other therapies, including sacituzumab, abemaciclib, and trastuzumab-emtansine, showed stable disease as the best response. Among AAs, HR-positive was the most common receptor type (50%). These patients had ORR of 35% and DCR of 65%. TDxd maintained ORR of 60% and DCR of 80%. Of five patients with LMD, three were HER2- positive, and two were HR-positive, with an ORR of 60%, and DCR of 80%. Conclusions: This “real-world” experience highlights that, at our institution, most patients with breast cancer and CNS metastases considered for upfront systemic therapy lack measurable disease (91% having lesions < 10 mm) typically required for clinical trials. Nonetheless, the response rate aligns with published experiences. In addition, we included patients with LMD, who are often excluded in trials. Our data also suggests impressive CNS responses with T-Dxd, both overall and in AA patients. The management of brain metastases and LMD in these patients is best approached in a multidisciplinary format.

Neurosurgery

Huang-Vredevoogd J, **Doemer A**, **Siddiqui S**, **Shah MM**, **Asadi AA**, **DiCarlo A**, **Scarpace L**, **Robin A**, **Lee I**, **Moceri A**, and **Thind K**. PPP04 Expanding Treatment Options for Reirradiation: The First Case of Gammatile Implantation in the Spine. *Brachytherapy* 2025;24(4):S20-S21. Full Text

Purpose: GammaTile® surgically targeted radiation therapy is a form of low dose rate brachytherapy in which Cs-131 seeds are embedded into a resorbable collagen-based matrix, allowing the seeds to be easily placed along a resection cavity during surgery. GammaTile has been used in several intracranial applications including the treatment of recurrent glioblastomas, meningiomas, and brain metastases as well as newly diagnosed brain metastases. However, it has not been used extracranially. This study describes the first use of GammaTile in the spine, for a patient who had rectosigmoid adenocarcinoma with recurrent metastatic disease in the sacrum. They received their first course of radiation in 2022 with external beam (54Gy in 30 fractions), followed by fractionated stereotactic radiation therapy to the recurrent lumbosacral disease in 2023 (30Gy in 5 fractions), and presented with pain in the legs and progressive disease in the sacrum. Given the patient's two prior courses of external beam radiation therapy, off-label use of GammaTile was pursued due to its ability to minimize dose to the nearby thecal sac, cauda equina and sacral nerve roots. Methods: GammaTile workflow for cranial applications involves estimating the surface area of the resection cavity to calculate the expected number of tiles needed. However, for this novel application, the number of tiles was estimated using a mock-up of the anticipated tile configuration based on the patient's MRI (Figure 1b), as well as a personalized 3D-printed replica of the patient's spine (Figure 1a).Following surgical resection, which included a partial L5 laminectomy and partial sacrectomy (Figure 1c), four tiles (16 sources) were placed “upside down” from the typical orientation, i.e., with the larger 3mm spacing facing toward the thecal sac to maximize separation and minimize dose to the cauda. Additionally, Fibrin sealant and absorbable gelatin were placed in between the tiles and the thecal sac to create further separation. Immediately after surgery, CT images were acquired in the OR for post-implant dosimetry and to verify the desired tile placement. These images were then used to calculate the delivered dose to the patient using the Eclipse planning system, and MIM was used to convert physical dose to biological effective dose to the thecal sac (BED3Gy) using the linear quadratic model for a permanent LDR implant and published values for the repair time, potential doubling time, and alpha values.1 Results: The post-implant calculated BED3Gy distribution is shown in Figure 1d. The D0.035cc physical dose and BED3Gy dose to the thecal sac was 89.8Gy and 106.4Gy respectively. At a 3-month post-operative appointment, the patient reported improved pain and was able to ambulate for longer distances with a walker. Conclusions: This study presents our institution's experience with the first use of Gammatile for the spine, highlighting the ability of our multi-disciplinary team to offer a novel treatment technique for a patient faced with either disease progression or a more extensive, life-altering surgery.

Neurosurgery

Walbert T, **Schultz L**, **Snyder JM**, and **Mohn DJ**. Electronic Assessment of Quality of Life in Glioma Patients Using the EORTC-QLQ-C30/ EORTC-BN20 and the PROMIS System in Clinical Practice (P3-6.008). *Neurology* 2025;104(7_Supplement_1). Full Text

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Objective: We aim to assess feasibility of computer adaptations of the Patient-Reported Outcomes Measurement Information System (PROMIS) questionnaire in the clinical setting and compare it with outcomes of the EORTC-QLQ-C30 and EORTC-BN20 questionnaires. Background: Glioblastoma (GBM) is the most aggressive malignant primary brain tumor causing high levels of distress and morbidity. Electronic assessment of quality of life (HRQoL) with standardized methods is of importance. Design/Methods: Newly diagnosed patients with GBM were enrolled to assess feasibility. The PROMIS modules were selected to reflect the HRQoL domains assessed in the EORTC-QLQ-C30 and EORTC-BN20 questionnaires. PROMIS modules selected included anxiety, depression, fatigue, physical function, sleep disturbance, sleep-related impairment, social satisfaction role, applied cognitive ability and global health. Results: 31 patients completed the survey prior to or within 14 days of start of radiation, 12 patients completed a survey outside of the radiation window, and a total of 60 completed surveys were obtained between both patient groups. Descriptive analysis was performed. The median times to complete the EORTC-QLQ-C30 and the EORTC-BN20 surveys were 4.77 (range=2.05- 18.6) and 2.63 (range=1.17-24.83) minutes respectively. For the PROMIS instruments except global health, the median times to complete different modules ranged from 0.6-1 minute (range= 0.15-7.77). For global health, the median time was 2.35 minutes (range= 1.02-21.12). Average time to complete all PROMIS questions was 8.65 minutes (range=3.32-66.01). Conclusions: Real-time prospective assessment without integration into the clinic work-flow is a limiting factor of the PROMIS/EORTC.Online assessment from home was challenging for patients with less social support, low computer literacy and the burdenof disease also limits quantity of responses. Electronic assessment of QoL is preferred, but not all patients were able toparticipate.

Neurosurgery
Zhang Y, **Zhang Y**, **Chopp M**, **Pang H**, **Wang X**, **Lu M**, **Chen L**, **Lu M**, **Zhang ZG**, **Mahmood A**, and **Xiong Y**. POB.066 - Therapeutic effects of miRNAs of exosomes derived from human bone marrow mesenchymal stem cells on histologi_cal outcome in rats after traumatic brain injury. *J Neurotrauma* 2025;42(13-14):e1186. Full Text

Y. Zhang, Department of Neurosurgery, Henry Ford Health, Detroit, United States

We previously showed that exosomes from naïve and engineered bone marrow mesenchymal stem cells (MSCs) improve functional recovery in rats after traumatic brain injury (TBI). This study examines the effects of MSC-derived exosomes with varying miRNA expression levels on histological outcomes following TBI. Young male rats with moderate TBI induced by controlled cortical impact injury (CCI) were randomly assigned to receive phosphate-buffered solution (PBS, control) or one dose of exosomes (100 lg/rat) from naïve MSCs (MSC group), MSCs overexpressing miR-17-92 (miR- 17-92 group), MSCs with an empty vector (miR-17-92-Empty group), MSCs with Argonaute 2 knockout with reduction of miRNAs (Ago2-KO group), or MSCs with an empty vector (Ago2-Vector group), administered 24 hours post-injury. Rat brains were collected 2 days post-injury for immunostaining of inflammatory markers (CD68, TNF alpha, CCR2), cell death (caspase-3), neurotrophic factors (BDNF, NGF), BBB breakdown (fibrin/fibrinogen), and synaptogenesis (Synaptophysin). Analysis of variance (ANOVA) followed by post hoc Tukey's tests was used for data analyses. PBS-treated TBI rats significantly increased neuroinflammation, cell death, and BBB damage and decreased synaptogenesis and neurotrophic factor expression in the injured brain vs Sham group ($p<0.05$). Treatments from MSC, miR-17-92-Empty or Ago2- Vector groups significantly decreased neuroinflammation, cell death, and BBB damage and increased synaptogenesis and neurotrophic factor expression in the injured brain vs PBS group ($p<0.05$). Exosomes from the miR-17-92 group provided further benefits while exosomes from the Ago2-KO group exhibited opposite effects vs MSC group ($p<0.05$). These results support use of engineered exosomes enriched with select miRNAs as a potential treatment for TBI.

Nursing

Jindal D, **Hirko K**, **Cassidy-Bushrow A**, **Ghosh S**, **Susick L**, **Latack K**, **Shetty P**, and **Neslund-Dudas C**. Racial differences in prevalence of coronary artery calcification among patients undergoing lung cancer screening. *J Clin Oncol* 2025;43(16). Full Text

D. Jindal

Background: Coronary artery calcification (CAC) is a known risk factor for coronary heart disease. Lung cancer screening (LCS) with low-dose computed tomography (LDCT) can detect lung cancer at earlier stages and reduce mortality. Additionally, CAC are common incidental findings among patients undergoing LDCT for LCS. However, racial differences in incidental findings of CAC among LCS patients have not been thoroughly investigated. We examined the association between race and presence of moderate to severe CAC among patients undergoing LDCT for LCS. Methods: We conducted a retrospective analysis of electronic health records (EHR) from Henry Ford Health (2016-2023) among patients undergoing LDCT for LCS. CAC was classified as moderate or severe (vs. none or mild). Race was categorized as Black, White, Asian, American Indian/Alaskan Native, Other and Unknown. We focused on Black and White patients, owing to the small sample size in the other groups. Multivariable logistic regression was used to examine the association between race and presence of moderate to severe CAC, adjusting for age, sex, and tobacco smoking status. Results: A total of 15,911 patients who were eligible for LCS and completed at least one screen during our study period were included. Of these, 79.6% were White and 20.4% were Black. The mean age of patients was 63.865.8 years; 50.4% were male and 61.4% reported current tobacco smoking. Demographic comparisons show that White patients were more frequently male compared to Black patients (50.9% vs 47.9%, p = 0.002). In addition, Black patients were slightly older (64.365.7 vs 63.665.8 years) and reported a higher current tobacco smoking status (67.9% vs 59.7%, p < 0.0001) compared to White patients. The prevalence of moderate to severe CAC was 10.9% overall and was higher among Black vs White patients (16.1% vs 9.6%, p < 0.0001). After covariate adjustment, Black patients had significantly higher odds of moderate to severe CAC compared to White patients (odds ratio [OR] = 1.8, 95% CI 1.6-1.9, p < 0.0001). Conclusions: The study findings suggest significant racial differences in the prevalence of CAC among patients undergoing LCS. Race may be an important factor when assessing cardiovascular risk in patients undergoing LCS and may have implications for screening protocols and preventive strategies. Future research is needed to explore the impact of these differences on risk and mortality from cardiovascular diseases.

Nursing

Kreitler K, **Fitzmaurice M**, **Wright S**, **Khoury N**, **Shrivastava P**, **Patel A**, and **Prashar R**. Safety of Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2is) in Kidney Transplant Recipients. *Am J Transplant* 2025;25(8):S413. Full Text

Purpose: SGLT2is have the potential to improve kidney function in kidney transplant recipients (KTRs) by reducing proteinuria and preserving eGFR, but safety concerns exist due to increased risk of urinary tract infections (UTI), volume depletion and genital infections in immunocompromised patients. We present a single center retrospective study assessing the safety of SGLT2i in KTRs. Methods: Data from 130 KTRs who were started on SGLT2i following KT were retrospectively collected from a single academic center. Data at drug initiation, and 12 months were assessed. T-test was performed to assess statistical significance in difference in clinical characteristics of KTRs at baseline and at 1 year post SGLT2i initiation. Results: Baseline characteristics are summarized in Table 1. Empagliflozin was the most prescribed SGLT2i and median time from transplant to drug initiation was 731 days. 45% of patients had diabetes pre-transplant, 37% had new onset diabetes post-transplant, and 18% were non-diabetics. Mean baseline estimated eGFR was 55.2 mL/min/1.73 m2. Mean HgbA1c at initiation was 6.9%, and urine albumin creatinine ratio (UACR) was 262 mg/g. 26% of patients had glycosuria at baseline. At 12 months, 88% patients developed glycosuria, 13 (10 %) had UTIs, and but only 16 (12.3%) patients had discontinued the needed to discontinue the SGLT2i. The reasons for drug discontinuation were recurrent UTIs (7), AKI acute kidney injury (3), lack of continued insurance coverage (3), nausea (1), foot infection (1) and new onset neurologic disease with urinary retention (1). When comparing mean eGFR, HbA1C and UACR at baseline and 12 months, no statistically significant difference was noted. The mean eGFR, however, was maintained at 12 months at 53.1 mL/min/1.73 m2. UACR at 6 months was 216 mg/g. Mean

BMI improved at 12 months as compared to baseline (29.6 vs 31.6, p=0.03). A statistically significant improvement in mean magnesium levels was also observed (1.8 vs 1.7 mg/dl, p=0.001) Conclusions: SGLT2is appear to be safe for use in KTRs with low risk of UTI, AKI, or foot infections, and overall low incidence of drug discontinuation. Further studies are needed to study long-term impact of SGLT2i on allograft and patient survival. [Formula presented] [Formula presented] CITATION INFORMATION: Kreitler K., Fitzmaurice M., Wright S., Khoury N., Shrivastava P., Patel A., Prashar R. Safety of Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2is) in Kidney Transplant Recipients AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES:

Ophthalmology and Eye Care Services

Deshmukh S, **Alsumait A**, Wang C, and Leffler C. Comparative Evaluation of ChatGPT-4 andOphthalmologist-in-training in the Triage ofPatient Messages Sent to the Eye Clinic viaElectronic Medical Record. *Invest Ophthalmol Vis Sci* 2025;66(8). Full Text

S. Deshmukh, Virginia Commonwealth University, School of Medicine, Richmond, VA, United States

Purpose : Chat Generative Pre-Trained Transformer (GPT-4), an artificial Intelligencemodel, has been proposed to have many applications in the field of medicine includingdiagnosis, triage, medical recordkeeping, education, and literature analysis. The role ofGPT-4 in Ophthalmology has previously been studied only to process queries posted in anonline medical forum. We conducted a restrospective cohort study to test theeffectiveness of GPT-4 in triaging real patient messages sent to our eye clinic. Methods : Messages from patients sent via Epic MyChart to Virginia CommonwealthUniversity (VCU) General Eye Clinic from January 2023 - August 2023 were recorded.Patient messages sent to the general eye clinic were de-identified and triaged by anophthalmologist-in-training as well as GPT-4. Ophthalmologists and GPT-4 were bothasked to direct patients to either general or specialty eye clinics, urgently or non-urgently,depending on the severity of the condition. Our two main outcome measures includedGPT-4's ability to accurately direct patient messages to 1) a general or specialty eye clinicand 2) determine the time frame within which the patient needed to be seen (triageacuity). Accuracy of recommendations made by GPT-4 were determined by comparingpercent agreement with those made by the Ophthalmologist.Results : The study included 139 patient messages. We noted agreement betweenrecommendations made by ChatGPT and Ophthalmologist in the majority of the cases.Similar recommendations were made with regard to general/specialty clinic (64.7%) andtriage acuity (60.4%). We also noted that GPT-4 recommended a triage acuity equal to orsooner than ophthalmologist for 93.5% of cases, and only recommended a less urgenttriage acuity in 6.5% of cases.Conclusions : To our knowledge, this is the first time that GPT-4 was assessed using realpatient queries in an Ophthalmology clinic. Our study indicates an Artifical Intelligencesystem such as GPT-4 would complement physician judgment in triaging ophthalmiccomplaints. These systems may assist providers and reduce the workload ofophthalmologists and ophthalmic .

Ophthalmology and Eye Care Services

Hicks PM, Dobson JN, Mitchell J, **Darnley-Fisch D**, Heisler M, Resnicow K, **Imami NR**, and Newman-Casey PA. Barriers and Facilitators of Glaucoma Medication Adherence by Patient and Neighborhood-level Factors in the Support, Educate, Empower Personalized Glaucoma Coaching Program Pilot Study. *Invest Ophthalmol Vis Sci* 2025;66(8). Full Text

P.M. Hicks, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, MI, United States

Purpose : To identify barriers and facilitators to glaucoma medication adherence for participants in the Support, Educate, Empower Personalized Glaucoma Coaching Program Pilot Study and assess any differences by age, sex, race, and Area Deprivation Index (ADI). Methods : This was a mixed-methods study of patients that reported glaucoma medication adherence of ≤80.00%. Patient (age, sex, and race) and neighborhood (ADI) factors were obtained, and patients completed an interview. To better understand the barriers and facilitators to glaucoma medication adherence, patient interviews were transcribed and analyzed using the modified Penchansky and Thomas framework. This framework is instrumental in identifying and analyzing potential barriers to accessing healthcare services, and it helps in developing strategies to improve service delivery and patient outcomes. Results : Of the 44 patients,

52.27% were ≥65 years old, 45.45% female, 50% Black, and 34.09% lived in high ADI neighborhoods. Barriers and facilitators were reported across all domains except accommodation/adequacy. The most frequent barriers were patient-level factors (50%), and the most common facilitator were patient-level factors (45%). Difficulty with medication schedule was the top barrier for various demographics, including age groups, genders, races, and ADI levels. A daily routine around taking eye drops was the leading facilitator for 40-64-year-olds (19%). Location of eye drops was the leading facilitator for patients ≥65 years old (33%), females (25%), Black race (20%), White race (30%), low-ADI (36%) and mid-ADI (16%). Having an additional medication supply was the leading facilitator for males (25%) and social support for high-ADI (13%). Conclusions : Among glaucoma patients with poor adherence, difficulty with the medication schedule was the most frequent barrier to optimal adherence among all patients regardless of age, race, or ADI score, while having a daily routine around taking eye drops was reported as the most common facilitator to optimal medication adherence among patients of all ages and races, women, and those who lived in low and medium ADI areas. The issue of providing support to integrate glaucoma medication taking into the daily routine is a highly salient issue to address in coaching for glaucoma disease selfmanagement.

Ophthalmology and Eye Care Services
Newman-Casey PA, Niziol L, Lu MC, **Darnley-Fisch D**, Resnicow K, Mitchell J, **Imami NR**, and Heisler M. The Support, Educate, Empower (SEE) Personalized Glaucoma Coaching Trial Results. *Invest Ophthalmol Vis Sci* 2025;66(8). Full Text

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Purpose : Test the effect of the Support, Educate, Empower (SEE) personalized glaucomacoaching program in a sample of medically-treated glaucoma participants with poor self-reported adherence on the following outcomes: 1) the primary outcome, medicationadherence; 2) the secondary outcome, glaucoma-related distress (GRD); 3) the exploratoryoutcome, intraocular pressure (IOP).Methods : Patients with glaucoma taking ≥1 eyedrop medications and self-reportingadherence ≤85% were recruited from two sites (University of Michigan [UM] and HenryFord Health System [HFHS]). Eligible participants were randomized 1:1 to the SEEintervention or usual care. The SEE intervention included motivational interviewing-basedcoaching alongside personalized glaucoma education at three in-person sessions from atrained non-physician counselor, four between-visit phone calls to discuss adherencescore, and automated medication reminders. All participants were followed for 6 monthsduring which medication adherence was monitored electronically (AdhereTech, New York,NY), and GRD (Modified Diabetes Distress Scale) and IOP (iCare tonometer; Tiolat Oy,Helsinki, Finland) were measured at study enrollment and exit. Medication adherence wascalculated as the percentage of doses taken by doses prescribed over the 6-month studyperiod. Outcomes were compared between SEE intervention and usual care groups with 2-sample t- and Wilcoxon tests.Results : 235 participants were enrolled (107 UM, 128 HFHS) and randomized (117 SEEintervention, 118 control). Participants were 67±11 (mean±standard deviation) years old,53% female, 30% White and 61% Black, and 63% reported income <$60k, 24% $61-$120k,and 13% >$120k. Electronically monitored adherence was significantly better in SEEintervention participants than usual care (77.6%±19.7 vs 58.0%±25.2, respectively,p<0.0001), as was change in GRD (-0.58±0.87 vs -0.23±0.74, p=0.003), and IOP in the eyewith worse mean deviation trended towards improvement (-1.01±4.54 vs 0.15±3.72,p=0.12) while IOP in the eye with better mean deviation showed no difference (-0.36±3.43vs -0.14±4.91, p=0.49).Conclusions : The SEE personalized glaucoma coaching program was a multi-facetedintervention that improved medication adherence and glaucoma related distress inglaucoma patients with poor self-reported adherence. There was a trend towards animprovement in IOP control.

Ophthalmology and Eye Care Services
Qureshi M, **Katz B**, **Bansal P**, and **Cerghet M**. IgG4 Related Disease Presenting as Persistent Intracranial Hypertension (P9-11.011). *Neurology* 2025;104(7_Supplement_1). Full Text

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Objective: We report a case of IgG4 related disease with isolated meningeal involvement resulting in persistent intracranial hypertension. Background: IgG4 related disease is a chronic, immune mediated fibroinflammatory disorder with a wide range of manifestations. Design/Methods: N/A Results: 32-year-old obese female presented to outside hospital with progressive headaches, blurred vision and new onset seizures. Initial examination revealed visual acuity of 20/40 with bilateral grade 4 disc edema. MRI brain demonstrated dural enhancement, hydrocephalus, and Chiari 1 malformation. A ventriculoperitoneal shunt was placed and meningeal biopsy demonstrated nonspecific acute and chronic inflammation with adjacent cerebritis. The patient improved following shunt placement but required shunt removal later due to intracranial infection. Nasal biopsy done showed acute on chronic inflammation. Following shunt removal, the patient noted worsening vision prompting presentation to the ED. She was found to have 20/400 vision in both eyes with pale edematous disc. MRI again showed diffuse dural and leptomeningeal enhancement. Lumbar puncture showed opening pressure of 29 with positive oligoclonal bands and IgG index of 1.3 -- consistent with CSF inflammation. Repeat brain biopsy and nasal biopsy showed similar findings to prior. Disc edema improved with oral acetazolamide, however, patient had persistent seizures prompting re-admission. Broad infectious and autoimmune lab workup, including serum IgG4 levels were within normal limits. The third repeat meningeal biopsy met criteria for probable IgG4 related disease. The patient had stabilization of symptoms on oral steroids. She has been maintained on Rituximab without recurrent symptoms. Conclusions: IgG4 related disease has a wide range of manifestations that can include intracranial hypertension due to meningealinflammation. Serum IgG4 levels in IgG4 related disease may not be elevated if disease process is isolated to a single organsystem. Repeat biopsy may be warranted in cases of persistent inflammation to achieve the diagnosis, as in this case whichrequired multiple biopsies to confirm diagnosis.

Otolaryngology – Head and Neck Surgery

Boakye EA, **Jin J**, **Williams AM**, **Chang SS**, **Suhael M**, **Siddiqui F**, **Ghanem T**, and **Tam S**. Evaluation of sleep quality and quality of life among patients newly diagnosed with head and neck cancer. *J Clin Oncol* 2025;43(16). Full Text

E.A. Boakye, Henry Ford Health System, Detroit, MI, United States

Background: Patients diagnosed with head and neck cancer (HNC) often suffer from distress attributed to their cancer diagnosis which may disturb their sleep, in turn impacting their quality of life (QoL). However, there is lack of research about the association between poor sleep quality and QoL among patients newly diagnosed with HNC. We assessed the association between in poor sleep quality and QoL among patients with HNC before starting treatment. Methods: This is a retrospective cohort study of patients with HNC between January 2019 and September 2022. All patients with HNC treated at this tertiary care health system are evaluated prior to starting treatment by psych-oncology, using a semi-structured assessment and validated measures including the FACT-HN and Insomnia Severity Index (ISI). The FACTHN is a 27-item validated instrument that consists of five subscales: that assesses the patient's quality of life in the physical, social/family, emotional, functional domains, and HNC-specific domains. Sleep quality was assessed via ISI, a 7-item self-report questionnaire assessing the nature, severity, and impact of sleep difficulties (defined as absence, sub-threshold, moderate, or severe). We used five beta regression models to examine the association between sleep quality via the ISI and QoL via the FACT-HN (one for each subscale: emotional, social, physical, functional, and hand and neck). These models are adjusted with a variety of demographic covariates and social factors along with clinical factors. To estimate confidence intervals, bootstrap methods with bias correction were employed. Results: The analysis included 312 patients, 5.4% reported severe and 15.1% moderate sleep difficulties. After adjusting for other covariates, sleep difficulties were significantly associated with all FACT-HN subscales. Compared to patients with no sleep difficulties, patients with severe difficulties had a decrease in emotional (β=-1.33, 95% CI, -1.67, -0.93), social (β=-0.90, 95% CI, -1.66, -0.37), physical (β=-2.27, 95% CI, -2.67, -1.74), functional (β=-1.64, 95% CI, -2.10, -0.87), and head and neck (β=-1.11, 95% CI, -1.58, -0.65) QoL. Similarly, compared to patients with no sleep difficulties, those with severe difficulties had a decrease in emotional (β=-1.34,95%CI, -1.66, -0.98), social (β=-0.61, 95% CI, -0.99, -0.17), physical (β=-1.85, 95% CI, -2.18, -1.49), functional (β=-1.37, 95% CI, -1.71, -0.89), and head and neck (β=-1.04, 95% CI, -1.34, -0.69) QoL. Conclusions: We found that patients with moderate or severe sleep difficulties had poor QoL. Early evaluation and tailored intervention to improve sleep quality are necessary to prepare

these patients for HNCtreatment and its consequences. Future studies are needed on sleep quality among patients during and after treatment.

Otolaryngology – Head and Neck Surgery
Surapaneni S, Baxter Z, **Tam S**, Bernacchi V, **Chang SS**, **Yaremchuk K**, and **Boakye EA**. A scoping review of uptake and interventions in specialty and non-primary care clinical settings. *J Clin Oncol* 2025;43(16). Full Text

S. Surapaneni

Background: Persistent human papillomavirus (HPV) infection significantly increases the risk of developing several cancers, including cervical, anal, and oropharyngeal cancers. According to CDC guidelines, vaccinations are recommended for individuals ages 9-26 and have been expanded to include some adults aged 27-45 based on a shared decision-making process with their clinician. It is estimated that over 90% of the HPV-associated cancers could be prevented with the HPV vaccine. Despite substantial evidence regarding the safety and effectiveness of the HPV vaccine, vaccination rates remain below the Healthy People 2030 goal of 80%, with vaccines primarily administered in primary care settings. Specialty clinics and non-primary care clinics that do not traditionally offer HPV vaccination, present an opportunity to improve vaccine uptake. This scoping review evaluates the potential impact of HPV vaccination in non-primary care settings. Methods: Our approach to data collection and analysis was guided by Arksey and O'Malley's scoping review framework, and the Preferred Reporting Items for Systematic reviews and meta-analyses extension for Scoping Reviews (PRISMA-ScR). Ovid MEDLINE, Embase, and Web of Science were queried to include articles published in the US from 2006 to 2024 using search terms such as human papillomavirus vaccination and specialty clinics by an academic librarian. Original empirical studies were included, there were no restrictions on study design. Results: Out of the 1752 studies identified, 10 studies met the inclusion criteria, including 5 retrospective observational studies, 2 cross sectional studies, 1 randomized control trial, 1 pre-post study, and 1 survey study. Sample size for studies included ranged from 50 to 3709 participants, age range 18-45 years. Settings included otolaryngology, OBGYN, family planning, and substance health services. Baseline vaccination rate ranged from 5.2% to 47%. Five studies were interventional, and evaluated the effects of patient counseling, pharmacistphysician education, free vaccination or mailed reminders on HPV vaccination rates. The interventions resulted in increases in vaccination from 5.6% to 16%. Conclusions: Practice settings for interventions included in this scoping review focused on specialties that treat the downstream effects of HPV vaccination or high-risk populations. For adults eligible for HPV vaccination, specialty outpatient clinics may present a unique additional opportunity to discuss and deliver HPV vaccination, especially since providers in these settings also treat HPV-related diseases and are well equipped to engage in shared decision making with patients. Future research should focus on the acceptability, feasibility, and effectiveness of implementation of an HPV vaccination program in these settings.

Palliative Medicine
Zimmer M, **Abad J**, **Gupta J**, **Ghosh S**, and **Kuriakose P**. MM-423: Secondary Hematologic Malignancies in Patients With Multiple Myeloma: A Retrospective Analysis of Risk Factors and Incidence in a Large Urban Health System. *Clin Lymphoma Myeloma Leuk* 2025;25:S919. Full Text

Multiple myeloma (MM) is a common hematologic malignancy. While overall survival has improved due to advances in therapy, there is concern regarding the risk of secondary hematologic malignancies (SHM). Objective: To identify patients treated for MM who subsequently developed SHM and estimate the incidence and timing of SHM. Design: Retrospective, observational study. Setting: Henry Ford Health, a large urban, tertiary care network in Detroit, MI. Patients: Patients age 18 years or more with a confirmed diagnosis of MM between January 2005 and December 2022 and a subsequent SHM diagnosis were identified through electronic medical records review. Results: Of 3122 patients with MM, 297 were identified by automatic data pull as having a diagnosis of SHM. After manual review, nine patients met the inclusion criteria. Six patients (66.7%) were male. Median age at MM diagnosis was 62 (range: 53–73) years. About 44.4% were African American, 33.3% were Caucasian, 11.1% were Asian, and 11.1% identified as other. At a median follow-up of 58 (range: 35–144) months, most patients (66.6%) had

received only one line of therapy, some had two lines (22.25%), and one patient had received 12 lines of therapy. Five patients (55.6%) underwent autologous stem cell transplantation. Most patients (77.8%) received maintenance therapy, most commonly with lenalidomide (66.7%), for a median duration of 11 (range: 0–29) months. SHM were diagnosed at a median of 4 years after MM diagnosis, being primarily myeloid in origin (77.8%). Median time from MM diagnosis to death was 64 (range: 49–78) months, and median time from SHM diagnosis to death was 5 (range: 0–9) months. Conclusion: Despite the sample size and retrospective nature, our study has some key findings. First, the incidence of SHM was 0.2%, which is significantly less than the 8–18% in previous studies. Second, most patients were not heavily pretreated, often receiving only 1–2 lines of therapy and shorter duration of lenalidomide maintenance prior to the development of SHM. Accordingly, further work needs to be done to evaluate the impact of both patient- and disease-dependent factors, as well as MM therapy, on the development of SHM.

Pathology and Laboratory Medicine

Nagai S, **Nowicki M**, **Oki R**, **Rajendran L**, **Kerby E**, **Mohamed A**, **Nassar A**, **Al-Kurd A**, **Yoshida A**, and **Abouljoud M**. Cost Analysis of Machine Perfusion in DCD Liver Transplantation: Balancing Expenses and Post-Transplant Outcomes. *Am J Transplant* 2025;25(8):S739. Full Text

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Purpose: Organ utilization has increased, along with the adoption of machine perfusion (MP). While MP may improve liver utilization, concerns about medical costs remain. This study analyzes expenses based on MP use and post-transplant complications. Methods: Data on medical expenses were collected for donation after circulatory death (DCD) liver translants (LT) between Jan 2019 and Jan 2024. Patients were classified: static cold storage (SCS) without complications (Group 1), SCS with complications (Group 2), MP without complications (Group 3), and MP with complications (Group 4). Complications included reoperations, biliary complications requiring stenting, and readmissions within 1-year post-transplant for any reason. Costs associated at initial admission and all encounters within 1-year post-transplant were compared. The cost at initial admission included the organ acquisition cost (MP management, transportation), surgery, reoperations, and procedures at initial admission. The cost for all encounters within 1-year post-transplant encompassed follow-ups, readmissions, and necessary procedures after discharge. Results: A total of 116 LT-alone were performed, with 5 patients excluded from the analysis due to mortality within 1 year. Thus, 111 cases were included. The number of patients in Groups 1, 2, 3, and 4 was 14, 35, 23, and 39, respectively. No significant differences in patient characteristics were observed among the four groups. Post-transplant complications occurred in 71.4% (35/49, including 8 cases of ischemic cholangiopathy) of the SCS group and 62.9% (39/62) of the MP group. The cost at initial admission was significantly higher in Group 3 ($231,368) and Group 4 ($233,204) compared to Group 1 ($139,043) and Group 2 ($159,267), primarily due to the increased organ acquisition cost associated with MP use ($p < 0.001$). No significant difference in total cost was observed between Groups 2 and 3 ($p=0.266$, Fig.1). When comparing the sum of the initial admission cost and all encounters 1-year post-transplant cost, significant differences were observed between Group 1 and 2 ($p < 0.001$) as well as between Group 3 and 4 ($p = 0.017$). The absolute cost difference was larger between Groups 1 and 2 ($80,103 per case) compared to Group 3 and 4 ($29,135 per case). Conclusions: While MP use increased the initial admission cost in DCD LT, total costs over one year were comparable between SCS with complications and MP without complications. MP was associated with fewer and less costly complications, suggesting that complications after SCS DCD LT may lead to more severe or persistent issues. Financial concerns about MP should be weighed against its potential to reduce complications and long-term costs.

Pathology and Laboratory Medicine

Saleem A, **Obri M**, **Ilyas O**, **Alomari A**, **Faisal M**, **Abusuliman M**, **Chaudhary A**, **Rehman S**, **Franco-Palacios D**, **Nagai S**, **Venkat D**, and **Jafri S**. Outcomes and Risk Factors for Post-Operative Rejection and Transaminitis Following Dual Liver-Lung Transplantation: A Retrospective Cohort Study. *Am J Transplant* 2025;25(8):S468-S469. Full Text

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Purpose: Dual liver-lung transplantation (DLLT) is a rare and complex procedure, with limited data on post-operative rejection and liver function abnormalities. Understanding risk factors for acute cellular rejection and transaminitis is critical for optimizing immunosuppressive management. This study evaluates post-transplant outcomes in DLLT recipients and explores associations with recipient demographics, transplant indication, and underlying liver/lung disease etiology. Methods: A retrospective analysis was conducted on patients at our center who underwent DLLT between 2013 and 2024. Data collected included demographics, transplant indications, length of stay, incidence of acute rejection, and subsequent infections. Post-operative liver function tests (LFTs) beyond one month post-transplant were analyzed, and their relationship with age at transplant, liver disease etiology, and lung disease etiology was assessed. Results: A total of 10 patients (5 males, 5 females, mean age 53.7 years) underwent DLLT between 2013 and 2024. Liver disease etiologies were ethanol-related cirrhosis (n=2), hepatitis C (n=1), cryptogenic cirrhosis (n=1), autoimmune hepatitis (n=1), cystic fibrosis (n=1), and other unspecified causes (n=4). Lung transplant indications included idiopathic pulmonary fibrosis (n=5), pulmonary hypertension (n=2), other forms of interstitial lung disease (n=2), and cystic fibrosis (n=1).Post-operatively, 4 of 10 patients developed transaminitis beyond one month post-transplant, with liver biopsy confirming acute cellular rejection. Three patients received IV solumedrol, while one was managed with an oral steroid taper. Transaminitis resolved in all four cases after steroid treatment. Within three months, two patients treated with IV solumedrol developed infections from Candida and Aspergillus, though none developed CMV viremia. Two deaths occurred in the cohort. One patient passed away four years after transplant due to multifocal pneumonia, while the second patient passed away nine years post-transplant due to septic shock secondary to pneumonia in the setting of a new diagnosis of angiosarcoma. Neither patient had experienced rejection. Rejection and transaminitis were not significantly associated with age at transplant, liver disease etiology, or lung disease etiology. Conclusions: This study provides one of the first detailed assessments of rejection and liver function abnormalities following DLLT. While transaminitis and acute cellular rejection occurred in 40% of patients, no clear predisposing factors were identified. IV solumedrol use for rejection was associated with increased infection risk, emphasizing the need for careful immunosuppressive management in this population. Further research with larger cohorts is essential to improve risk stratification and post-transplant care in DLLT recipients. CITATION INFORMATION: Saleem A., Obri M., Ilyas O., Alomari A., Faisal M., Abusuliman M., Chaudhary A., Rehman S., Franco-Palacios D., Nagai S., Venkat D., Jafri S. Outcomes and Risk Factors for Post-Operative Rejection and Transaminitis Following Dual Liver-Lung Transplantation: A Retrospective Cohort Study AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Saleem: None.

Pharmacy

Eshaya M, **Franco-Palacios D**, **Jakupovic L**, **Patel A**, **Tong M**, **Poparad-Stezar A**, and **Fitzmaurice M**. Real-World Use of Maribavir vs. Valganciclovir in Solid Organ Transplant (SOT) Patients with or without Refractory Cytomegalovirus Disease. *Am J Transplant* 2025;25(8):S590. Full Text

Henry Ford Transplant Inst, Detroit, MI USA

Purpose: Cytomegalovirus (CMV) infection is a major complication in solid organ transplant (SOT) recipients, impacting graft function and survival. The SOLSTICE trial demonstrated maribavir's (MBV) superiority to investigator-assigned therapy for CMV clearance by week 8, yet data on MBV use in SOT patients with non-refractory CMV remains limited, and the impact of MBV on calcineurin inhibitor (CNI)-based immunosuppression (IS) has not been well characterized. The purpose of this study was to assess the efficacy of MBV for viremia clearance in a variety of SOT recipients and the real-world impact of MBV on CNI levels. Methods: This was a retrospective, single-center study of SOT recipients treated with MBV or valganciclovir (VGC) between 2021 to 2024. The primary outcome was CMV viremia clearance by

week 8. Secondary outcomes included impact of antiviral therapy on CNI trough levels, adjustments to IS during treatment, treatment-related adverse events, and therapy discontinuation. Results: 55 SOT patients were included (MBV: 25; VGC: 30) with a median age of 58 (kidney 34.5%, liver 29.1%, lung 23.6%, heart 5.5%, multivisceral 5.5%, simultaneous liver-kidney 1.9%). Baseline demographics were comparable between groups (table 1). Notably, patients in MBV group had a median of 15 days of prior VGC exposure before switching therapies. By week 8, CMV clearance was achieved in 48% of MBV-treated patients versus 40% of VGC-treated patients (p=0.551). Among patients receiving tacrolimus in MBV group, a notable increase in FK trough levels was observed. Median FK level before treatment was 6.9, which increased to 9.2 by day 7 (+39%). To counteract this, tacrolimus doses were reduced early in therapy, with median daily dose decreasing from 6 mg to 4 mg by day 7 (−25%) and remaining stable by day 14. VGC-treated patients experienced significant leukopenia (37%). Initial WBC counts were lower in the MBV group but remained stable throughout therapy. In contrast, VGC patients had a median 50% WBC reduction, necessitating granulocyte-colony stimulating factor use in 27% of cases, while no MBV patients required it (p=0.005). Conclusions: MBV demonstrated comparable efficacy to VGC in CMV clearance. It was associated with fewer hematologic complications but led to increased CNI levels, requiring dose adjustments. These findings support MBV as an alternative for CMV treatment in SOT recipients, particularly those at risk for VGC-induced leukopenia. Close monitoring of CNI levels is required, thus larger studies validating degree of interaction are warranted. [Formula presented] CITATION INFORMATION: Eshaya M., Franco-Palacios D., Jakupovic L., Patel A., Tong M., Poparad-Stezar A., Fitzmaurice M. Real-World Use of Maribavir vs. Valganciclovir in Solid Organ Transplant (SOT) Patients with or without Refractory Cytomegalovirus Disease AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Eshaya: None.

Pharmacy

Kreitler K, **Fitzmaurice M**, **Wright S**, **Khoury N**, **Shrivastava P**, **Patel A**, and **Prashar R**. Safety of Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2is) in Kidney Transplant Recipients. *Am J Transplant* 2025;25(8):S413. Full Text

Purpose: SGLT2is have the potential to improve kidney function in kidney transplant recipients (KTRs) by reducing proteinuria and preserving eGFR, but safety concerns exist due to increased risk of urinary tract infections (UTI), volume depletion and genital infections in immunocompromised patients. We present a single center retrospective study assessing the safety of SGLT2i in KTRs. Methods: Data from 130 KTRs who were started on SGLT2i following KT were retrospectively collected from a single academic center. Data at drug initiation, and 12 months were assessed. T-test was performed to assess statistical significance in difference in clinical characteristics of KTRs at baseline and at 1 year post SGLT2i initiation. Results: Baseline characteristics are summarized in Table 1. Empagliflozin was the most prescribed SGLT2i and median time from transplant to drug initiation was 731 days. 45% of patients had diabetes pre-transplant, 37% had new onset diabetes post-transplant, and 18% were non-diabetics. Mean baseline estimated eGFR was 55.2 mL/min/1.73 m2. Mean HgbA1c at initiation was 6.9%, and urine albumin creatinine ratio (UACR) was 262 mg/g. 26% of patients had glycosuria at baseline. At 12 months, 88% patients developed glycosuria, 13 (10 %) had UTIs, and but only 16 (12.3%) patients had discontinued the needed to discontinue the SGLT2i. The reasons for drug discontinuation were recurrent UTIs (7), AKI acute kidney injury (3), lack of continued insurance coverage (3), nausea (1), foot infection (1) and new onset neurologic disease with urinary retention (1). When comparing mean eGFR, HbA1C and UACR at baseline and 12 months, no statistically significant difference was noted. The mean eGFR, however, was maintained at 12 months at 53.1 mL/min/1.73 m2. UACR at 6 months was 216 mg/g. Mean BMI improved at 12 months as compared to baseline (29.6 vs 31.6, p=0.03). A statistically significant improvement in mean magnesium levels was also observed (1.8 vs 1.7 mg/dl, p=0.001) Conclusions: SGLT2is appear to be safe for use in KTRs with low risk of UTI, AKI, or foot infections, and overall low incidence of drug discontinuation. Further studies are needed to study long-term impact of SGLT2i on allograft and patient survival. [Formula presented] [Formula presented] CITATION INFORMATION: Kreitler K., Fitzmaurice M., Wright S., Khoury N., Shrivastava P., Patel A., Prashar R. Safety of Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2is) in Kidney Transplant Recipients AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES:

Pharmacy

Stratton P, **Fitzmaurice M**, **Jakupovic L**, **Moonka D**, **Tong M**, and **Poparad-Stezar A**. Rejection Outcomes in Simultaneous Liver-Kidney Transplant versus Liver Transplant Alone in Recipients with Chronic Kidney Disease. *Am J Transplant* 2025;25(8):S773. Full Text

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Purpose: As more patients with renal dysfunction receive liver transplants, chronic kidney disease (CKD) has been identified as a risk factor for post-transplant morbidity and mortality. Since the addition of serum creatinine in the Model of End Stage Liver Disease (MELD), the number of simultaneous liver kidney transplants (SLKT) have increased by 177% (Thompson, 2009). Despite the vast number of SLKTs performed across the country, there is no standardized immunosuppression (IS) strategy. Our study aims to compare outcomes of recipients of SLKT to liver transplant alone (LTA) with pre-existing CKD. Methods: This retrospective analysis evaluated SLKTs compared to LTAs with pre-existing CKD from January 2018-December 2023. LTA patients had diagnosed CKD with an estimated glomerular filtration rate (eGFR) of 30-44 mL/min/1.73 m2 (CKD stage 3b). The primary outcome was acute rejection (AR) within 1 year (antibody and T-cell mediated), and secondary outcomes included maintenance IS, AR treatment, infection, renal function, malignancy, and death, assessed for 1 year. Results: 51 SLKT patients and 31 LTA patients were included, with baseline characteristics evenly matched, however patients in the SLKT were younger with worse renal function (table 1). Table 2 contains secondary outcomes. Patients in the SLKT group had higher rates of AR compared to LTA (21.6 vs 12.8%; p=0.282). 3 drug IS regimens were more common in SLKT (27.5 vs 17.9%; p=0.291) and use of mammalian target of rapamycin inhibitors (mTORi) was higher in LTA (11.8 vs 43.6%; p<0.001). Tacrolimus troughs were significantly higher in the SLKT group at 6-12 months. Clostridiodes difficile infections and a composite infection endpoint (cytomegalovirus, blood stream, urinary tract, and intra-abdominal infections) were higher in SLKT (76.5 vs 59%; p=0.076). eGFR was significantly higher for the SLKT group through 1 year. LTA patients' eGFRs were maintained around their pre-LTA baseline. Malignancy and mortality rates were low, but the SLKT group had more deaths (2.6 vs 11.8%; p=0.134). Conclusions: Despite significantly improved eGFR post-transplant, the SLKT group suffered more complications including AR, infection, malignancy, and mortality, possibly in part due to differences in IS management. The SLKT group had greater IS requirements. This suggests that although there is evident renal benefit of SLKT, there may be unknown factors that heighten the risk of non-renal complications. Future studies can work to establish optimal IS regimens in this complex dual-organ population to help mitigate these risks. [Formula presented] CITATION INFORMATION: Stratton P., Fitzmaurice M., Jakupovic L., Moonka D., Tong M., Poparad-Stezar A. Rejection Outcomes in Simultaneous Liver-Kidney Transplant versus Liver Transplant Alone in Recipients with Chronic Kidney Disease AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: P. Stratton: None.

Pharmacy

Stratton P, **Jakupovic L**, **Fitzmaurice M**, and **Poparad-Stezar A**. You Want a Piece of Me? Evaluating Living Liver Donor Pain Management Outcomes After Donation. *Am J Transplant* 2025;25(8):S731. Full Text

Purpose: While multimodal analgesia and Enhanced Recovery After Surgery (ERAS) protocols have shown to effectively control pain while promoting early recovery in living liver donors undergoing hepatectomy, there is a paucity of data on sustained pain control beyond index discharge. Our review aims to evaluate the strategies utilized to ensure effective and sustained postoperative pain management in living liver donors for up to 12 months after surgery. Methods: This is a single center retrospective cross-sectional analysis evaluating post-operative pain management in adults who underwent elective hepatectomy between 2016-2023. The protocol includes pre and post- hepatectomy pain management counseling by PharmD, and use of a multimodal pain regimen including muscle relaxers, local analgesics, NSAIDs, and regional anesthesia along with opioids. The primary outcome was opioid requirements in Morphine Milligram Equivalents (MME) during inpatient stay, at discharge, 1-month, 6 weeks, 6 months and 12 months post hepatectomy. Secondary outcomes evaluated length of stay, multimodal pain regimen during inpatient stay and at discharge, average pain scores per each post-operative day while admitted, opioid-related adverse events, and re-admissions. Results: There were 55 patients included (30

females and 25 males, median age 37) with baseline characteristics as shown in Table 1. The majority of donors were opioid naive. All patients received multi-modal pain regimens post-hepatectomy, most commonly including regional anesthesia (76%) and intramuscular ketorolac (95%). The average pain score was 3.5 during an average 5-day stay. Only one patient required a pain management consult post-op. At 1-month post-hepatectomy, 85% of patients did not require new or additional pain medication and 91% did not require new or additional opioids. Pain requirements continued to decrease with time and minimal analgesic prescriptions were needed at 6 weeks and 6 months after donation (7% and 4%, respectively). At 1-year post-hepatectomy, analgesic prescriptions were not utilized by any of the donors. Conclusions: Few patients required pain-related medical visits and additional pain medication prescriptions post-hepatectomy. Pain control was adequately achieved with a multi-modal pain regimen during index admission which allowed for minimal opioid use outpatient and pain related re-admissions. Additionally, all patients received PharmD education pre-op and at time of discharge on prescribed pain medications and bowel regimen, which may have contributed to low incidence of opioid related adverse events. [Formula presented] CITATION INFORMATION: Stratton P., Jakupovic L., Fitzmaurice M., Poparad-Stezar A. You Want a Piece of Me? Evaluating Living Liver Donor Pain Management Outcomes After Donation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Poparad-Stezar: None.

Plastic Surgery

Al-Juburi S, **Oki R**, **Rocha I**, **Rajendran L**, **Kerby E**, **Mohamed A**, **Nassar A**, **Al-Kurd A**, **Kim D**, **Yoshida A**, **Abouljoud M**, and **Nagai S**. Temporal Trends in the Influence of Socioeconomic Factors on Kidney Transplant Outcomes. *Am J Transplant* 2025;25(8):S890-S891. Full Text

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Purpose: Socioeconomic status is widely recognized as a factor influencing graft survival (GS) in adult kidney transplant (KT) recipients. We hypothesized that the influence of socioeconomic status on GS varies across different post-transplantation periods. We evaluated the longitudinal impact of socioeconomic status on GS over time. Methods: Adult KT alone performed from 2003-2013 were evaluated using the United Network for Organ Sharing database. The period of post-transplantation was divided into 3 categories; Group1: 1-year survival in all patients, Group2: conditional 5-year survival in 1 year-survivors, Group3: conditional 10-year survival in 5-year survivors (Fig.1). Socioeconomic factors included patient education level, employment status at transplant and distance from transplant center to patient residence at transplant. The impact of socioeconomic factors on graft survival in each period was evaluated using the Cox proportional hazards model, stratified by deceased and living donor KT. Results: In total, 186,342 adult KT were performed from 2003-2013 (Group1), of which 176,656 recipients survived at 1 year (Group2) and 126,405 recipients survived at 5 years (Group3) post-transplant. Multivariable Cox hazard model revealed that employment status at transplant was independently associated with better graft survival in all groups in both deceased (Fig.2) and living (Fig.3) KT. While lower education level (high school or lower, reference; postcollege graduate degree) was not the risk factor in Group1, it increased the risk of graft failure in the later periods for both deceased donor and living donor KT. There was no association between the distance and patient outcomes in all groups. Conclusions: The impact of socioeconomic status on GS changed over time in both living and deceased KT.To improve the very long-term outcomes in later periods, consideration of the patient's education level in follow-up care might be necessary. [Formula presented] [Formula presented] [Formula presented] CITATION INFORMATION: Al-Juburi S., Oki R., Rocha I., Rajendran L., Kerby E., Mohamed A., Nassar A., Al-Kurd A., Kim D., Yoshida A., Abouljoud M., Nagai S. Temporal Trends in the Influence of Socioeconomic Factors on Kidney Transplant Outcomes AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: S. Al-Juburi: None.

Plastic Surgery

Hannoudi A, **Gonte MR**, **Cannella C**, **Sawar K**, **Yono SS**, **Atisha NM**, **Walker EM**, **Bensenhaver J**, **Evangelista MS**, and **Atisha DM**. ASO Visual Abstract: The Effect of Oncoplastic Reduction Mammoplasty on the Incidence of Breast Lymphedema in Women Undergoing Breast-Conservation Surgery. *Ann Surg Oncol* 2025:2. Full Text

[Hannoudi, Andrew; Gonte, Madeleine R.; Sawar, Kinan] Wayne State Univ, Sch Med, Detroit, MI 48202 USA; [Gonte, Madeleine R.; Cannella, Cara; Yono, Summer S.; Atisha, Noah M.; Walker, Eleanor M.; Bensenhaver, Jessica; Evangelista, Maristella S.; Atisha, Dunya M.] Henry Ford Hosp, Div Plast & Reconstruct Surg, Detroit, MI USA
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Public Health Sciences
Boakye EA, **Jin J**, **Williams AM**, **Chang SS**, **Suhael M**, **Siddiqui F**, **Ghanem T**, and **Tam S**. Evaluation of sleep quality and quality of life among patients newly diagnosed with head and neck cancer. *J Clin Oncol* 2025;43(16). Full Text

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Background: Patients diagnosed with head and neck cancer (HNC) often suffer from distress attributed to their cancer diagnosis which may disturb their sleep, in turn impacting their quality of life (QoL). However, there is lack of research about the association between poor sleep quality and QoL among patients newly diagnosed with HNC. We assessed the association between in poor sleep quality and QoL among patients with HNC before starting treatment. Methods: This is a retrospective cohort study of patients with HNC between January 2019 and September 2022. All patients with HNC treated at this tertiary care health system are evaluated prior to starting treatment by psych-oncology, using a semi-structured assessment and validated measures including the FACT-HN and Insomnia Severity Index (ISI). The FACTHN is a 27-item validated instrument that consists of five subscales: that assesses the patient's quality of life in the physical, social/family, emotional, functional domains, and HNC-specific domains. Sleep quality was assessed via ISI, a 7-item self-report questionnaire assessing the nature, severity, and impact of sleep difficulties (defined as absence, sub-threshold, moderate, or severe). We used five beta regression models to examine the association between sleep quality via the ISI and QoL via the FACT-HN (one for each subscale: emotional, social, physical, functional, and hand and neck). These models are adjusted with a variety of demographic covariates and social factors along with clinical factors. To estimate confidence intervals, bootstrap methods with bias correction were employed. Results: The analysis included 312 patients, 5.4% reported severe and 15.1% moderate sleep difficulties. After adjusting for other covariates, sleep difficulties were significantly associated with all FACT-HN subscales. Compared to patients with no sleep difficulties, patients with severe difficulties had a decrease in emotional (β=-1.33, 95% CI, -1.67, -0.93), social (β=-0.90, 95% CI, -1.66, -0.37), physical (β=-2.27, 95% CI, -2.67, -1.74), functional (β=-1.64, 95% CI, -2.10, -0.87), and head and neck (β=-1.11, 95% CI, -1.58, -0.65) QoL. Similarly, compared to patients with no sleep difficulties, those with severe difficulties had a decrease in emotional (β=-1.34,95%CI, -1.66, -0.98), social (β=-0.61, 95% CI, -0.99, -0.17), physical (β=-1.85, 95% CI, -2.18, -1.49), functional (β=-1.37, 95% CI, -1.71, -0.89), and head and neck (β=-1.04, 95% CI, -1.34, -0.69) QoL. Conclusions: We found that patients with moderate or severe sleep difficulties had poor QoL. Early evaluation and tailored intervention to improve sleep quality are necessary to prepare these patients for HNCtreatment and its consequences. Future studies are needed on sleep quality among patients during and after treatment.

Public Health Sciences
Gor D, **Rehman T**, **Pradeep A**, **Ghosh S**, and **Kuriakose P**. MM-259: Impact of the International Myeloma Working Group (IMWG) SLiM Criteria on Multiple Myeloma Management: A Tertiary Care Center Experience. *Clin Lymphoma Myeloma Leuk* 2025;25:S911. Full Text

Multiple myeloma (MM) is a hematologic malignancy characterized by the proliferation of plasma cells. IMWG's introduction of the SLiM criteria in 2014 expanded the diagnosis of MM. Our retrospective study evaluated the adoption and impact of these criteria at Henry Ford Cancer Institute (HFCI), focusing on patient demographics and outcomes of those diagnosed exclusively using the SLiM criteria. Methods: Electronic medical records at HFCI (January 2015–December 2023) were reviewed to identify MM patients meeting at least one SLiM criterion (≥60% plasma cells, free light chain (FLC) ratio >100, or MRI lesion), excluding those with CRAB features. Data on demographics, staging, treatment, and outcomes (through December 2024) were analyzed. Results: Between 2015 and 2023, 495MMpatients were

diagnosed; 190 met at least one SLiM criterion. After excluding 177 with CRAB features, 13 patients remained who were diagnosed solely by SLiM criteria. Of these, 6 had plasma cells >60%, 11 had FLC ratio >100, and 3 met MRI criteria. The mean age was 63.6 years; 53.8% were female, 53.8% African American, and 38.4% Caucasian. High-risk cytogenetics were present in 53.8% patients. By Revised International Staging System (R-ISS) staging, 61.5% of patients had stage 1, 30.7% had stage 2, and 7.6% had stage 3 disease. Twelve patients received treatment with induction regimen, which included bortezomib, lenalidomide, dexamethasone (VRd) (n = 9), daratumumab-VRd (n = 1), carfilzomib, lenalidomide, dexamethasone (KRd) (n = 1), or bortezomib, dexamethasone (Vd) (n = 1), all starting treatment at diagnosis. Among them, there was one death (hospice, age/comorbidities), two relapses (both in remission after second-line therapy), and nine remained in remission. One patient, diagnosed in 2017, has not required treatment to date. Conclusion: Our study highlights real-world data on the impact of the IMWG SLiM criteria for MM diagnosis. Patients diagnosed solely based on SLiM criteria, who would previously have been classified as having smoldering myeloma, were treated at diagnosis, reflecting real-time adoption of the updated guidelines. This underscores the positive impact and practical applicability of the revised criteria. Interestingly, one untreated patient has not progressed, suggesting the need for appropriately powered randomized studies to better understand outcomes in this specific subset of patients.

Public Health Sciences

Jindal D, **Hirko K**, **Cassidy-Bushrow A**, **Ghosh S**, **Susick L**, **Latack K**, **Shetty P**, and **Neslund-Dudas C**. Racial differences in prevalence of coronary artery calcification among patients undergoing lung cancer screening. *J Clin Oncol* 2025;43(16). Full Text

D. Jindal

Background: Coronary artery calcification (CAC) is a known risk factor for coronary heart disease. Lung cancer screening (LCS) with low-dose computed tomography (LDCT) can detect lung cancer at earlier stages and reduce mortality. Additionally, CAC are common incidental findings among patients undergoing LDCT for LCS. However, racial differences in incidental findings of CAC among LCS patients have not been thoroughly investigated. We examined the association between race and presence of moderate to severe CAC among patients undergoing LDCT for LCS. Methods: We conducted a retrospective analysis of electronic health records (EHR) from Henry Ford Health (2016-2023) among patients undergoing LDCT for LCS. CAC was classified as moderate or severe (vs. none or mild). Race was categorized as Black, White, Asian, American Indian/Alaskan Native, Other and Unknown. We focused on Black and White patients, owing to the small sample size in the other groups. Multivariable logistic regression was used to examine the association between race and presence of moderate to severe CAC, adjusting for age, sex, and tobacco smoking status. Results: A total of 15,911 patients who were eligible for LCS and completed at least one screen during our study period were included. Of these, 79.6% were White and 20.4% were Black. The mean age of patients was 63.865.8 years; 50.4% were male and 61.4% reported current tobacco smoking. Demographic comparisons show that White patients were more frequently male compared to Black patients (50.9% vs 47.9%, $p = 0.002$). In addition, Black patients were slightly older (64.365.7 vs 63.665.8 years) and reported a higher current tobacco smoking status (67.9% vs 59.7%, $p < 0.0001$) compared to White patients. The prevalence of moderate to severe CAC was 10.9% overall and was higher among Black vs White patients (16.1% vs 9.6%, $p < 0.0001$). After covariate adjustment, Black patients had significantly higher odds of moderate to severe CAC compared to White patients (odds ratio [OR] = 1.8, 95% CI 1.6-1.9, $p < 0.0001$). Conclusions: The study findings suggest significant racial differences in the prevalence of CAC among patients undergoing LCS. Race may be an important factor when assessing cardiovascular risk in patients undergoing LCS and may have implications for screening protocols and preventive strategies. Future research is needed to explore the impact of these differences on risk and mortality from cardiovascular diseases.

Public Health Sciences

Surapaneni S, Baxter Z, **Tam S**, Bernacchi V, **Chang SS**, **Yaremchuk K**, and **Boakye EA**. A scoping review of uptake and interventions in specialty and non-primary care clinical settings. *J Clin Oncol* 2025;43(16). Full Text

S. Surapaneni

Background: Persistent human papillomavirus (HPV) infection significantly increases the risk of developing several cancers, including cervical, anal, and oropharyngeal cancers. According to CDC guidelines, vaccinations are recommended for individuals ages 9-26 and have been expanded to include some adults aged 27-45 based on a shared decision-making process with their clinician. It is estimated that over 90% of the HPV-associated cancers could be prevented with the HPV vaccine. Despite substantial evidence regarding the safety and effectiveness of the HPV vaccine, vaccination rates remain below the Healthy People 2030 goal of 80%, with vaccines primarily administered in primary care settings. Specialty clinics and non-primary care clinics that do not traditionally offer HPV vaccination, present an opportunity to improve vaccine uptake. This scoping review evaluates the potential impact of HPV vaccination in non-primary care settings. Methods: Our approach to data collection and analysis was guided by Arksey and O'Malley's scoping review framework, and the Preferred Reporting Items for Systematic reviews and meta-analyses extension for Scoping Reviews (PRISMA-ScR). Ovid MEDLINE, Embase, and Web of Science were queried to include articles published in the US from 2006 to 2024 using search terms such as human papillomavirus vaccination and specialty clinics by an academic librarian. Original empirical studies were included, there were no restrictions on study design. Results: Out of the 1752 studies identified, 10 studies met the inclusion criteria, including 5 retrospective observational studies, 2 cross sectional studies, 1 randomized control trial, 1 pre-post study, and 1 survey study. Sample size for studies included ranged from 50 to 3709 participants, age range 18-45 years. Settings included otolaryngology, OBGYN, family planning, and substance health services. Baseline vaccination rate ranged from 5.2% to 47%. Five studies were interventional, and evaluated the effects of patient counseling, pharmacistphysician education, free vaccination or mailed reminders on HPV vaccination rates. The interventions resulted in increases in vaccination from 5.6% to 16%. Conclusions: Practice settings for interventions included in this scoping review focused on specialties that treat the downstream effects of HPV vaccination or high-risk populations. For adults eligible for HPV vaccination, specialty outpatient clinics may present a unique additional opportunity to discuss and deliver HPV vaccination, especially since providers in these settings also treat HPV-related diseases and are well equipped to engage in shared decision making with patients. Future research should focus on the acceptability, feasibility, and effectiveness of implementation of an HPV vaccination program in these settings.

Public Health Sciences

Toiv A, **Yoshida A**, **Roberman J**, **Doshi N**, **Poisson L**, **Abouljoud M**, **Moonka D**, and **Jesse M**. Listed or Left Behind: The Impact of Social Support on Liver Transplant Access. *Am J Transplant* 2025;25(8):S493. Full Text

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Purpose: Liver transplantation (LT) is the only curative therapy for patients with decompensated liver disease, but the complex evaluation process for selecting LT recipients limits access for many. “Social support” is a subjective and controversial criterion often used for determining LT eligibility. However, transplant centers inconsistently apply this criterion, and using social support to determine LT eligibility contributes to racial, ethnic, and socioeconomic inequities in transplant listing. Here we investigated the impact of using social support as a criterion for LT listing. Methods: We conducted a retrospective analysis of all patients evaluated for LT between January 1, 2019, and December 31, 2021 at an academic liver center with a clearly defined objective social support evaluation criterion. Logistic regression analysis was used to determine the association between social support inadequacy (unable to report ≥2 support people and/or other significant concerns) and LT listing status. Kaplan-Meier analysis was used to examine the relationship between social support and time-to-decision. Results: Of 711 LT candidates who had social support information available, 498 (70%) were not listed for LT, of whom 13 (2.6%) were not listed for LT solely due to having inadequate social support. After controlling for several variables, having inadequate social support was significantly associated with decreased odds of being

listed for LT (odds ratio 0.38; 95% CI, 0.13-0.93). Other predictors of non-listing included female sex and having recommendations for substance use treatment. Conversely, being married/partnered and higher education levels were positively associated with listing. Kaplan-Meier analysis did not show significant differences in time-to-decision based on social support status; however, patients with inadequate social support exhibited a steeper decline in evaluation completion during the initial 125 days. Conclusions: At our transplant center, <3% of patients who were excluded from LT listing were not listed solely due to having inadequate social support, and inadequate social support was significantly associated with a lower likelihood of listing. Social support remains a critical and controversial criterion for determining LT eligibility, and the subjective nature of social support evaluations can perpetuate disparities in access to life-saving transplantation. Standardizing assessments and implementing interventions to strengthen social support systems could reduce inequities and ensure more equitable access to transplantation. CITATION INFORMATION: Toiv A., Yoshida A., Roberman J., Doshi N., Poisson L., Abouljoud M., Moonka D., Jesse M. Listed or Left Behind: The Impact of Social Support on Liver Transplant Access AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Toiv: None.

Public Health Sciences

Wood M, Guthrie KA, Park Y, Ngo-Metzger Q, Kaltman RD, Lee CB, **Rybicki B**, Liao JC, and Ramsey SD. The Vanguard study: An NCI cancer screening research network multi-cancer detection feasibility study. *J Clin Oncol* 2025;43(16). Full Text

M. Wood

Background: Multi-cancer detection (MCD) tests are promising; however, large-scale trials are needed to establish their harms, benefits, and clinical utility. The NCI has established the Cancer Screening Research Network (CSRN) to evaluate novel screening technologies. The first study of CSRN, the Vanguard study, is designed to establish the feasibility of recruiting individuals from diverse backgrounds into randomized cancer screening trials and to evaluate trial design and diagnostic evaluation processes. Methods: The Vanguard study is a randomized, three-arm trial of two novel MCD assays and a usual care group (n = 24,000). Adults ages 45-75 without cancer in the last 5 years will be eligible. The primary outcomes are feasibility and equitable recruitment. Recruitment sites include nine US Hubs (ACCESS Hubs) selected for ability to recruit racially, ethnically, geographically and socioeconomically diverse participants. Participants randomized to an intervention arm will receive anMCDtest at baseline and year 1 followup. MCD platforms selected for investigation demonstrate ability to screen for lung, breast, colorectal, prostate, bladder, ovarian, pancreatic, esophageal, liver and gastric cancers. All participants will provide blood samples and complete questionnaires centered around demographics, social determinants of health, cancer risk and screening history, anxiety, and cancer worry, at baseline and year 1. Year 2 will include the same questionnaires without a blood sample. All participants will be encouraged to participate in standard-of-care (SOC) cancer screenings. Those with abnormal MCD results will undergo a cancer site-specific, protocolguided diagnostic evaluation. will be followed for SOC screening behavior, cancer incidence, mortality, and quality of life. Results: The Vanguard study protocol, developed in partnership between the CSRN Communications and Coordinating Center, Statistics and Data Management Center, ACCESS Hubs, and the NCI, will be launched in 2025. ACCESS Hubs will accrue participants over a two-year period. Several unique design elements have been integrated into this study: 1) Facilitation of recruitment and retention of underrepresented and rural populations using features such as remote consenting, remote blood collection, electronic surveys. 2) Results of a positive MCD will always be returned to participants but participants in 4 Hubs will be blinded to whether they have undergone testing with an MCD. 3) Results of MCD testing will identify a likely tissue of origin (e.g., ovary or pancreas) to guide diagnostic workup. Conclusions: The Vanguard study is a critical step to ensure rigorous design and implementation of future large RCTs evaluating the clinical efficacy and safety of MCDs. Results from this study will inform a larger RCT to evaluate whetherMCDsare beneficial in detecting cancer early, and any potential harms of the tests.

Public Health Sciences

Zhang Y, **Zhang Y**, **Chopp M**, **Pang H**, **Wang X**, **Lu M**, **Chen L**, **Lu M**, **Zhang ZG**, **Mahmood A**, and **Xiong Y**. POB.066 - Therapeutic effects of miRNAs of exosomes derived from human bone marrow mesenchymal stem cells on histologi_cal outcome in rats after traumatic brain injury. *J Neurotrauma* 2025;42(13-14):e1186. Full Text

Y. Zhang, Department of Neurosurgery, Henry Ford Health, Detroit, United States

We previously showed that exosomes from naïve and engineered bone marrow mesenchymal stem cells (MSCs) improve functional recovery in rats after traumatic brain injury (TBI). This study examines the effects of MSC-derived exosomes with varying miRNA expression levels on histological outcomes following TBI. Young male rats with moderate TBI induced by controlled cortical impact injury (CCI) were randomly assigned to receive phosphate-buffered solution (PBS, control) or one dose of exosomes (100 lg/rat) from naïve MSCs (MSC group), MSCs overexpressing miR-17-92 (miR- 17-92 group), MSCs with an empty vector (miR-17-92-Empty group), MSCs with Argonaute 2 knockout with reduction of miRNAs (Ago2-KO group), or MSCs with an empty vector (Ago2-Vector group), administered 24 hours post-injury. Rat brains were collected 2 days post-injury for immunostaining of inflammatory markers (CD68, TNF alpha, CCR2), cell death (caspase-3), neurotrophic factors (BDNF, NGF), BBB breakdown (fibrin/fibrinogen), and synaptogenesis (Synaptophysin). Analysis of variance (ANOVA) followed by post hoc Tukey's tests was used for data analyses. PBS-treated TBI rats significantly increased neuroinflammation, cell death, and BBB damage and decreased synaptogenesis and neurotrophic factor expression in the injured brain vs Sham group ($p<0.05$). Treatments from MSC, miR-17-92-Empty or Ago2- Vector groups significantly decreased neuroinflammation, cell death, and BBB damage and increased synaptogenesis and neurotrophic factor expression in the injured brain vs PBS group ($p<0.05$). Exosomes from the miR-17-92 group provided further benefits while exosomes from the Ago2-KO group exhibited opposite effects vs MSC group ($p<0.05$). These results support use of engineered exosomes enriched with select miRNAs as a potential treatment for TBI.

Public Health Sciences

Zimmer M, **Abad J**, **Gupta J**, **Ghosh S**, and **Kuriakose P**. MM-423: Secondary Hematologic Malignancies in Patients With Multiple Myeloma: A Retrospective Analysis of Risk Factors and Incidence in a Large Urban Health System. *Clin Lymphoma Myeloma Leuk* 2025;25:S919. Full Text

Multiple myeloma (MM) is a common hematologic malignancy. While overall survival has improved due to advances in therapy, there is concern regarding the risk of secondary hematologic malignancies (SHM). Objective: To identify patients treated for MM who subsequently developed SHM and estimate the incidence and timing of SHM. Design: Retrospective, observational study. Setting: Henry Ford Health, a large urban, tertiary care network in Detroit, MI. Patients: Patients age 18 years or more with a confirmed diagnosis of MM between January 2005 and December 2022 and a subsequent SHM diagnosis were identified through electronic medical records review. Results: Of 3122 patients with MM, 297 were identified by automatic data pull as having a diagnosis of SHM. After manual review, nine patients met the inclusion criteria. Six patients (66.7%) were male. Median age at MM diagnosis was 62 (range: 53–73) years. About 44.4% were African American, 33.3% were Caucasian, 11.1% were Asian, and 11.1% identified as other. At a median follow-up of 58 (range: 35–144) months, most patients (66.6%) had received only one line of therapy, some had two lines (22.25%), and one patient had received 12 lines of therapy. Five patients (55.6%) underwent autologous stem cell transplantation. Most patients (77.8%) received maintenance therapy, most commonly with lenalidomide (66.7%), for a median duration of 11 (range: 0–29) months. SHM were diagnosed at a median of 4 years after MM diagnosis, being primarily myeloid in origin (77.8%). Median time from MM diagnosis to death was 64 (range: 49–78) months, and median time from SHM diagnosis to death was 5 (range: 0–9) months. Conclusion: Despite the sample size and retrospective nature, our study has some key findings. First, the incidence of SHM was 0.2%, which is significantly less than the 8–18% in previous studies. Second, most patients were not heavily pretreated, often receiving only 1–2 lines of therapy and shorter duration of lenalidomide maintenance prior to the development of SHM. Accordingly, further work needs to be done to evaluate the impact of both patient- and disease-dependent factors, as well as MM therapy, on the development of SHM.

Pulmonary and Critical Care Medicine

Eshaya M, **Franco-Palacios D**, **Jakupovic L**, **Patel A**, **Tong M**, **Poparad-Stezar A**, and **Fitzmaurice M**. Real-World Use of Maribavir vs. Valganciclovir in Solid Organ Transplant (SOT) Patients with or without Refractory Cytomegalovirus Disease. *Am J Transplant* 2025;25(8):S590. Full Text

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Purpose: Cytomegalovirus (CMV) infection is a major complication in solid organ transplant (SOT) recipients, impacting graft function and survival. The SOLSTICE trial demonstrated maribavir's (MBV) superiority to investigator-assigned therapy for CMV clearance by week 8, yet data on MBV use in SOT patients with non-refractory CMV remains limited, and the impact of MBV on calcineurin inhibitor (CNI)-based immunosuppression (IS) has not been well characterized. The purpose of this study was to assess the efficacy of MBV for viremia clearance in a variety of SOT recipients and the real-world impact of MBV on CNI levels. Methods: This was a retrospective, single-center study of SOT recipients treated with MBV or valganciclovir (VGC) between 2021 to 2024. The primary outcome was CMV viremia clearance by week 8. Secondary outcomes included impact of antiviral therapy on CNI trough levels, adjustments to IS during treatment, treatment-related adverse events, and therapy discontinuation. Results: 55 SOT patients were included (MBV: 25; VGC: 30) with a median age of 58 (kidney 34.5%, liver 29.1%, lung 23.6%, heart 5.5%, multivisceral 5.5%, simultaneous liver-kidney 1.9%). Baseline demographics were comparable between groups (table 1). Notably, patients in MBV group had a median of 15 days of prior VGC exposure before switching therapies. By week 8, CMV clearance was achieved in 48% of MBV-treated patients versus 40% of VGC-treated patients (p=0.551). Among patients receiving tacrolimus in MBV group, a notable increase in FK trough levels was observed. Median FK level before treatment was 6.9, which increased to 9.2 by day 7 (+39%). To counteract this, tacrolimus doses were reduced early in therapy, with median daily dose decreasing from 6 mg to 4 mg by day 7 (−25%) and remaining stable by day 14. VGC-treated patients experienced significant leukopenia (37%). Initial WBC counts were lower in the MBV group but remained stable throughout therapy. In contrast, VGC patients had a median 50% WBC reduction, necessitating granulocyte-colony stimulating factor use in 27% of cases, while no MBV patients required it (p=0.005). Conclusions: MBV demonstrated comparable efficacy to VGC in CMV clearance. It was associated with fewer hematologic complications but led to increased CNI levels, requiring dose adjustments. These findings support MBV as an alternative for CMV treatment in SOT recipients, particularly those at risk for VGC-induced leukopenia. Close monitoring of CNI levels is required, thus larger studies validating degree of interaction are warranted. [Formula presented] CITATION INFORMATION: Eshaya M., Franco-Palacios D., Jakupovic L., Patel A., Tong M., Poparad-Stezar A., Fitzmaurice M. Real-World Use of Maribavir vs. Valganciclovir in Solid Organ Transplant (SOT) Patients with or without Refractory Cytomegalovirus Disease AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Eshaya: None.

Pulmonary and Critical Care Medicine

Saleem A, **Obri M**, **Ilyas O**, **Alomari A**, **Faisal M**, **Abusuliman M**, **Chaudhary A**, **Rehman S**, **Franco-Palacios D**, **Nagai S**, **Venkat D**, and **Jafri S**. Outcomes and Risk Factors for Post-Operative Rejection and Transaminitis Following Dual Liver-Lung Transplantation: A Retrospective Cohort Study. *Am J Transplant* 2025;25(8):S468-S469. Full Text

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Purpose: Dual liver-lung transplantation (DLLT) is a rare and complex procedure, with limited data on post-operative rejection and liver function abnormalities. Understanding risk factors for acute cellular rejection and transaminitis is critical for optimizing immunosuppressive management. This study

evaluates post-transplant outcomes in DLLT recipients and explores associations with recipient demographics, transplant indication, and underlying liver/lung disease etiology. Methods: A retrospective analysis was conducted on patients at our center who underwent DLLT between 2013 and 2024. Data collected included demographics, transplant indications, length of stay, incidence of acute rejection, and subsequent infections. Post-operative liver function tests (LFTs) beyond one month post-transplant were analyzed, and their relationship with age at transplant, liver disease etiology, and lung disease etiology was assessed. Results: A total of 10 patients (5 males, 5 females, mean age 53.7 years) underwent DLLT between 2013 and 2024. Liver disease etiologies were ethanol-related cirrhosis (n=2), hepatitis C (n=1), cryptogenic cirrhosis (n=1), autoimmune hepatitis (n=1), cystic fibrosis (n=1), and other unspecified causes (n=4). Lung transplant indications included idiopathic pulmonary fibrosis (n=5), pulmonary hypertension (n=2), other forms of interstitial lung disease (n=2), and cystic fibrosis (n=1).Post-operatively, 4 of 10 patients developed transaminitis beyond one month post-transplant, with liver biopsy confirming acute cellular rejection. Three patients received IV solumedrol, while one was managed with an oral steroid taper. Transaminitis resolved in all four cases after steroid treatment. Within three months, two patients treated with IV solumedrol developed infections from Candida and Aspergillus, though none developed CMV viremia. Two deaths occurred in the cohort. One patient passed away four years after transplant due to multifocal pneumonia, while the second patient passed away nine years post-transplant due to septic shock secondary to pneumonia in the setting of a new diagnosis of angiosarcoma. Neither patient had experienced rejection. Rejection and transaminitis were not significantly associated with age at transplant, liver disease etiology, or lung disease etiology. Conclusions: This study provides one of the first detailed assessments of rejection and liver function abnormalities following DLLT. While transaminitis and acute cellular rejection occurred in 40% of patients, no clear predisposing factors were identified. IV solumedrol use for rejection was associated with increased infection risk, emphasizing the need for careful immunosuppressive management in this population. Further research with larger cohorts is essential to improve risk stratification and post-transplant care in DLLT recipients. CITATION INFORMATION: Saleem A., Obri M., Ilyas O., Alomari A., Faisal M., Abusuliman M., Chaudhary A., Rehman S., Franco-Palacios D., Nagai S., Venkat D., Jafri S. Outcomes and Risk Factors for Post-Operative Rejection and Transaminitis Following Dual Liver-Lung Transplantation: A Retrospective Cohort Study AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Saleem: None.

Radiation Oncology

Boakye EA, **Jin J**, **Williams AM**, **Chang SS**, **Suhael M**, **Siddiqui F**, **Ghanem T**, and **Tam S**. Evaluation of sleep quality and quality of life among patients newly diagnosed with head and neck cancer. *J Clin Oncol* 2025;43(16). Full Text

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Background: Patients diagnosed with head and neck cancer (HNC) often suffer from distress attributed to their cancer diagnosis which may disturb their sleep, in turn impacting their quality of life (QoL). However, there is lack of research about the association between poor sleep quality and QoL among patients newly diagnosed with HNC. We assessed the association between in poor sleep quality and QoL among patients with HNC before starting treatment. Methods: This is a retrospective cohort study of patients with HNC between January 2019 and September 2022. All patients with HNC treated at this tertiary care health system are evaluated prior to starting treatment by psych-oncology, using a semi-structured assessment and validated measures including the FACT-HN and Insomnia Severity Index (ISI). The FACTHN is a 27-item validated instrument that consists of five subscales: that assesses the patient's quality of life in the physical, social/family, emotional, functional domains, and HNC-specific domains. Sleep quality was assessed via ISI, a 7-item self-report questionnaire assessing the nature, severity, and impact of sleep difficulties (defined as absence, sub-threshold, moderate, or severe). We used five beta regression models to examine the association between sleep quality via the ISI and QoL via the FACT-HN (one for each subscale: emotional, social, physical, functional, and hand and neck). These models are adjusted with a variety of demographic covariates and social factors along with clinical factors. To estimate confidence intervals, bootstrap methods with bias correction were employed. Results: The analysis included 312 patients, 5.4% reported severe and 15.1% moderate sleep difficulties. After adjusting for other covariates, sleep difficulties were significantly associated with all FACT-HN subscales. Compared to patients with no sleep difficulties, patients with severe difficulties had a decrease in

emotional (β=-1.33, 95% CI, -1.67, -0.93), social (β=-0.90, 95% CI, -1.66, -0.37), physical (β=-2.27, 95% CI, -2.67, -1.74), functional (β=-1.64, 95% CI, -2.10, -0.87), and head and neck (β=-1.11, 95% CI, -1.58, -0.65) QoL. Similarly, compared to patients with no sleep difficulties, those with severe difficulties had a decrease in emotional (β=-1.34,95%CI, -1.66, -0.98), social (β=-0.61, 95% CI, -0.99, -0.17), physical (β=-1.85, 95% CI, -2.18, -1.49), functional (β=-1.37, 95% CI, -1.71, -0.89), and head and neck (β=-1.04, 95% CI, -1.34, -0.69) QoL. Conclusions: We found that patients with moderate or severe sleep difficulties had poor QoL. Early evaluation and tailored intervention to improve sleep quality are necessary to prepare these patients for HNCtreatment and its consequences. Future studies are needed on sleep quality among patients during and after treatment.

Radiation Oncology

Gwede CK, Harris J, Machtay M, Le QTX, Thorstad W, Nguyen-Tan F, Siu LL, Dorth JA, Lee NY, Dunlap NE, Chan J, Bar-Ad V, Patel PR, Chakravarti A, Rao S, Shipstone A, Lanning RM, Attwood K, Yom SS, and **Movsas B**. Quality of life in a phase III study of prospective radiation therapy (IMRT) +/- cetuximab for locally advanced resected head and neck cancer: NRG/RTOG 0920. *J Clin Oncol* 2025;43(16). Full Text

C.K. Gwede

Background:Wetested the primary question whether the addition of cetuximab to postoperative radiotherapy (IMRT) results in poorer patient reported outcomes (PROs) at 12 months compared to IMRT alone. We also examined changes in PROs over time. Methods: Randomized and eligible patients who consented to quality of life (QOL) assessment completed PROs measured by 5 instruments, prior to treatment (baseline) and at 3, 12, and 24 months after IMRT. Instruments included: 1) Functional Assessment of Cancer Therapy-Head&Neck (FACT-HN), a multidimensional QOL instrument for use with head and neck cancer patients; 2) University of Michigan Xerostomia- Related Quality of Life Scale (XeQOLS) covering mouth/throat dryness and its impact on oral health-related QOL; 3) Dermatology Life Quality Index (DLQI) for skin-related changes; 4) EuroQol (EQ-5D-3L) covering usual activities and perceived current health state; 5) Performance Status Scale for Head and Neck Cancer (PSS-HN) assessing normalcy of diet, public eating, and understandability of speech. Higher scores on XeQOLS and DLQI indicate worse QOL; otherwise higher scores indicate better QOL for other measures. For FACT-HN, XeQOLS, DLQI, and EQ-5D- 3L, changes from baseline were compared by Van Elteren test, and for PSS-HN, the% < 50 was compared by Z test. 158 patients per arm provided 80% power to test the difference between IMRT + cetuximab and IMRT alone. Changes in PROs over time were evaluated using mixed models. Two-sided tests were used with a=0.05. Results: 499 of 577 eligible patients (86%) consented to QOL. There were no significant differences between treatment arms (IMRT vs. IMRT + cetuximab) for all PRO measures in change from baseline to 3 or 12 months post-IMRT (see table). At 24 months, the change from baseline was significantly different for DLQI (p=0.02), but the difference was not clinically meaningful; other PROs were not significantly different. There were no significant differences between treatment arms forPSS-HN diet, eating, or speech at any time point (see table). Regarding treatment effect over time, in both treatment groups, all PRO measures showed greatest decline at 3 months followed by improvement towards baseline by 24 months. Conclusions: Treatment with IMRT + cetuximab was not associated with worse PROs compared to IMRT alone. Furthermore, findings demonstrate important recovery trends in QOL with return to baseline for most measures in both study arms.

Radiation Oncology

Hannoudi A, **Gonte MR**, **Cannella C**, **Sawar K**, **Yono SS**, **Atisha NM**, **Walker EM**, **Bensenhaver J**, **Evangelista MS**, and **Atisha DM**. ASO Visual Abstract: The Effect of Oncoplastic Reduction Mammoplasty on the Incidence of Breast Lymphedema in Women Undergoing Breast-Conservation Surgery. *Ann Surg Oncol* 2025:2. Full Text

[Hannoudi, Andrew; Gonte, Madeleine R.; Sawar, Kinan] Wayne State Univ, Sch Med, Detroit, MI 48202 USA; [Gonte, Madeleine R.; Cannella, Cara; Yono, Summer S.; Atisha, Noah M.; Walker, Eleanor M.; Bensenhaver, Jessica; Evangelista, Maristella S.; Atisha, Dunya M.] Henry Ford Hosp, Div Plast & Reconstruct Surg, Detroit, MI USA

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Radiation Oncology

Huang-Vredevoogd J, **Doemer A**, **Siddiqui S**, **Shah MM**, **Asadi AA**, **DiCarlo A**, **Scarpace L**, **Robin A**, **Lee I**, **Moceri A**, and **Thind K**. PPP04 Expanding Treatment Options for Reirradiation: The First Case of Gammatile Implantation in the Spine. *Brachytherapy* 2025;24(4):S20-S21. Full Text

Purpose: GammaTile® surgically targeted radiation therapy is a form of low dose rate brachytherapy in which Cs-131 seeds are embedded into a resorbable collagen-based matrix, allowing the seeds to be easily placed along a resection cavity during surgery. GammaTile has been used in several intracranial applications including the treatment of recurrent glioblastomas, meningiomas, and brain metastases as well as newly diagnosed brain metastases. However, it has not been used extracranially. This study describes the first use of GammaTile in the spine, for a patient who had rectosigmoid adenocarcinoma with recurrent metastatic disease in the sacrum. They received their first course of radiation in 2022 with external beam (54Gy in 30 fractions), followed by fractionated stereotactic radiation therapy to the recurrent lumbosacral disease in 2023 (30Gy in 5 fractions), and presented with pain in the legs and progressive disease in the sacrum. Given the patient's two prior courses of external beam radiation therapy, off-label use of GammaTile was pursued due to its ability to minimize dose to the nearby thecal sac, cauda equina and sacral nerve roots. Methods: GammaTile workflow for cranial applications involves estimating the surface area of the resection cavity to calculate the expected number of tiles needed. However, for this novel application, the number of tiles was estimated using a mock-up of the anticipated tile configuration based on the patient's MRI (Figure 1b), as well as a personalized 3D-printed replica of the patient's spine (Figure 1a).Following surgical resection, which included a partial L5 laminectomy and partial sacrectomy (Figure 1c), four tiles (16 sources) were placed “upside down” from the typical orientation, i.e., with the larger 3mm spacing facing toward the thecal sac to maximize separation and minimize dose to the cauda. Additionally, Fibrin sealant and absorbable gelatin were placed in between the tiles and the thecal sac to create further separation. Immediately after surgery, CT images were acquired in the OR for post-implant dosimetry and to verify the desired tile placement. These images were then used to calculate the delivered dose to the patient using the Eclipse planning system, and MIM was used to convert physical dose to biological effective dose to the thecal sac (BED3Gy) using the linear quadratic model for a permanent LDR implant and published values for the repair time, potential doubling time, and alpha values.1 Results: The post-implant calculated BED3Gy distribution is shown in Figure 1d. The D0.035cc physical dose and BED3Gy dose to the thecal sac was 89.8Gy and 106.4Gy respectively. At a 3-month post-operative appointment, the patient reported improved pain and was able to ambulate for longer distances with a walker. Conclusions: This study presents our institution's experience with the first use of Gammatile for the spine, highlighting the ability of our multi-disciplinary team to offer a novel treatment technique for a patient faced with either disease progression or a more extensive, life-altering surgery.

Surgery

Aceituno L, Magyar C, Li Z, Claasen M, **Ivanics T**, Winter E, Bucur R, Rukavina N, Choi WJ, Selzner N, Bhat M, Lilly L, Tsien C, Patel K, Selzner M, McGilvray I, Reichman T, Shwaartz C, Ghanekar A, Cattral MS, Sayed B, Jaeckel E, and Sapisochin G. Impact of recipient sex on long-term survival after liver transplantation in patients with high MELD. *J Hepatol* 2024;80:S381. Full Text

Background and aims: The MELD score is used to prioritize liver transplant (LT) candidates for deceased donor organs, with a “sickest first” approach. However, it has been shown that MELD score does not accurately reflect disease severity in females. It remains controversial whether recipient sex affects long-term post-transplantation survival. This study aimed to assess the impact of sex in a high MELD cohort on (1) long-term survival post-LT, (2) and its association with underlying diseases, cause of transplant, and comorbidities. Method: Retrospective cohort study at Toronto General Hospital, including adult LT recipients with a MELD ≥25 at transplant between January 2007 and December 2019. Patients were stratified by sex. Survival analysis was performed using a priori multivariable Cox regression and Kaplan-Meier analysis. A post hoc sex-stratified multivariable Cox regression model was performed. Results: 478 patients with MELD ≥25 were included; 196 (40%) were females, with a median BMI of 27.4 kg/m2 (IQR

23.7–31.2). The median follow-up post-LT was 5.7 years (IQR 2.2, 9.2) with a median waitlist of 23.5 days (IRQ 0.0, 75.5). The median listing and pretransplant MELD scores were 28 (IQR 21–34), and 31 (IQR 26–35) respectively. Male recipients had pre-transplant higher rates of ascites (39.8% vs. 53.5%; p = 0.003) and hepatic encephalopathy (34.2% vs. 44.3%; p = 0.026). Autoimmune hepatitis as underlying disease was more prevalent among females (26.5% vs. 12.4%; p < 0.005). Conversely, viral hepatitis (8.7% vs. 24.8%; p < 0.001), alcoholrelated cirrhosis (ALD) (13.3% vs. 28.7%; p < 0.001), and mixed ALD + viral cirrhosis (1.0% vs. 5.0%; p = 0.018) were more frequent in males. Females were more frequently transplanted for acute liver failure (16.8% vs. 4.6%; p < 0.001) and fewer for cancer (4.6% vs. 11.3%; p = 0.009). No statistically significant differenceswere observed between sex crude overall long-term survival (log-rank p = 0.681), or estimated effect (HR 0.92; p = 0.686). In the a priori multivariable analysis, sex was not significant (HR 0.94, CI 95% 0.61–1.43; p = 0.779).There were no sex differences in early post-transplant mortality (<90 days) (6.6% females vs. 9.2% males; p = 0.309; HR 0.71, p = 0.329), mortality in the 1st year (10.7% females vs. 14.5% males; p = 0.221), 5th (16.8% females vs. 18.8% males; p = 0.584) and 10th year (20.4% females vs. 22.0% males; p = 0.679). There was no difference in risk of postoperative complications. On post hoc multivariable analysis stratified by sex, re-transplantation (HR 2.80; CI 95% 1.53–5.14; p = 0.001) and ICU stay (HR 1.009; CI 95% 1.005– 1.01; p < 0.001) were significant risk factors for female mortality. Conclusion: Our findings show no sex differences in the overall survival in high MELD liver transplant recipients. Female patients with longer ICU admission, or requiring re-transplantation, were at higher risk of all-cause mortality.

Surgery

Al-Juburi S, **Oki R**, **Rocha I**, **Rajendran L**, **Kerby E**, **Mohamed A**, **Nassar A**, **Al-Kurd A**, **Kim D**, **Yoshida A**, **Abouljoud M**, and **Nagai S**. Temporal Trends in the Influence of Socioeconomic Factors on Kidney Transplant Outcomes. *Am J Transplant* 2025;25(8):S890-S891. Full Text

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Purpose: Socioeconomic status is widely recognized as a factor influencing graft survival (GS) in adult kidney transplant (KT) recipients. We hypothesized that the influence of socioeconomic status on GS varies across different post-transplantation periods. We evaluated the longitudinal impact of socioeconomic status on GS over time. Methods: Adult KT alone performed from 2003-2013 were evaluated using the United Network for Organ Sharing database. The period of post-transplantation was divided into 3 categories; Group1: 1-year survival in all patients, Group2: conditional 5-year survival in 1 year-survivors, Group3: conditional 10-year survival in 5-year survivors (Fig.1). Socioeconomic factors included patient education level, employment status at transplant and distance from transplant center to patient residence at transplant. The impact of socioeconomic factors on graft survival in each period was evaluated using the Cox proportional hazards model, stratified by deceased and living donor KT. Results: In total, 186,342 adult KT were performed from 2003-2013 (Group1), of which 176,656 recipients survived at 1 year (Group2) and 126,405 recipients survived at 5 years (Group3) post-transplant. Multivariable Cox hazard model revealed that employment status at transplant was independently associated with better graft survival in all groups in both deceased (Fig.2) and living (Fig.3) KT. While lower education level (high school or lower, reference; postcollege graduate degree) was not the risk factor in Group1, it increased the risk of graft failure in the later periods for both deceased donor and living donor KT. There was no association between the distance and patient outcomes in all groups. Conclusions: The impact of socioeconomic status on GS changed over time in both living and deceased KT.To improve the very long-term outcomes in later periods, consideration of the patient's education level in follow-up care might be necessary. [Formula presented] [Formula presented] [Formula presented] CITATION INFORMATION: Al-Juburi S., Oki R., Rocha I., Rajendran L., Kerby E., Mohamed A., Nassar A., Al-Kurd A., Kim D., Yoshida A., Abouljoud M., Nagai S. Temporal Trends in the Influence of Socioeconomic Factors on Kidney Transplant Outcomes AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: S. Al-Juburi: None.

Surgery

Axelrod D, Reich D, Schlegel A, Mao S, Hashimoto K, **Nassar A**, Foley D, Florman S, Arvelakis A, de Vera M, Pinna A, Bohorquez H, Roll G, Kubal S, Saharia A, Akoad M, Melcher M, Merani S, Mihaylov P, and Schnitzler M. Economic Assessment of Hypothermic Oxygenated Machine Perfusion in Liver Transplantation. *Am J Transplant* 2025;25(8):S185. Full Text

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Purpose: Liver transplantation (LT) has been fundamentally changed by the development of novel machine preservation (MP) technology, although widespread adoption has been limited by financial considerations. Back-to-base hypothermic oxygenated perfusion (HOPE) is a potential solution, as it improves outcomes following LT using both donors after brain death (DBD) and circulatory death (DCD) but requires fewer resources than other MP technologies. This study aimed to assess the financial benefits of HOPE using results from a contemporary randomized controlled trial. Methods: We examined the financial implications of key post-LT outcomes reported in the Bridge to Life clinical trial comparing HOPE following ex vivo liver preservation with static cold storage (SCS) to SCS alone (clinicaltrials.gov: Nct05045794). Financial analyses were assessed using a Markov model. The cost of key events (LT, re-transplant (re-LT), death, and biliary complications [BC]) requiring invasive intervention were estimated from Medicare payment data. National hospital cost accounting data were used to assess cost per hospital day. Credible Interval (CrI) was determined using robust sensitivity analysis. Results: Compared to SCS only (N=110), LT using HOPE (N=109) reduced initial post-LT hospital length of stay (10.8 vs. 12.9 days), BCs (20.2% vs. 24.6%), re-LT(1.8% vs. 4.5%), and death (2.8% vs. 3.6%). HOPE reduced 1 year cost of LT by $28,565 (CrI: 23,027-$34,541). Savings was greater for DCD LT ($64,370: CrI $52,507 to $78,761) than DBD organs ($16,929: CrI $13,203 to $19,805).. Conclusions: HOPE for a minimum 1.5 hours at the recipient hospital reduced the cost of LT by shortening the index hospitalization and decreasing late complications (BCs, graft failure and death). Additional financial benefits may include increased organ utilization, reduced staff overtime, and fewer high MELD transplants. [Formula presented] CITATION INFORMATION: Axelrod D., Reich D., Schlegel A., Mao S., Hashimoto K., Nassar A., Foley D., Florman S., Arvelakis A., de Vera M., Pinna A., Bohorquez H., Roll G., Kubal S., Saharia A., Akoad M., Melcher M., Merani S., Mihaylov P., Schnitzler M. Economic Assessment of Hypothermic Oxygenated Machine Perfusion in Liver Transplantation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: D. Axelrod: Consultant; Bridge to Life, CareDx. Scientific/Medical Advisory Board Member; Specialist Direct. Consultant; BMI Organ Bank.

Surgery

Dar W, Ng Y, Haver D, **Jesse M**, and Engel K. The Relationship of Pre-Kidney Transplant Cognitive Function and Post-Kidney Transplant Medical and Biological Outcomes. *Am J Transplant* 2025;25(8):S516-S517. Full Text

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Purpose: Pre-transplant cognitive function (CF) in kidney transplant (KT) recipients is emerging as an important component of the KT evaluation. However, the effect of pre-KT CF on post-KT medical outcomes is not clear. We sought to better understand the effect of pre-KT CF on post-KT patient and graft survival and biological outcomes by conducting a systematic review of the available literature. Methods: We conducted a systematic review based on a query of "cognitive function in kidney transplantation." Literature was reviewed and screened as demonstrated in Figure 1. Key inclusion criteria were that studies included for final review had to measure CF both pre and post KT and report on medical outcomes. Results: We identified 24 studies which reported on the relationship between pre-KT CF and post-KT medical outcomes. Only one found a relationship between global pre-KT cognitive impairment and post-KT all cause graft loss. One study identified pre-KT cognitive impairment in the domain of executive function as a risk factor for post-KT mortality. No studies found a correlation between pre-KT global CF and post-KT changes in biochemical markers such as BUN, Cr, hemoglobin, or blood pressure. Seven of 24 studies reported on the relationship of domain specific pre-KT CF and post-KT neuro-imaging, neuro-functional, neural biochemical marker findings with all seven studies correlating pre-KT CF in the domains of executive function and psychomotor speed with changes seen in imaging, functional, or marker studies. Conclusions: This comprehensive systematic review demonstrates the limited data on the relationship of pre-KT CF on post-KT medical outcomes. The data is further limited in that some studies that met the inclusion criteria utilized global measures to test CF while others utilized only domain specific testing. Studies examining neural function, neuro-imaging, neural specific biochemical markers demonstrated a consistent physiologic relationship between pre-KT domain specific CF and biologic outcomes. This suggests that pre-KT CF is correlated with physiologic changes in the CKD/ESRD population. However, when examining pre-KT global CF and post-KT medical outcomes, no relationship emerged. As cognitive impairment is associated with increased mortality in the pre-KT population, these findings suggests more work is needed to define the nature of cognitive impairment in the pre-KT population to better guide clinical care in both the pre-KT and post-KT settings. [Formula presented] CITATION INFORMATION: Dar W., Ng Y., Haver D., Jesse M., Engel K. The Relationship of Pre-Kidney Transplant Cognitive Function and Post-Kidney Transplant Medical and Biological Outcomes AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: W. Dar: None.

Surgery
Engel K, Yek M, Haver D, Dar W, and **Jesse M**. Measures of Cognitive Function in Patients Awaiting and Undergoing Kidney Transplant. *Am J Transplant* 2025;25(8):S628. Full Text

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Purpose: The effect of pre-kidney transplant (KT) cognitive function (CF) on post-KT outcomes is unclear, in part due to the use of variable cognitive assessment measures in the pre-KT setting. As part of a larger systematic review to assess the effects of pre-KT CF on post-KT outcomes, we examined the methodologies employed in assessing pre-KT CF in intended kidney transplant recipients (KTRs) within the existing literature. Methods: We conducted a systematic review to identify studies that measured pre-KT CF and related that to post-KT outcomes. Studies were included if they reported an objective assessment of pre-KT CF and related that to post-KT medical and/or psychosocial outcomes. We screened 1491 studies and 33 were included. Results: Sixty-seven different measures of CF were used across 33 studies. Eight studies assessed CF with one measure only, while 25 studies used more than one measure. Eighteen studies utilized a global cognitive screening measure: Montreal Cognitive

Assessment (n=4), Mini Mental Status Exam (n=7), Modified Mini Mental Status Exam (n=6), and Mini-Cog (n=1). The remainder utilized measures focused on specific cognitive domains. The two cognitive domains that were most studied were executive functioning (n=17) and complex attention (n=21), with at least 12 different measures used across studies to assess each domain. Identification of cognitive impairment was inconsistent across studies even when the same assessment measure was used and many studies (n=17) did not include a cut-off score to identify cognitive impairment. Further, not all studies controlled for the effects of variables such as age, education, dialysis time, or biochemical derangements on CF in the pre-KT setting. Conclusions: There were no consistent practices for examining pre-KT CF in terms of assessment tools used or interpretation of results. This variability indicates a lack of a universal, validated approach to assessing CF and identifying cognitive impairment in this population, thus making comparison across studies difficult. Further, variables known to impact cognitive performance (e.g., age, education, dialysis time, and uremia) were not uniformly accounted for. Given these gaps, it is imperative to identify a validated measure of CF in KTRs so that deficits may not only be consistently identified but also intervened on to potentially improve post-KT outcomes. CITATION INFORMATION: Engel K., Yek M., Haver D., Dar W., Jesse M., Workgroup C. Measures of Cognitive Function in Patients Awaiting and Undergoing Kidney Transplant AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: K. Engel: None.

Surgery

Eshaya M, **Franco-Palacios D**, **Jakupovic L**, **Patel A**, **Tong M**, **Poparad-Stezar A**, and **Fitzmaurice M**. Real-World Use of Maribavir vs. Valganciclovir in Solid Organ Transplant (SOT) Patients with or without Refractory Cytomegalovirus Disease. *Am J Transplant* 2025;25(8):S590. Full Text

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Purpose: Cytomegalovirus (CMV) infection is a major complication in solid organ transplant (SOT) recipients, impacting graft function and survival. The SOLSTICE trial demonstrated maribavir's (MBV) superiority to investigator-assigned therapy for CMV clearance by week 8, yet data on MBV use in SOT patients with non-refractory CMV remains limited, and the impact of MBV on calcineurin inhibitor (CNI)-based immunosuppression (IS) has not been well characterized. The purpose of this study was to assess the efficacy of MBV for viremia clearance in a variety of SOT recipients and the real-world impact of MBV on CNI levels. Methods: This was a retrospective, single-center study of SOT recipients treated with MBV or valganciclovir (VGC) between 2021 to 2024. The primary outcome was CMV viremia clearance by week 8. Secondary outcomes included impact of antiviral therapy on CNI trough levels, adjustments to IS during treatment, treatment-related adverse events, and therapy discontinuation. Results: 55 SOT patients were included (MBV: 25; VGC: 30) with a median age of 58 (kidney 34.5%, liver 29.1%, lung 23.6%, heart 5.5%, multivisceral 5.5%, simultaneous liver-kidney 1.9%). Baseline demographics were comparable between groups (table 1). Notably, patients in MBV group had a median of 15 days of prior VGC exposure before switching therapies. By week 8, CMV clearance was achieved in 48% of MBV-treated patients versus 40% of VGC-treated patients (p=0.551). Among patients receiving tacrolimus in MBV group, a notable increase in FK trough levels was observed. Median FK level before treatment was 6.9, which increased to 9.2 by day 7 (+39%). To counteract this, tacrolimus doses were reduced early in therapy, with median daily dose decreasing from 6 mg to 4 mg by day 7 (−25%) and remaining stable by day 14. VGC-treated patients experienced significant leukopenia (37%). Initial WBC counts were lower in the MBV group but remained stable throughout therapy. In contrast, VGC patients had a median 50% WBC reduction, necessitating granulocyte-colony stimulating factor use in 27% of cases, while no MBV patients required it (p=0.005). Conclusions: MBV demonstrated comparable efficacy to VGC in CMV clearance. It was associated with fewer hematologic complications but led to increased CNI levels, requiring dose adjustments. These findings support MBV as an alternative for CMV treatment in SOT recipients, particularly those at risk for VGC-induced leukopenia. Close monitoring of CNI levels is required, thus larger studies validating degree of interaction are warranted. [Formula presented] CITATION INFORMATION: Eshaya M., Franco-Palacios D., Jakupovic L., Patel A., Tong M., Poparad-Stezar A., Fitzmaurice M. Real-World Use of Maribavir vs. Valganciclovir in Solid Organ Transplant (SOT) Patients with or without Refractory Cytomegalovirus Disease AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Eshaya: None.

Surgery

Halabi M, **Chamseddine H**, **Shepard A**, **Kabbani L**, **Nypaver T**, **Weaver M**, **Kavousi Y**, **Onofrey K**, **Gould J**, and **Peshkepija A**. Comparative Outcomes of Physician-modified Endografts and Zenith Fenestrated Endografts in Juxtarenal Abdominal Aortic Aneurysms. *J Vasc Surg* 2025;82:e81. Full Text

Objectives: To evaluate the early outcomes of physician modified endografts (PMEGs) vs Zenith fenestrated (ZFEN) grafts for juxtarenal aneurysms (JAAA). Methods: A retrospective review was conducted for all patients who underwent endovascular repair of a JAAA with either PMEG or ZFEN at a quaternary care center between 2014 and 2024. Demographic data, procedural metrics, and postoperative outcomes were collected. Technical success was defined on an intention-to-treat basis. Descriptive statistics summarized baseline characteristics, operative variables, and follow-up outcomes. Bivariate analysis was performed to compare perioperative outcomes between the PMEG and ZFEN groups. Results: A total of 60 patients underwent fenestrated endovascular aortic repair for JAAA using either PMEG (n = 25) or ZFEN (n = 35). Patients treated with ZFEN had a higher comorbidity burden, including diabetes (66% vs 24%; P =.001), hypertension (97% vs 76%; P =.012), hyperlipidemia (97% vs 68%; P =.002), and chronic kidney disease (71% vs 6%; P <.001). Operative metrics demonstrated comparable median procedure times between groups (273 minutes vs 270 minutes; P =.382). PMEG cases had significantly longer fluoroscopy times (86 minutes vs 58.5 minutes; P =.011) but total radiation dose was similar between the two groups (Table I). Technical success was 100% in both cohorts. At 30 days, pneumonia (12% vs 0%; P =.035) and acute kidney injury (28% vs 6%; P =.017) were more frequent in the PMEG group. Other postoperative outcomes, including spinal cord ischemia, stroke, and reintervention, were similar. No 30-day mortality occurred in either group. Type Ia endoleak occurred more frequently in the ZFEN group (5.5% vs 0%; P =.809) (Table 2). At 1 year, mortality was higher in the ZFEN group (11% vs 4%; P =.390), while reintervention rates remained similar (8% vs 6%; P =.557). Conclusions: Both PMEG and ZFEN demonstrated high technical success rates for JAAA repair, with similar procedural times and no 30-day mortality. ZFEN use is limited by strict instruction for use criteria and long delivery times, making PMEG a timely alternative for anatomically unsuiTable cases. Long-term follow-up is needed to evaluate durability and reintervention rates between techniques. [Formula presented] [Formula presented]

Surgery

Halabi M, **Chamseddine H**, **Shepard A**, **Kabbani L**, **Nypaver T**, **Weaver M**, **Onofrey K**, **Sullivan B**, **Hafeez MS**, and **Peshkepija A**. Physician-modified Endografts in Real-world Practice: Comparable Outcomes to IDE Centers and the Need for Quality Registries. *J Vasc Surg* 2025;82:e50. Full Text

Objectives: To evaluate early outcomes of physician-modified endografts (PMEGs) for complex abdominal aortic aneurysms (CAAAs) at our institution and compare results to those of investigational new device (IDE) centers. Methods: A retrospective review of all patients at a quaternary medical center who received a PMEG for CAAA repair between 2022 and 2024 was performed. Demographics, procedural metrics, and postoperative outcomes were collected. Descriptive statistics summarized baseline characteristics, operative variables, and follow-up outcomes. Technical success was defined on an intention-to-treat basis. Bivariate analysis was performed to compare our outcomes with those reported by IDE centers. Results: A total of 70 (68% male; mean age, 75 years) patients underwent repair. The majority were former smokers (52%) and had hypertension (78%) or hyperlipidemia (68%). History included prior open aortic repair (3%) and prior endovascular aneurysm repair (22%), 32% of patients were symptomatic. Mean aneurysm diameter was 67 mm. Aneurysm types treated include juxtarenal (37%), pararenal (22%), and thoracoabdominal (38%; 11% type IV) aneurysms. Median operative time was 270 minutes, fluoroscopy time was 80 minutes, median contrast volume was 131.5 mL, and technical success was 95%. Within the first 30 days, type I endoleaks were absent, and type III endoleaks occurred in 2.8%, acute kidney injury in 24.2%, spinal cord ischemia in 7.1% (three patients permanent and two transient), mortality was 5.7%, and 14.2% required reintervention. At 12 months (n = 14), branch stent graft patency was 96% with no additional mortality. Comparisons to IDE centers are detailed in Table I (operative metrics) and Table II (postoperative outcomes). Conclusions: This study demonstrates the feasibility and safety of PMEGs in real-world practice, with outcomes comparable with IDE centers despite higher radiation and AKI rates. The technical success rate (95%) and midterm branch patency (96%) support PMEG as a viable option for CAAA repair. Our data suggest centers outside IDE

may achieve similar results with adequate institutional support and expertise. These findings underscore the need for standardized quality registries to validate PMEG outcomes and guide broader adoption. [Formula presented] [Formula presented]

Surgery
Halabi M, **Chamseddine H**, **Shepard A**, **Nypaver T**, **Weaver M**, **Peshkepija A**, Rashid A, Kashyap V, and **Kabbani L**. Comparative Learning Curves in Carotid Artery Stenting: TCAR Is More Forgiving Than TFCAS. *J Vasc Surg* 2025;82:e54. Full Text

Objectives: To compare the learning curves for transcarotid artery revascularization (TCAR) and transfemoral carotid artery stenting (tfCAS). Methods: Patients undergoing TCAR or tfCAS from 2005 to 2024 were identified in the Vascular Quality Initiative registry. Operator experience was measured by numbering each physician's cases chronologically. Stroke was the primary outcome; secondary outcomes included major adverse cardiovascular events (MACEs) and procedural metrics (procedure time, fluoroscopy time, contrast volume). A machine learning model predicted outcome risk based on experience. Proficiency was defined as the point when predicted outcomes fell below the overall mean. Learning curves were generated over time and stratified by symptomatic status. Results: The study included 48,538 TCAR and 37,561 tfCAS procedures, averaging 20 TCAR and 16 tfCAS procedures per operator. Stroke rates declined with experience for both procedures. In TCAR, symptomatic patient rates fell from 1.9% (95% confidence interval [CI], 1.6%-2.1%) to 0.85% (95% CI, 0.8%-0.9%), reaching the mean by 37 cases (Fig 1). For tfCAS, symptomatic rates declined from 3.0% (95% CI, 1.95%-4.2%) to 1.5% (95% CI, 1.45%-1.61%), reaching the mean by 40 cases (Fig 1). MACE outcomes followed similar improvement trends with increased experience. Operative time declined from 79 minutes (95% CI, 76-81) to 40 minutes (95% CI, 37-41) in TCAR, reaching the average by case 23 (Fig 2); in tfCAS, time dropped from 76 minutes (95% CI, 74-78) to 56 minutes (95% CI, 54-58), reaching average by case 25 (Fig 2). Other technical efficiency metrics followed similar improvement patterns. Conclusions: While both TCAR and tfCAS show improved performance with experience, their learning curves are distinct. TCAR has low complication rates from the outset, with no significant change in slope over time. In contrast, tfCAS shows marked improvement until 50 cases, after which it runs parallel to the TCAR curve. The curves never converge, with TCAR maintaining lower complication rates at all experience levels. These findings suggest TCAR is a safer, more accessible option for a broader range of operators, while tfCAS requires higher-volume specialization to reduce risk. [Formula presented] [Formula presented]

Surgery
Hannoudi A, **Gonte MR**, **Cannella C**, **Sawar K**, **Yono SS**, **Atisha NM**, **Walker EM**, **Bensenhaver J**, **Evangelista MS**, and **Atisha DM**. ASO Visual Abstract: The Effect of Oncoplastic Reduction Mammoplasty on the Incidence of Breast Lymphedema in Women Undergoing Breast-Conservation Surgery. *Ann Surg Oncol* 2025:2. Full Text

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Surgery
Lu Z, **Kumar V**, **Kumaresan K**, **Prashar R**, and **Patel A**. Renal Transplant Outcomes in Elderly Recipients: Age Alone Should Not Be a Barrier. *Am J Transplant* 2025;25(8):S893-S894. Full Text

Purpose: Elderly patients undergo fewer renal transplants due to concerns of increased mortality. We compared outcomes and risk factors for graft loss and mortality in our program's elderly recipients to evaluate these concerns and inform decision-making. Methods: Retrospective analysis of recipients from 1/2013 to 6/2022. Those aged 65 years (yrs.) and older who received primary renal transplants were included. Recipients were grouped into younger (RY; age 65-70 yrs.) and older (RO; age 70+ yrs.). Baseline recipient and donor variables and transplant outcomes were compared between the groups.

Primary outcomes of interest were patient survival (PS) and graft survival (GS). Kaplan-Meier (KM) survival analysis and multivariate Cox regression analysis was performed on all variables with censoring date 11/26/23. Results: 199 recipients were included; 116 were RY, 83 were RO. RY had higher preoperative serum albumin, shorter EPTS, and higher rates of hypertension (HTN), ischemic heart disease (IHD), and vascular disease (PVD). More RO had no induction agent and had a donor with diabetes (DM). Foley duration was longer and hydronephrosis rate was higher in RY, while RO had a higher rate of urine leak. Other characteristics and posttransplant complications did not differ significantly between groups (Table 1). [Formula presented] RY and RO had similar KM probabilities of 1-10 year GS (p=0.21 - 0.91) and PS (p=0.23 - 0.95). Median GS was longer in RY (8.5 vs 6.4 yrs., p=0.08), as was PS (8.9 vs 7.2 yrs., p=0.05). Median GS was similar between groups (8.5 vs 6.4 yrs., p=0.08), while PS was longer in RY (8.9 vs 7.2 yrs., p=0.05). On multivariate analysis, higher 1-year serum creatinine was significantly associated with graft loss in both groups. Recipient DM, IHD, and DGF was associated with risk of graft loss and patient mortality for RY, while higher serum albumin was associated with lower risk for both outcomes for RO. Induction with Simulect (vs. no agent) was associated with lower risk for patient mortality for RO (Figure 1). [Formula presented] Conclusions: Despite differences in baseline characteristics, we found comparable GS and PS between RY and RO groups, indicating that older age should not be a barrier to transplantation. Future analysis will include waitlisted and dialysis patients. CITATION INFORMATION: Lu Z., Kumar V., Kumaresan K., Prashar R., Patel A. Renal Transplant Outcomes in Elderly Recipients: Age Alone Should Not Be a Barrier AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: Z. Lu: None.

Surgery

Lu Z, **Patel A**, and **Yoshida A**. Toward Better Organ Utilization: Identifying Missed Opportunities in Kidney Transplantation. *Am J Transplant* 2025;25(8):S375-S376. Full Text

Purpose: Some deceased donor kidneys (DDKs) refused by one transplant program are then accepted and transplanted elsewhere, indicating missed opportunities. We compared characteristics and transplant outcomes of DDKs accepted vs. initially refused by programs within one OPTN region to assess acceptance and utilization patterns across the region. Methods: Retrospective analysis of DDKs offered by a regional OPO to adult kidney programs from 8/2022 to 8/2024. Only DDKs that were transplanted were included. DDKs were classified as “kidney accepted (KA)” if accepted and transplanted by a regional program, or “kidney refused (KR)” if turned down by a regional program for donor and/or organ reasons and transplanted elsewhere. Programs were grouped into 3 tiers based on acceptance rate. Donor and kidney features and recipient outcomes were compared between groups in each tier. Outcomes of interest were rate of delayed graft function (DGF), recipient 6-month and 1-year serum creatinine (Se Cr) and 1-year graft survival (GS). Kaplan Meier survival analysis was performed with censoring date 8/16/24 and a Cox proportional hazards model was used to quantify the effect of initial refusal on graft loss. Results: 1046 DDKs, offered to 12 programs, were included. Program-specific acceptance rates ranged 7.1 - 35.7%, with 3 programs in the top tier (acceptance rate >20%), 5 in the middle (rate 10-20%), and 4 in the bottom (rate <10%). Over 75% of KR were refused for organ quality reasons, most often unacceptable biopsy and/or organ-specific results. Selected results are shown in Table 1. Across all tiers, KR kidneys had older donors with higher KDPI, longer cold ischemia time, and higher biopsy rates. DDKs accepted by the top tier had the fewest number of significant between-group differences (8 of 16 examined features), while those accepted by the middle tier had the most (12 of 16). DGF rates were higher in KR groups in the top and bottom tiers. Other outcomes were similar between groups across all tiers. KR kidneys had a nonsignificant higher risk of graft loss in the middle and bottom tiers. [Formula presented] Conclusions: With few exceptions, program acceptance rates were low (<20%), reflecting a need to improve DDK utilization across the region. Despite differences in baseline characteristics, we found overall comparable allograft outcomes between KA and KR groups, indicating a need for programs to rethink their donor acceptance and exclusion criteria. CITATION INFORMATION: Lu Z., Patel A., Yoshida A. Toward Better Organ Utilization: Identifying Missed Opportunities in Kidney Transplantation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: Z. Lu: None.

Surgery

Lu Z, **Patel A**, and **Yoshida A**. Missed Opportunities in Kidney Transplantation: Time to Rethink Acceptance Practices. *Am J Transplant* 2025;25(8):S374-S375. Full Text

Purpose: Some deceased donor kidneys (DDKs) refused by one program are then accepted and transplanted elsewhere, suggesting missed opportunities for transplant. We compared characteristics and outcomes of transplanted DDKs accepted vs. initially refused by our program to assess the appropriateness of our acceptance criteria and identify adjustments needed to reduce missed opportunities. Methods: Retrospective analysis of OPTN data on DDKs offered by a regional OPO to a single center from 8/2022 to 8/2024. Only DDKs that were ultimately transplanted were included. DDKs were classified as either “kidney accepted (KA)” if accepted and transplanted by our program, or “kidney refused (KR)” if turned down by our program and transplanted elsewhere. Only DDKs refused for donor and/or organ reasons were included. Donor and organ characteristics and recipient outcomes were compared between the two groups. Outcomes of interest were rate of delayed graft function (DGF), recipient 6-month and 1-year serum creatinine (Se Cr), and 1-year graft survival (GS). Kaplan Meier (KM) survival analysis was performed with censoring date 8/16/24. Multivariate Cox regression of graft loss was performed on all variables. Results: 312 kidneys were included, with 65 (20.8%) in the KA group and 247 (79.2%) in the KR group. 89.5% of KR were turned down for organ-specific reasons, most often for unacceptable organ-specific test results (30%) and organ anatomical damage/defect (24.6%). KR kidneys had a higher degree of glomerulosclerosis and came from donors with higher KDPI and terminal creatinine. Other donor and kidney characteristics did not differ significantly between groups. Outcomes were similar between groups across all measures (Table 1). [Formula presented] On multivariate analysis, DGF was significantly associated with graft loss (HR 5.2, 95% CI [1.33 - 20.43], p=0.02) across the entire cohort. Kidneys that were initially refused (KR group) had a similar risk of failure as KA kidneys (HR 1.5, 95% CI [0.42 - 5.39], p=0.54). No significant risk factors for graft loss were identified within groups. Conclusions: Despite differences in donor and kidney characteristics, we found comparable allograft outcomes between KA and KR groups, indicating a need to rethink our acceptance filters and highlighting the importance of systematic review of donor exclusion criteria in every program. CITATION INFORMATION: Lu Z., Patel A., Yoshida A. Missed Opportunities in Kidney Transplantation: Time to Rethink Acceptance Practices AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: Z. Lu: None.

Surgery

Lu Z, **Patel A**, and **Yoshida A**. Expanding Transplant Opportunities: Rethinking the Role of Offer Biopsy in Kidney Selection. *Am J Transplant* 2025;25(8):S375. Full Text

Purpose: Biopsy findings are a common refusal reason for deceased donor kidneys (DDKs) and some of these refused DDKs are then accepted and transplanted elsewhere, suggesting missed opportunities for transplant. We compared characteristics and outcomes of transplanted DDKs accepted vs. initially turned down for biopsy reasons by our program to assess the appropriateness of our acceptance criteria and identify adjustments needed to reduce missed opportunities. Methods: Retrospective analysis of OPTN data on DDKs offered by a regional OPO to a single center from 8/2022 to 8/2024. Only DDKs that were biopsied and ultimately transplanted were included. DDKs were classified as “kidney accepted (KA)” if accepted and transplanted by our program, or “kidney refused (KR)” if turned down by our program and transplanted elsewhere. DDKs refused for non-biopsy reasons were excluded. Donor and kidney characteristics and recipient outcomes were compared between the two groups. Outcomes of interest were rate of delayed graft function (DGF), recipient 6-month and 1-year serum creatinine (Se Cr), and 1-year graft survival (GS). Kaplan Meier (KM) survival analysis was performed with censoring date 8/16/24. Multivariate Cox regression of graft loss was performed on all variables across the entire cohort and within groups. Results: 103 DDKs were included, with 46 (44.7%) in the KA group, 57 (55.3%) in the KR group. KR kidneys had a higher degree of glomerulosclerosis and longer cold ischemia time. Other donor and kidney characteristics did not differ significantly between groups. Outcomes were similar between groups across all measures (Table 1). [Formula presented] No significant risk for graft loss were identified on multivariate analysis. Biopsied kidneys that were initially turned down (KR group) had a similar risk of failure as KA kidneys (HR 1.33, 95% CI [0.08 - 21.73], p=0.84). Conclusions: Despite differences in kidney characteristics, we found comparable allograft outcomes between KA and KR groups, reaffirming that biopsy findings should not be a consistent factor for refusal and indicating a need to adjust our donor exclusion criteria to reflect this understanding. CITATION INFORMATION: Lu Z., Patel A., Yoshida A. Expanding Transplant Opportunities: Rethinking the Role of Offer Biopsy in Kidney Selection AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: Z. Lu: None.

Surgery

Malick A, **Tepe G**, **Nagai S**, **Muszkat Y**, **Beltran N**, **Pietrowsky T**, and **Jafri S**. Outcomes of Intestinal Biopsies Which Are Indeterminate for Rejection Following Intestine Transplant. *Am J Transplant* 2025;25(8):S839-S840. Full Text

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Purpose: We evaluated the impact of “indeterminate for rejection” (IFR) biopsy results and subsequent clinical outcomes. We aim to evaluate whether changes in immunosuppressive medications and cytomegalovirus (CMV) status at the time of IFR biopsy influence the likelihood of a subsequent biopsy also being classified as IFR or showing a definitive rejection outcome. Methods: Retrospective analysis of adult patients who underwent intestinal transplantation, including those who received multi-organ transplants with intestine with at least one biopsy classified as IFR. Data collected includes immunosuppressive changes, subsequent biopsy results, and infection status. Results: We evaluated 31 patients with long term follow-up following IFR biopsy. 17 (55%) were female. Mean age at time of transplant was 48 years (22-68). 18 (57.9%) patients had intestine transplant only, 13 had multiorgan transplant. There were 84 recorded instances of IFR biopsy results. 54 instances (64%) led to immunosuppression changes, while 30 (36%) did not. 4% of patients in the immunosuppression change group (ICG) and 7% in the no-change group (NCG) had positive CMV PCR at the time of biopsy. In ICG, 69% of cases were negative for rejection on follow-up biopsy. In NCG, 60% were negative for rejection on follow-up biopsy. Persistent indeterminate classification was observed in 9.3% of ICG cases and 20% of NCG. Mild rejection occurred in 20% of ICG cases and 17% of NCG cases. Moderate rejection was seen in 1.9% of ICG cases and 0% of NCG cases. Severe rejection was seen in 0% of ICG cases and 3.3% of NCG cases. There were no statistically significant differences between the two groups (Odds Ratio [OR] = 1.27, 95% Confidence Interval [CI]: 0.47-3.38, p = 0.6). A secondary analysis focused on only the first instance of an IFR biopsy for each patient. 71% of these cases were ICG. 77% of these ICG cases showed subsequent results negative for rejection. 44% of NCG cases showed negative subsequent results for rejection. Persistent IFR occurred in 4.5% of ICG cases and 22% of NCG. Mild rejection occurred in 14% of ICG cases and 22% of NCG. Moderate rejection occurred in 4.5% of ICG and 0% of NCG. Severe rejection occurred in 0% of ICG and 11% of NCG. Conclusions: While medication adjustments were frequently implemented following IFR biopsy, their effect on subsequent biopsy results was not statistically significant. The majority of patients who underwent immunosuppression changes had negative subsequent biopsy outcomes, similar to those without immunosuppression changes. The study highlights the complexity of managing IFR biopsy results in transplant recipients and underscores the need for further research to better understand the appropriate response to IFR biopsy. CITATION INFORMATION: Malick A., Tepe G., Nagai S., Muszkat Y., Beltran N., Pietrowsky T., Jafri S. Outcomes of Intestinal Biopsies Which Are Indeterminate for Rejection Following Intestine Transplant AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Malick: None.

Surgery

Mavilian C, Vega A, Alabi O, Arya S, Brooke BS, Chester C, Conte MS, Fereydooni A, George EL, Iannuzzi J, **Kabbani L**, Lee MH, Mize B, **Nguyen TM**, Tiu M, Woo K, and O'Banion LA. Validation of the Society for Vascular Surgery Appropriate Use Criteria for Management of Intermittent Claudication. *J Vasc Surg* 2025;82:e85-e86. Full Text

Objective: To perform a multi-institutional retrospective validation of the Society for Vascular Surgery appropriate use criteria (AUC) for the management of intermittent claudication (IC). Methods: A retrospective review of patients treated for IC from 2005 to 2024 was performed across seven institutions. Inclusion criteria followed AUC assumptions and all definitions aligned with AUC. All treated limbs were rated as appropriate (benefit outweighs risk, B>R), indeterminate (IND) or inappropriate (risk outweighs benefit, R>B) per AUC by two authors, who resolved discrepancies through discussion. Analysis was performed on the patient level. If one limb was rated as R>B, the patient was rated as R>B. B>R and IND were grouped together (B>R/IND). Results: Among 333 patients, mean age was 69, majority male with

typical comorbidities (Table). Mean follow-up was 4 years. Most had moderate lifestyle limitations, were low surgical risk, with short (<2 block) walking distance (Table). Femoropopliteal (FP, 47%) and aortoiliac (AI, 36%) were most commonly affected. There were 89 patients (27%) who received exercise therapy (ET) alone. Revascularization was performed in 217 (65%), of whom 142 (65%) were on optimal medical therapy at intervention, 54 (25%) received ET, and 79 (36%) underwent bilateral revascularization. Most interventions were AI (40%) or FP (42%) and endovascular (71%). Overall, 223 patients were categorized as B>R/IND and 110 as R>B. Among those who underwent revascularization, 110 (51%) were R>B and 107 (49%) B>R/IND. R>B patients had higher rates of symptom recurrence (58% vs 45%; P =.04), reintervention (45% vs 34%; P =.05), minor amputation (AMP) (8% vs 2%; P =.01), major AMP (8% vs 0; P <.001) and any AMP (14% vs 2%; P <.001). Conclusions: In this retrospective multi-institutional cohort, patients with IC who were treated inappropriately (R>B) per Society for Vascular Surgery AUC experienced significantly worse outcomes compared with those who received appropriate/indeterminate (B>R/IND) treatment. [Formula presented]

Surgery
Miyake K, Alaniz J, **Rocha I**, Kortan E, **Oki R**, Di Cocco P, **Denny J**, Alvarez JA, **Malinzak L**, **Kim D**, Bartlett S, Tzvetanov I, **Abouljoud M**, **Nagai S**, Benedetti E, Spaggiari M, and **Yoshida A**. Robotic Kidney Transplantation with Multiple Arteries: Safety and Efficacy in a Multicenter US Cohort. *Am J Transplant* 2025;25(8):S431. Full Text

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Purpose: Robot-assisted kidney transplantation (RAKT) is increasingly adopted, but outcomes for grafts with multiple arteries (GMA) remain unclear. This study evaluates early outcomes of RAKT using GMA compared to RAKT using grafts with single arteries (GSA) and open kidney transplantation with GMA (OKT-GMA). Methods: Retrospective review of 283 OKT-GMA, 276 RAKT-GSA, and 58 RAKT-GMA cases (January 2018-December 2023) extracted from 2 transplant centers. Primary outcome was 90-day Clavien-Dindo grade ≥3 complication rates. Secondary outcomes included one-year graft and patient survival. Results: Regarding baseline characteristics, age (51.6, 47.4, and 49.1 years, respectively; p=0.21) showed no significant difference between OKT-GMA, RAKT-GSA, and RAKT-GMA groups. BMI was 29.6, 38.7, and 35.2, respectively (p=0.08). The rate of diabetes as a past medical history was also comparable (46.4%, 46.9%, and 44.2%, respectively; p=0.94). For the primary outcome, 90-day complication rates were higher in RAKT-GMA vs. RAKT-GSA (19.3% vs. 9.4%, p=0.031) but not different from OKT-GMA (19.3% vs. 21.1%, p=0.52). One-year graft survival was comparable across groups (96.1% OKT-GMA, 95.3% RAKT-GSA, 93.2% RAKT-GMA, p=0.28). One-year patient survival was also comparable (96.8% OKT-GMA, 96.8% RAKT-GSA, 94.7% RAKT-GMA, p=0.34). Conclusions: RAKT using GMA demonstrates comparable 90-day complication rates to open surgery and acceptable one-year graft/patient survival, despite higher complications than RAKT with single arteries. RAKT using GMA is a viable option in select patients. [Formula presented] CITATION INFORMATION: Miyake K., Alaniz J., Rocha I., Kortan E., Oki R., Di Cocco P., Denny J., Almario Alvarez J., Malinzak L., Kim D., Bartlett S., Tzvetanov I., Abouljoud M., Nagai S., Benedetti E., Spaggiari M., Yoshida A. Robotic Kidney Transplantation with Multiple Arteries: Safety and Efficacy in a Multicenter US Cohort AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: K. Miyake: None.

Surgery
Nabaty R, **Muszkat Y**, **Nagai S**, **Beltran N**, **Pietrowsky T**, and **Jafri S**. Intestinal Transplantation for Short Bowel Syndrome from Gun Shot Wounds: A Case Series. *Am J Transplant* 2025;25(8):S843-S844. Full Text

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Purpose: Short bowel syndrome (SBS) is a malabsorption disorder leading to nutritional deficiencies and high morbidity. Gunshot wounds (GSWs) and other abdominal traumas are known causes of SBS. Intestinal transplantation offers a unique therapeutic option for this patient population; however, outcomes are not well elucidated. We present two cases of patients who developed SBS secondary to GSWs, underwent intestinal transplantation, and subsequently required transplant enterectomy. Methods: We evaluated patients with SBS due to GSW receiving an intestinal transplant at a single center for outcomes including rejection, infection, graft survival, and patient survival. Results: Two males sustained GSWs necessitating small bowel and colon resection, leading to SBS that became dependent on parenteral nutrition with multiple line-related complications. Both patients underwent isolated small bowel transplantation. Patient 1: A 21-year-old underwent transplant with post operative course remaining largely unremarkable for 102 months until he presented with abdominal pain and found to be in cellular and humoral rejection. He developed septic shock due to bacteremia and adenovirus enteritis and did not respond to medical management, necessitating eventual transplant enterectomy. Afterwards, he was managed with parenteral nutrition, however clinical course was complicated by multiple infections and opioid misuse. Patient ultimately expired 12 months post-transplant enterectomy. Patient 2: A 37-year-old underwent transplant and remained hospitalized for 41 days afterwards. Three weeks post-transplant he was noted to have cellular and humoral rejection requiring plasmapheresis and immunoglobulin. Approximately 12 months post-transplant, he presented with septic shock and multiorgan failure. Endoscopy revealed ulcerated and friable mucosa, leading to transplant enterectomy. Despite surgical intervention, his clinical status deteriorated, and he expired shortly thereafter. Conclusions: Patients undergoing intestinal transplantation for SBS secondary to GSW represent a unique and understudied population. These cases highlight the significant risks of rejection, transplant enterectomy, and morbidity. Despite these risks, outcomes are robust as illustrated with the first patient who had many years of normal bowel function, post-transplant. Further research is warranted to optimize management strategies and improve survival rates for this vulnerable population as advancements in transplantation continue. CITATION INFORMATION: Nabaty R., Muszkat Y., Nagai S., Beltran N., Pietrowsky T., Jafri S. Intestinal Transplantation for Short Bowel Syndrome from Gun Shot Wounds: A Case Series AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: R. Nabaty: None.

Surgery

Nagai S, **Nowicki M**, **Oki R**, **Rajendran L**, **Kerby E**, **Mohamed A**, **Nassar A**, **Al-Kurd A**, **Yoshida A**, and **Abouljoud M**. Cost Analysis of Machine Perfusion in DCD Liver Transplantation: Balancing Expenses and Post-Transplant Outcomes. *Am J Transplant* 2025;25(8):S739. Full Text

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Purpose: Organ utilization has increased, along with the adoption of machine perfusion (MP). While MP may improve liver utilization, concerns about medical costs remain. This study analyzes expenses based on MP use and post-transplant complications. Methods: Data on medical expenses were collected for donation after circulatory death (DCD) liver translants (LT) between Jan 2019 and Jan 2024. Patients were classified: static cold storage (SCS) without complications (Group 1), SCS with complications (Group 2), MP without complications (Group 3), and MP with complications (Group 4). Complications included reoperations, biliary complications requiring stenting, and readmissions within 1-year post-transplant for any reason. Costs associated at initial admission and all encounters within 1-year post-transplant were compared. The cost at initial admission included the organ acquisition cost (MP management, transportation), surgery, reoperations, and procedures at initial admission. The cost for all encounters within 1-year post-transplant encompassed follow-ups, readmissions, and necessary procedures after discharge. Results: A total of 116 LT-alone were performed, with 5 patients excluded from the analysis due to mortality within 1 year. Thus, 111 cases were included. The number of patients in Groups 1, 2, 3, and 4 was 14, 35, 23, and 39, respectively. No significant differences in patient characteristics were observed among the four groups. Post-transplant complications occurred in 71.4% (35/49, including 8 cases of ischemic cholangiopathy) of the SCS group and 62.9% (39/62) of the MP group. The cost at initial admission was significantly higher in Group 3 ($231,368) and Group 4 ($233,204) compared to Group 1 ($139,043) and Group 2 ($159,267), primarily due to the increased organ acquisition cost associated with MP use ($p < 0.001$). No significant difference in total cost was

observed between Groups 2 and 3 (p=0.266, Fig.1). When comparing the sum of the initial admission cost and all encounters 1-year post-transplant cost, significant differences were observed between Group 1 and 2 (p < 0.001) as well as between Group 3 and 4 (p = 0.017). The absolute cost difference was larger between Groups 1 and 2 ($80,103 per case) compared to Group 3 and 4 ($29,135 per case). Conclusions: While MP use increased the initial admission cost in DCD LT, total costs over one year were comparable between SCS with complications and MP without complications. MP was associated with fewer and less costly complications, suggesting that complications after SCS DCD LT may lead to more severe or persistent issues. Financial concerns about MP should be weighed against its potential to reduce complications and long-term costs. [Formula presented] CITATION INFORMATION: Nagai S., Nowicki M., Oki R., Rajendran L., Kerby E., Mohamed A., Nassar A., Al-Kurd A., Yoshida A., Abouljoud M. Cost Analysis of Machine Perfusion in DCD Liver Transplantation: Balancing Expenses and Post-Transplant Outcomes AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: S. Nagai: None.

Surgery

Oki R, **Rajendran L**, **Kerby E**, **Mohamed A**, **Nassar A**, **Al-Kurd A**, **Kim D**, **Yoshida A**, **Abouljoud M**, and **Nagai S**. Exploring Disease-Specific Waitlist Dynamics in Simultaneous Liver-Kidney Transplantation. *Am J Transplant* 2025;25(8):S276. Full Text

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Purpose: Model for End-Stage Liver Disease (MELD) score system has been used to determine liver transplant (LT) waitlist ranking. While LT candidates have variety of primary liver diseases, the score systems have been used regardless of their disease etiology. In fact, our group previously reported that waitlist outcomes differed between those with major liver diseases in LT alone candidates. We hypothesized that waitlist outcomes varied depending on the etiology of liver disease in those who need simultaneous liver-kidney transplant (SLKT). We assessed the difference in in waitlist outcomes among major liver disease groups in SLKT candidates. Methods: Adult listed for SLKT from 2017-2023 were evaluated using the United Network for Organ Sharing database. Waitlist outcomes were compared between the five-disease groups, including alcohol-related liver disease (ALD), Metabolic dysfunction-Associated Steatohepatitis (MASH), hepatitis C virus infection (HCV), biliary diseases, and others. Waitlist outcomes including mortality or SLKT were assessed using Fine-Gray proportional hazard regression for competing events. Results: In total, 9,089 adult candidates for SLKT were enrolled.There were no significant differences in 90-day waitlist mortality and 90-day transplant rate among 5 etiologies adjusted with initial age, ascites, BMI, hemodialysis, MELD-Na-score and race. (Fig.1) When patients were categorized by initial MELD score (6-20, 21-29, and ≥30), biliary disease demonstrated better 90-day mortality compared to ALD in the lower MELD score group (p<0.001). In contrast, MASH had significantly worse 1-year waitlist mortality compared to ALD. (HR1.36, 95%CI 1.15-1.59, p<0.001, Fig. 2) There were no difference in 1-year transplant rate. (Fig. 2) MASH demonstrated significantly worse 1-year mortality compared to ALD in the lower and middle MELD score groups (p=0.005, p=0.003) but showed no significant difference in the higher score group (p=0.390). Conclusions: There were significant differences in waitlist outcomes according to the liver etiologies in SLKT. Patients with MASH often had chronic metabolic diseases, which may include chronic kidney failure, which may be attributable to the findings of this study. MELD score systems failed to stratify patients' medical urgency. [Formula presented] [Formula presented] CITATION INFORMATION: Oki R., Rajendran L., Kerby E., Mohamed A., Nassar A., Al-Kurd A., Kim D., Yoshida A., Abouljoud M., Nagai S. Exploring Disease-Specific Waitlist Dynamics in Simultaneous Liver-Kidney Transplantation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: R. Oki: None.

Surgery

Oki R, **Rocha I**, **Al-Juburi S**, **Rajendran L**, **Kerby E**, **Kim D**, **Yoshida A**, **Abouljoud M**, and **Nagai S**. The Role of Machine Perfusion in Expanding Donor Utilization for Simultaneous Liver and Kidney Transplantation. *Am J Transplant* 2025;25(8):S273-S274. Full Text

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Purpose: The use of MP(Machine perfusion) for both the kidney and liver has the potential to increase organ utilization in simultaneous liver-kidney transplantation (SLKT). The purpose of this study was to examine: 1) the trends over time in donor types and the use of MP for kidney and liver transplantation, and 2) whether medically complex donors pose a risk factor for 1-year graft survival between the use of MP and without MP for each organ in SLKT. Methods: We analyzed SLKT performed between 2015 and 2024 using the United Network for Organ Sharing database. Donor types and MP use for liver and/or kidney were captured and associations with outcomes were evaluated. Cox proportional hazard model was used for analyzing the factors related to 1-year liver or kidney graft failure. Results: IIn total, 6,956 adult SLKT were performed during the study period. SLK from circulatory death donors (DCD) increased from 4.5% in 2015 to 16% in 2023. (Figure 1)The median Kidney Donor Profile Index (KDPI) has shown an increasing trend from 23% in 2015 to 28% in 2023. MP use for kidney and liver increased from 21% to 51% and 0% to 17%, respectively. (Figure 1) Overall, 37.8% of kidney allografts were placed on MP (N=2632) and 3.2% of liver allografts were placed on MP (N=222). KDPI>85% was an independent risk factor of 1-year kidney graft failure in the no kidney MP group [HR 2.03, 95%CI 1.20-3.44, p=0.009], but not in the kidney MP group. (Table1) DCD was found to be an independent risk factor of 1-year liver graft failure in the no liver MP group [HR 1.56, 95%CI 1.19-2.03, p=0.001], but not in the liver MP group. (Table2) Conclusions: Although DCD was a risk factor for liver graft failure without MP for liver, it ceased to be a risk factor when MP was applied. Likewise, although KDPI >85% was linked to a higher risk of kidney graft failure without MP for kidney, MP for kidney might help reduce this risk. MP might also enable the use of lower-quality organs, thereby further expanding the donor pool in SLKT. [Formula presented] [Formula presented] [Formula presented] CITATION INFORMATION: Oki R., Rocha I., Al-Juburi S., Rajendran L., Kerby E., Kim D., Yoshida A., Abouljoud M., Nagai S. The Role of Machine Perfusion in Expanding Donor Utilization for Simultaneous Liver and Kidney Transplantation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: R. Oki: None.

Surgery

Oki R, **Varban O**, **Carlin A**, **Al-Kurd A**, **Nagai S**, **Yoshida A**, **Abouljoud M**, **Prashar R**, **Khoury N**, and **Shrivastava P**. Trends in Bariatric Surgery and Kidney Transplantation Status Among Patients with Advanced Chronic Kidney Disease: A 12-Year Retrospective Review. *Am J Transplant* 2025;25(8):S891-S892. Full Text

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Purpose: The prevalence of obesity is increasing among patients with end-stage renal disease (ESRD). Metabolic and bariatric surgery (MBS) is an effective method for weight loss in this population. This study aims to examine the trends and outcomes in kidney transplant (KT) among patients with advanced chronic kidney disease (CKD) who underwent MBS. Methods: A retrospective review was conducted of all patients undergoing MBS between January 1, 2012, and Dec 31, 2024, within a large metropolitan health care system. Patients with CKD stage 5, ESRD, or history of KT at the time of MBS were identified and demographic information and comorbidities were examined. The log-rank test was used to compare patient and graft survival. Results: Fifty-eight patients were included, with a median age of 47 years and a median BMI of 43.8 kg/m2. Forty-one (70.7%) patients were female and 42 (73.4%) were Black. Hypertension and/or diabetes accounted for 75.8% of etiology, while cardiovascular disease (CVD) was present in 94.6%. (Table1)Twenty-nine patients underwent KT, of which 18 received KT before MBS and 11 after. No significant differences were observed in patient characteristics between the two groups(Table1). There was no significant difference in patient survival (p=0.979) between patients with or without KT(Fig.1). Among patients undergoing KT, no significant difference in patient (p=0.326) or graft survival (p=0.078) was observed based on timing of KT either before or after MBS. Black patients tended to have lower graft survival (p=0.070). A total of 13 (32.5%) patients were declined listing for KT after MBS. The reasons for decline included low cardiac function (30.8%), persistent obesity (15.4%), and other physical problems (15.4%). (Fig.2) Conclusions: MBS appears to be associated with similar patient and graft survival both before and after KT. Despite undergoing MBS nearly one-third of patients with

CKD are declined listing for KT. [Formula presented] [Formula presented] [Formula presented] CITATION INFORMATION: Oki R., Varban O., Carlin A., Al-Kurd A., Nagai S., Yoshida A., Abouljoud M., Prashar R., Khoury N., Shrivastava P. Trends in Bariatric Surgery and Kidney Transplantation Status Among Patients with Advanced Chronic Kidney Disease: A 12-Year Retrospective Review AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: R. Oki: None.

Surgery

Oluborode B, **Malinzak L**, **Nagai S**, **Abouljoud M**, and **Yoshida A**. Long-Term Survival Outcomes of Liver Transplantation, Liver Resection, Ablative Therapy Among Patients with Early Solitary Primary Hepatocellular Carcinoma: A Population-Based Longitudinal Study. *Am J Transplant* 2025;25(8):S706. Full Text

Purpose: While treatment options for early solitary primary hepatocellular carcinoma (HCC) include radiofrequency ablation (RFA), liver resection (LR), and liver transplantation (LT), controversy exists on the optimal treatment choice. Due to ethical reasons, a randomized trial comparing these options has not been conducted. Furthermore, previous studies have primarily evaluated the treatment effect among smaller cohorts and are often limited to individual institutions and conducted over shorter period. Hence, using a population-based database that span several decades, we aimed to evaluate the long-term survival outcomes in patients with solitary early-stage primary HCC carcinoma who had either LT, LR or RFA Methods: This was a longitudinal cohort study using data obtained from the Surveillance, Epidemiology, and End Results registry database which covers about 30% of USA's population. In this study, patients who were ≥18 years, with solitary primary HCC ≤ 3cm, without vascular invasion, between 2004 and 2021 were included. Excluded were those with unknown follow-up status or those with survival time < 1 month. The outcome of interest was cancer-related survival, which was assessed with the Kaplan-Meier method. A multivariate analysis was conducted using the Cox proportional hazard model to identify factors associated with survival. The significance level was assessed at $p < 0.05$. Results: 5,115 patients with early solitary primary HCC met the inclusion criteria, out of which 1,156 (22.6%) underwent LT; 1,071(20.9%) underwent SR; and 2,888 (56.5%) underwent RFA. The 1 yr survival rate in the LT group was 97% compared to 95% in the SR and RFA cohort (Fig 1). In the adjusted model, patients who had RFA had a lower long-term survival when compared to the LT cohort. The RFA cohort had a 5-fold risk of cancer-related death (HR: 5.37 [95% CI 4.37-6.60]; $p < 0.001$), while the risk of cancer-related death was 3-fold higher in the SR group (HR: 3.30 [95% CI 2.62-4.15]; $p < 0.001$) when compared to the LR group. Furthermore, patients with elevated AFP had a 32% increased risk of cancer-related death [HR:1.32 (95%CI: 1.18,1.49)]. Also, for every cm increase in the size of the tumor, there was a 3% increased risk of death [HR:1.03 (95%CI:1.02,1.04)]. The risk of death was 43% lower among Asians/Pacific Islanders [HR: 0.57 (95%CI:0.59,0.67)] compared to Caucasians. Conclusions: Although LT confers improved long-term survival since LT reduces the risk of recurrence. The comparable one-year survival rate with SR & RFA suggests that SR & RFA could be used as a bridging treatment option. [Formula presented] CITATION INFORMATION: Oluborode B., Malinzak L., Nagai S., Abouljoud M., Yoshida A. Long-Term Survival Outcomes of Liver Transplantation, Liver Resection, Ablative Therapy Among Patients with Early Solitary Primary Hepatocellular Carcinoma: A Population-Based Longitudinal Study AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: B. Oluborode: None.

Surgery

Ramthun M, Engel K, Haver B, Dar W, and Jesse M. Psychosocial Factors Associated with Cognitive Functioning in Patients Who Are Being Considered or Listed for Kidney Transplant. *Am J Transplant* 2025;25(8):S636. Full Text

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Wellstar Hlth Syst, Marietta, GA USA

Purpose: As a component of a broader systematic review examining the impact of pre-kidney transplant (KT) cognitive functioning (CF) on post-transplant outcomes, we sought to identify the psychosocial

factors associated with pre-KT cognitive impairment in patients who are being considered for or listed for KT. Methods: A systematic review was performed with the primary aim of identifying whether CF, as measured in the pre-transplant period, impacts post-transplant medical and/or psychosocial outcomes. Studies were eligible if they provided an evaluation of pre-KT CF and linked it to medical and/or psychosocial outcomes after transplant. After screening 1,491 studies, 33 studies were included in the review. Results: Only six of the included studies assessed for a relationship between pre-KT CF and psychosocial variables. Three studies assessed for the association between pre-KT CF and race. One study found that non-white race was associated with increased odds of cognitive impairment while two studies did not find a significant association, although one had a significantly limited sample (four non-white participant out of 88 total). There were four studies that assessed the association between education and CF, all of which found an association between cognitive impairment and lower educational attainment. There was one study that evaluated the relationship between income and CF and found that less annual household income was associated with cognitive impairment. Two studies evaluated the association between depression and CF pre-transplant though used different self-report measures to assess for symptoms of depression. One of the studies found a significant association between depression and CF though the other did not. It is notable that 15 studies excluded participants with varying mental health histories and/or current symptoms. Conclusions: In conclusion, our systematic review highlights the limited research on the psychosocial factors influencing pre-KT CF. Despite extensive research on the impact of variables such as education and depression in other populations, available research with KT patients has largely failed to take these things into consideration. This makes interpretation of results related to cognitive assessment in this population limited. Further research is needed to explore these psychosocial variables more comprehensively and their potential confounding effect on CF pre-transplant. CITATION INFORMATION: Ramthun M., Engel K., Haver B., Dar W., Jesse M. Psychosocial Factors Associated with Cognitive Functioning in Patients Who Are Being Considered or Listed for Kidney Transplant AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: M. Ramthun: None.

Surgery

Reich DJ, Schlegel A, Mao S, Hashimoto K, **Nassar A**, **Rizzari M**, Foley D, Florman S, Arvelakis A, de Vera M, Pinna A, Bohorquez H, Roll G, Mihaylov P, Kubal C, Saharia A, Akoad M, Melcher M, and Merani S. Decreased Rejection Severity with Hypothermic Oxygenated Perfusion: Sub Analysis from a Pivotal Multicenter Trial of HOPE for Liver Transplantation. *Am J Transplant* 2025;25(8):S238-S239. Full Text

Purpose: Hypothermic oxygenated perfusion (HOPE) mitigates ischemia reperfusion injury and downstream immune mediated complications in liver transplant (LT) recipients. We analyzed allograft rejection outcomes in the US multicenter Bridge to HOPE RCT comparing static cold storage (SCS) alone with SCS followed by end ischemic HOPE for increased risk DBD and DCD LTs. The trial, completed in 11/2024, demonstrated significant reduction in Early Allograft Dysfunction in the HOPE arm (primary endpoint superiority, p=.005) and other improved outcomes, including shorter hospital stays, reduced severity of cholangiopathy, and fewer graft failures. The rejection outcomes haven't previously been reported. Methods: The trial has been described (clinicaltrials.gov: Nct05045794). We analyzed data from the full cohort of 219 patients; each had 1-yr follow-up except 7 that died (3 HOPE, 4 SCS). Biopsy proven rejection (BPR) was graded by Banff Classification and assessed for treatment with steroids and anti-thymocyte globulin (ATG). Results: Baseline demographics and immunosuppression were similar between arms (Table); autoimmune liver disease trended higher in SCS. Rejection prevalences were comparable between arms (HOPE: 25 pts [23%], 27 events; SCS: 26 pts [24%], 28 events). Seven of 51 patients with presumed rejection lacked biopsy confirmation (2 HOPE, 5 SCS); there were 44 BPRs, also with similar prevalences between arms (Table). Mycophenolate use at the time of BPR was more common in SCS. Moderate/severe BPR was less common in HOPE than SCS (32% v 67%, p=.033; Figure). Ten patients developed steroid resistant BPR (SRR) requiring ATG, 1 in HOPE and 9 in SCS (4% v 43%, p=.003; Figure); 1 of the 9 SCS patients failed ATG and underwent urgent re-LT on day 13 for accelerated BPR and another 3/9 SCS patients had unresolved SRR at the end of study follow-up. Conclusions: While the prevalence of BPR was similar in HOPE and SCS, HOPE was associated with significantly less severe BPR and a significantly lower risk of SRR. These results highlight the immunomodulatory benefits of HOPE and warrant further research. [Formula presented] CITATION INFORMATION: Reich D., Schlegel A., Mao S., Hashimoto K., Nassar A., Rizzari M., Foley D., Florman S., Arvelakis A., de Vera M., Pinna A., Bohorquez H., Roll G., Mihaylov P., Kubal C., Saharia A., Akoad

M., Melcher M., Merani S. Decreased Rejection Severity with Hypothermic Oxygenated Perfusion: Sub Analysis from a Pivotal Multicenter Trial of HOPE for Liver Transplantation AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: D.J. Reich: None.

Surgery
Rocha I, **Oki R**, **Nishimagi A**, **Al-Juburi S**, **Rajendran L**, **Kerby E**, **Mohamed A**, **Nassar A**, **Al-Kurd A**, **Kim D**, **Yoshida A**, **Abouljoud M**, and **Nagai S**. Long-Term Conditional Graft Survival in Liver and Kidney Transplants: Does Race Matter Differently? *Am J Transplant* 2025;25(8):S277. Full Text

Purpose: Racial and ethnic disparities in outcomes after liver transplantation (LT) and kidney transplantation (KT) are important to address. Previous studies showed that Black has lower graft survival (GS) than White in both LT and KT. However, it remains unclear about the impact of race on very long-term post-transplant outcomes. This study aimed to evaluate and compare the influence of race on very long-term GS in LT and KT. Methods: Adult LT or KT performed from 2003-2013 were evaluated respectively, using the United Network for Organ Sharing database. To mitigate the prognostic effects of early post-transplant complications, we assessed conditional 10-year GS in 5-year graft survivors post-transplant,defined as the probability of GS at 10 years after 5 years in those whose graft function was maintained during the first 5 years. Race was classified into White, Black, Hispanic, Asian and Others. The impact of race on GS was evaluated by Cox proportional hazard model. Risks were adjusted with recipients' age, gender, BMI, diabetes mellitus, employment status, educational level, distance from transplant center to patients' residence at transplant and donor's age gender, BMI, race, donor type. Results: In total, 71,679 adult LT and 186,342 adult KT were performed from 2003-2013, of which 46,659LT/126,405KT recipients maintained graft function at 5 years post-transplantation. Kaplan-Meier analysis showed that Asian had the best and Black had the worst 10-year conditional GS in both KT and LT. ($p<0.01$) Black showed significantly lower 10-year conditional GS in KT, compared to White, after risk adjustment. (HR 1.07, 95%CI 1.03-1.11, $p<0.01$, Fig.1) In contrast, in LT, Black demonstrated comparable 10-year conditional GS to White after risk adjustment. (HR 1.07, 95%CI 0.95-1.20, $p=0.259$, Fig.2). In LT, the rate of cardiovascular disease (CVD) and malignancy as a cause of death was higher in White compared to Black. (28.5% vs 24.8%, 34.4% vs 23.8%, $p<0.001$) Conclusions: Black was associated with lower 10-year conditional GS in KT, whereas in LT, 10-year conditional GS between Black and White was comparable. Higher incidence of deaths due to CVD or malignancy in White LT patients might contribute to this finding. Further evaluations of factors contributing to disparities are necessary to address racial inequities in long-term post-transplant outcomes. [Formula presented] [Formula presented] CITATION INFORMATION: Rocha I., Oki R., Nishimagi A., Al-Juburi S., Rajendran L., Kerby E., Mohamed A., Nassar A., Al-Kurd A., Kim D., Yoshida A., Abouljoud M., Nagai S. Long-Term Conditional Graft Survival in Liver and Kidney Transplants: Does Race Matter Differently? AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: I. Rocha: None.

Surgery
Smith B, **Rajendran L**, and **Nassar A**. Safety of Robotic Cholecystectomy in Cirrhotic Patients. *Am J Transplant* 2025;25(8):S481. Full Text

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Purpose: Over the years there have been many studies that investigate the safety of laparoscopic cholecystectomy in patients who have cirrhosis. However, evidence on the safety and outcomes of robotic cholecystectomy in cirrhotic patients is limited. The goal of this study was to evaluate the post-operative complications for patients with cirrhosis who underwent robotic cholecystectomy. Methods: A database search was done for robotic cholecystectomies performed for any reason by our facility's Transplant or Hepatobiliary surgeons between 2014 -2024. Patient demographic and operative variables were collected including: body mass index, etiology and grade of liver disease, surgery indications, and need for conversion to open surgery. The outcomes examined included: 30-day postoperative complications, re-admission to hospital, and overall 1-year patient survival. Complications were graded based on the Clavien-Dindo classification. The overall incidence of complications was calculated. Results: 146 patients were identified. Twenty of these patients were identified to have cirrhosis. The patients

ranged in age from 41-75 (mean 59.8 years old), with an average BMI of 33.97kg/m2. Model of end stage disease (MELD) score ranged from 6-18 (mean 10.05). There were 14 patients who were Child-Pugh Class A and 6 who were Class B. Of these 20 cirrhotic patients, there were 2 who had postoperative complications requiring re-admission in the first 30 days postop. Both post-op complications were Clavien-Dindo grade 3. Incidence rate of complications after robotic cholecystectomy was 0.1 over 10 years. Conclusions: Based on this study with a small sample size, overall the incidence of complications after robotic cholecystectomy is low in patients who are Child-Pugh score B or less. More analysis is needed to evaluate incidence of complication in relation to grade and etiology of liver disease, surgical indications and laboratory data. More data is needed to compare outcomes of cirrhotics with non-cirrhotics after robotic cholecystectomy. CITATION INFORMATION: Smith B., Rajendran L., Nassar A. Safety of Robotic Cholecystectomy in Cirrhotic Patients AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: B. Smith: None.

Surgery

Taber D, **Jesse M**, Peipert J, Myaskovsky L, George R, Gordon E, Chisholm-Burns M, and Gill J. Burdens of Therapy: AST's National Patient Survey of Unmet Immunosuppressant Needs. *Am J Transplant* 2025;25(8):S25-S26. Full Text

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Purpose: AST commissioned the development, dissemination, and analysis of a national survey assessing organ transplant (Tx) recipients' perceptions of unmet immunosuppressant (IS) needs. Side effect (SE) frequency, severity, and overall burden were assessed and presented here. Methods: In partnership with 25 transplant recipients, an AST workgroup of 9 transplant professionals developed, disseminated, and analyzed an online survey containing 17 constructs. Topics included IS SEs, treatment burden, quality of life, adherence, self-efficacy, costs, and others. The survey, active from 06/2023 to10/2024, resulted in >10,000 valid responses. Patient recruitment strategies involved direct advertising and engaging clinicians to invite participants via a weblink or QR code in Tx clinics. Statistics included: descriptive, Item Response Theory to estimate SE burden, and generalized linear modeling to assess variables associated with SE burden. Results: After removing invalid responses,10,091 surveys were analyzed (9,543 adults, 548 peds) from 232 Tx centers. Respondents were a mean of 6.6 years post- Tx and were well represented across sociodemographic characteristics. Nearly all (92%) respondents reported at least one SE (median 3 [IQR 1-5]). Of the recorded SEs, 63% were reported as occurring 'often' or 'always,' and 54% were rated as having a 'moderate' or 'great deal' of impact on daily life (Figure A). Write-in SEs (which was allowed in addition to specific selections) were ranked highest in severity, and included cancer, pain/neuropathy, skin issues, kidney disease, diabetes, hypertension, memory/brain fog, and infection (Figure B). SEs of fatigue, insomnia, mood/depression/anxiety, and tremor were common, with varying degrees of severity (Figure C). Baseline characteristics significantly associated with SE burden included current IS, past IS, and demographics. Belatacept, current mTOR use, and cyclosporine were not significantly associated with SE burden (Table D). Conclusions: Findings from a US survey of >10,000 Tx recipients demonstrate IS SEs are common and have a heavy burden on daily life. Cancers, kidney disease, diabetes, hypertension, and memory issues were common write-in SEs rated as having the highest burden. SE burden was strongly associated with certain IS regimens and demographics, which may inform future efforts to develop evidence- based IS individualization recommendations. [Formula presented] CITATION INFORMATION: Taber D., Jesse M., Peipert J., Myaskovsky L., George R., Gordon E., Chisholm-Burns M., Gill J. Burdens of Therapy: AST's National Patient Survey of Unmet Immunosuppressant Needs AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: D. Taber: Consultant; Takeda, Veloxis, CareDx. Research Grant Site Overall Principal Investigator; Takeda, Veloxis, Merck.

Surgery

Toiv A, **Yoshida A**, **Roberman J**, **Doshi N**, **Poisson L**, **Abouljoud M**, **Moonka D**, and **Jesse M**. Listed or Left Behind: The Impact of Social Support on Liver Transplant Access. *Am J Transplant* 2025;25(8):S493. Full Text

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Purpose: Liver transplantation (LT) is the only curative therapy for patients with decompensated liver disease, but the complex evaluation process for selecting LT recipients limits access for many. “Social support” is a subjective and controversial criterion often used for determining LT eligibility. However, transplant centers inconsistently apply this criterion, and using social support to determine LT eligibility contributes to racial, ethnic, and socioeconomic inequities in transplant listing. Here we investigated the impact of using social support as a criterion for LT listing. Methods: We conducted a retrospective analysis of all patients evaluated for LT between January 1, 2019, and December 31, 2021 at an academic liver center with a clearly defined objective social support evaluation criterion. Logistic regression analysis was used to determine the association between social support inadequacy (unable to report ≥2 support people and/or other significant concerns) and LT listing status. Kaplan-Meier analysis was used to examine the relationship between social support and time-to-decision. Results: Of 711 LT candidates who had social support information available, 498 (70%) were not listed for LT, of whom 13 (2.6%) were not listed for LT solely due to having inadequate social support. After controlling for several variables, having inadequate social support was significantly associated with decreased odds of being listed for LT (odds ratio 0.38; 95% CI, 0.13-0.93). Other predictors of non-listing included female sex and having recommendations for substance use treatment. Conversely, being married/partnered and higher education levels were positively associated with listing. Kaplan-Meier analysis did not show significant differences in time-to-decision based on social support status; however, patients with inadequate social support exhibited a steeper decline in evaluation completion during the initial 125 days. Conclusions: At our transplant center, <3% of patients who were excluded from LT listing were not listed solely due to having inadequate social support, and inadequate social support was significantly associated with a lower likelihood of listing. Social support remains a critical and controversial criterion for determining LT eligibility, and the subjective nature of social support evaluations can perpetuate disparities in access to life-saving transplantation. Standardizing assessments and implementing interventions to strengthen social support systems could reduce inequities and ensure more equitable access to transplantation. CITATION INFORMATION: Toiv A., Yoshida A., Roberman J., Doshi N., Poisson L., Abouljoud M., Moonka D., Jesse M. Listed or Left Behind: The Impact of Social Support on Liver Transplant Access AJT, Volume 25, Issue 8 Supplement 1 DISCLOSURES: A. Toiv: None.

Surgery

Wehrle CJ, Mao S, Satish S, Hashimoto K, **Nassar A**, Riz- zari M, Foley D, Florman S, DeVera M, Pinna A, Reich D, Bo- horquez H, Roll G, Mihaylov P, Kubal C, Saharia A, Akoad M, Melcher M, Merani S, and Schlegel A. Hypothermic-Oxygenated and Normothermic Machine Perfusion: A Risk-Matched Post-Hoc Comparison of the Bridge to Hope Randomized Trial with Prospectively Collected Institutional Outcomes. *Am J Transplant* 2025;25(8):S86. Full Text

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Purpose: Hypothermic-Oxygenated (HOPE) and Normothermic Machine Perfusion (NMP) are the two most popular techniques for ex-situ liver perfusion. Despite routine use in many countries, their clinical outcomes have never been directly compared. Methods: This is a post-hoc comparison of the Bridge to Hope (BtH) RCT (Nct05045794; VitaSmart®) with prospectively collected institutional outcomes with NMP (OrganOx metra®). Both were applied after static cold storage (SCS) in the recipient center. Institutional and RCT SCS-only cases were compared to assess whether differences were attributable to preservation type or other practices. HOPE vs. NMP and SCS vs. SCS cases with 12m active follow-up were propensity-matched (PSM) using donor age, donor-risk index (DRI), cold ischemia time, graft type (DBD vs. DCD), recipient age, and labMELD. Standardized Core Outcome Sets (COS) were used for complication reporting. Results: Overall, 1,029 transplantations were included: 407 perfusion (HOPE=109; NMP=308) and 622 SCS (BtH=110, Institution=512). After risk-matching, all measured risk-factors and post-LT outcomes for SCS cases were similar. Following PSM, 101 pairs (DBD=77, DCD=24) demonstrated balancing of all measured risk factors. Median DRI was 1.98 [1.7-2.3] and 2.1 [1.74-2.3] for NMP and HOPE. HOPE-treated grafts demonstrated improved graft (log-rank p=0.042) and recipient survival (log-rank p=0.029), and major complications (Clavien Grade III-V) in hospital (p=0.003), at 3- (p=0.030) and 6-months (p=0.031). Cumulative complications measured by CCI were reduced with HOPE at 3m (34.6 [IQR=27-48] vs. 43.3 [28-57], p=0.031), 6m (38.7 [29-52] vs. 48.3 [35-71], p<0.001) and 12m (39.4 [30-53] vs. 53.6 [41-76], p<0.001). Finally, HOPE reduced non-anastomotic strictures (NAS, 4% vs. 11%, p=0.04) in all patients. Within the DCD sub-cohort (HOPE=24 vs. NMP=24), NAS (8% vs. 21%) and AS (10% vs. 29%) were reduced though not significant. NAS-associated graft loss was HOPE=4% (n=1) and NMP=13% (n=3). Conclusions: HOPE-treatment may improve outcomes further over what has already been seen with NMP in the US.