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Henry Ford Health Publication List – March 2024

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health personnel. Searches were conducted in PubMed, Embase, Web of Science, CINAHL, and Google Books during the month, and then imported into EndNote for formatting. There are 191 unique citations listed this month, including 117 articles, 72 conference abstracts, and 2 books or book chapters.

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

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Articles

Conference Abstracts

Books and Book Chapters

Articles

Anesthesiology

Bao X, Kumar SS, Shah NJ, **Penning D**, Weinstein M, Malhotra G, Rose S, Drover D, Pennington MW, Domino K, Meng L, Treggiari M, Clavijo C, Wagener G, Chitilian H, and Maheshwari K. AcumenTM hypotension prediction index guidance for prevention and treatment of hypotension in noncardiac surgery: a prospective, single-arm, multicenter trial. *Perioper Med (Lond)* 2024; 13(1):13. PMID: 38439069. Full Text

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BACKGROUND: Intraoperative hypotension is common during noncardiac surgery and is associated with postoperative myocardial infarction, acute kidney injury, stroke, and severe infection. The Hypotension Prediction Index software is an algorithm based on arterial waveform analysis that alerts clinicians of the patient's likelihood of experiencing a future hypotensive event, defined as mean arterial pressure < 65 mmHg for at least 1 min. METHODS: Two analyses included (1) a prospective, single-arm trial, with continuous blood pressure measurements from study monitors, compared to a historical comparison cohort. (2) A post hoc analysis of a subset of trial participants versus a propensity score-weighted contemporaneous comparison group, using external data from the Multicenter Perioperative Outcomes Group (MPOG). The trial included 485 subjects in 11 sites; 406 were in the final effectiveness analysis. The post hoc analysis included 457 trial participants and 15,796 comparison patients. Patients were eligible if aged 18 years or older, American Society of Anesthesiologists (ASA) physical status 3 or 4, and scheduled for moderate- to high-risk noncardiac surgery expected to last at least 3 h. MEASUREMENTS: minutes of mean arterial pressure (MAP) below 65 mmHg and area under MAP < 65 mmHg. RESULTS: Analysis 1: Trial subjects (n = 406) experienced a mean of 9 ± 13 min of MAP below 65 mmHg, compared with the MPOG historical control mean of 25 ± 41 min, a 65% reduction ($p < 0.001$). Subjects with at least one episode of hypotension (n = 293) had a mean of 12 ± 14 min of MAP below 65 mmHg compared with the MPOG historical control mean of 28 ± 43 min, a 58% reduction ($p< 0.001$). Analysis 2: In the post hoc inverse probability treatment weighting model, patients in the trial demonstrated a 35% reduction in minutes of hypotension compared to a contemporaneous comparison group [exponentiated coefficient: -0.35 (95%CI - 0.43, - 0.27); $p < 0.001$]. CONCLUSIONS: The use of prediction software for blood pressure management was associated with a clinically meaningful reduction in the duration of intraoperative hypotension. Further studies must investigate whether predictive algorithms to prevent hypotension can reduce adverse outcomes. TRIAL REGISTRATION: Clinical trial number: NCT03805217. Registry URL: https://clinicaltrials.gov/ct2/show/NCT03805217 . Principal investigator: Xiaodong Bao, MD, PhD. Date of registration: January 15, 2019.

Anesthesiology
Chen F, Belgique ST, Canter C, Boscardin CK, Willie C, **Mitchell JD**, Sullivan K, and Martinelli SM. Unprofessionalism in anesthesiology: A qualitative study on classifying unprofessional behavior in anesthesiology residency education. *J Clin Anesth* 2024; 95:111429. PMID: 38460412. Full Text

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STUDY OBJECTIVE: This study aims to identify the domains that constitute behaviors perceived to be unprofessional in anesthesiology residency training programs. DESIGN: Qualitative study. SETTING: Anesthesiology residency training programs. PATIENTS: Not applicable. The participants involved residents, fellows, and faculty members purposefully sampled in four US-based anesthesiology residency programs. INTERVENTIONS: Participants were asked to submit examples of unprofessional behavior they witnessed in anesthesiology residents, fellows, or faculty members via a Qualtrics link. MEASUREMENTS: Not applicable. The behavior examples were independently reviewed and categorized into themes using content analysis. MAIN RESULTS: A total of 116 vignettes were collected, resulting in a final list of 111 vignettes after excluding those that did not describe behavior exhibited by anesthesiology faculty or trainees. Fifty-eight vignettes pertained to unprofessional behaviors observed in faculty members and 53 were observed in trainees (residents and fellows). Nine unprofessionalism themes emerged in the analysis. The most common themes were VERBAL, SUPERVISION, QUALITY, ENGAGEMENT, and TIME. As to the distribution of role group (faculty versus trainee) by theme, unprofessional behaviors falling into the categories of BIAS, GOSSIP, LEWD, and VERBAL were observed more in faculty; whereas themes with unprofessional behavior primarily attributed to trainees included ENGAGEMENT, QUALITY, TIME, and SUPERVISION. CONCLUSION: By reviewing reported professionalism-related vignettes within residency training programs, we identified classification descriptors for defining unprofessional behavior specific to anesthesiology residency education. Findings from this study enrich the definition of professionalism as a multi-dimensional competency pertaining to anesthesiology graduate medical education. This framework may facilitate preventative intervention and timely remediation plans for unprofessional behavior in residents and faculty.

Anesthesiology
Guerra-Londono CE, Dexter F, **Mitchell JD**, **Forrest PB**, and **Penning DH**. Effect of a non-reactive absorbent with or without environmentally oriented electronic feedback on anesthesia provider's fresh gas flow rates: A greening initiative. *J Clin Anesth* 2024; 95:111441. PMID: 38452428. Full Text

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STUDY OBJECTIVE: To examine the effects of a non-reactive carbon dioxide absorbent (AMSORB® Plus) versus a traditional carbon dioxide absorbent (Medisorb™) on the FGF used by anesthesia providers and an electronic educational feedback intervention using Carestation™ Insights (GE HealthCare) on provider-specific change in FGF. DESIGN: Prospective, single-center cohort study set in a greening initiative. SETTING: Operating room. PARTICIPANTS: 157 anesthesia providers (i.e., anesthesiology trainees, certified registered nurse anesthetists, and solo anesthesiologists). INTERVENTIONS: Intervention #1 was the introduction of AMSORB® Plus into 8 Aisys CS2,

Carestation™ Insights-enabled anesthesia machines (GE HealthCare) at the study site. At the end of week 6, anesthesia providers were educated and given an environmentally oriented electronic feedback strategy for the next 12 weeks of the study (Intervention #2) using Carestation™ Insights data. MEASUREMENTS: The dual primary outcomes were the difference in average daily FGF during maintenance anesthesia between machines assigned to AMSORB® Plus versus Medisorb™ and the provider-specific change in average fresh gas flows after 12 weeks of feedback and education compared to the historical data. MAIN RESULTS: Over the 18-week period, there were 1577 inhaled anesthetics performed in the 8 operating rooms (528 for intervention 1, 1049 for intervention 2). There were 1001 provider days using Aisys CS2 machines and 7452 provider days of historical data from the preceding year. Overall, AMSORB® Plus was not associated with significantly less FGF (mean - 80 ml/min, 97.5% confidence interval - 206 to 46, P = .15). The environmentally oriented electronic feedback intervention was not associated with a significant decrease in provider-specific mean FGF (-112 ml/min, 97.5% confidence interval - 244 to 21, P = .059). CONCLUSIONS: This study showed that introducing a non-reactive absorbent did not significantly alter FGF. Using environmentally oriented electronic feedback relying on data analytics did not result in significantly reduced provider-specific FGF.

Anesthesiology
Wahezi SE, Emerick TD, Caparó M, Choi H, Eshraghi Y, Naeimi T, Kohan L, Anitescu M, Wright T, Przkora R, Patel K, Lamer TJ, Moeschler S, Yener U, Alerte J, Grandhe R, Bautista A, Spektor B, Noon K, Reddy R, Osuagwu UC, Carpenter A, Gerges FJ, Horn DB, Murphy CA, Kim C, Pritzlaff SG, Marshall C, Kirchen G, Oryhan C, Swaran Singh TS, Sayed D, Lubenow TR, Sehgal N, Argoff CE, Gulati A, Day MR, Shaparin N, **Sibai N**, Dua A, and Barad M. The current state of training in pain medicine fellowships: An Association of Pain Program Directors (APPD) survey of program directors. *Pain Pract* 2024; Epub ahead of print. PMID: 38553945. Full Text

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INTRODUCTION: The Accreditation Council for Graduate Medical Education (ACGME) approved the first pain medicine fellowship programs over three decades ago, designed around a pharmacological philosophy. Following that, there has been a rise in the transition of pain medicine education toward a multidisciplinary interventional model based on a tremendous surge of contemporaneous literature in these areas. This trend has created variability in clinical experience and education amongst accredited pain medicine programs with minimal literature evaluating the differences and commonalities in education and experience of different pain medicine fellowships through Program Director (PD) experiences. This study aims to gather insight from pain medicine fellowship program directors across the country to assess clinical and interventional training, providing valuable perspectives on the future of pain medicine education. METHODS: This study involved 56 PDs of ACGME-accredited pain fellowship programs in the United States. The recruitment process included three phases: advanced notification, invitation, and follow-up to maximize response rate. Participants completed a standard online questionnaire, covering various topics such as subcategory fields, online platforms for supplemental education, clinical experience, postgraduate practice success, and training adequacy. RESULTS: Surveys were completed by 39/56 (69%) standing members of the Association of Pain Program Directors (APPD). All PDs allowed fellows to participate in industry-related and professional society-related procedural workshops, with 59% encouraging these workshops. PDs emphasized the importance of integrity, professionalism, and diligence for long-term success. Fifty-four percent of PDs expressed the need for extension of fellowship training to avoid supplemental education by industry or pain/spine societies. CONCLUSION: This study highlights the challenge of providing adequate training in all Pain Medicine subtopics within a 12-month pain medicine fellowship. PDs suggest the need for additional training for fellows and discuss the importance of curriculum standardization.

Cardiology/Cardiovascular Research

Alhuneafat L, Ta'ani OA, Tarawneh T, ElHamdani A, Al-Adayleh R, Al-Ajlouni Y, Naser A, Al-Abdouh A, Amoetang R, Taffe K, **Alqarqaz M**, and **Jabri A**. Burden of Cardiovascular Disease in Sub-Saharan Africa, 1990-2019: An analysis of the Global Burden of Disease Study. *Curr Probl Cardiol* 2024; Epub ahead of print. PMID: 38554891. Full Text

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INTRODUCTION: The rise in cardiovascular disease (CVD) in Sub-Saharan Africa (SSA) reflects a major shift from communicable to noncommunicable diseases as primary health challenges. Consequently, this study aims to explore the burden of CVD and associated risk factors in SSA using data from the Global Burden of Disease (GBD) database. METHODS: This study utilized data from the GBD 1990 to 2019 to examine CVD prevalence in 46 SSA countries. We employed Bayesian regression models, demographic techniques, and mortality-to-incidence ratios to analyze both prevalence and mortality rates. Additionally, disability-adjusted life years (DALYs) were computed, and various risk factors were examined using the GBD's comparative risk assessment framework. RESULTS: Between 1990 and 2019, CVD raw counts in SSA rose by 131.7%, with a 2.1% increase in age-standardized prevalence rates. The most prevalent conditions were ischemic heart disease, stroke, and rheumatic heart disease. During the same period, the age-standardized CVD deaths per 100,000 individuals decreased from 314 (1990) to 269 (2019), reflecting a -14.4% decline. Age-standardized CVD DALY rates also showed a decrease from 6,755 in 1990 to 5,476 in 2019, with translates to 18.9% reduction. By 2019, the Central African Republic, Madagascar, and Lesotho were the countries with the highest age-standardized DALY rates for all CVDs. CONCLUSIONS: The study highlights a contrasting trend in SSA's CVD landscape: a decrease in age-standardized mortality and DALYs contrasts with increasing CVD prevalence, emphasizing the need for targeted public health strategies that balance treatment advancements with intensified prevention and control measures.

Cardiology/Cardiovascular Research

Allana SS, Rempakos A, Alexandrou M, Mutlu D, **Alaswad K**, Azzalini L, Kearney K, Krestyaninov O, Khelimskii D, Gorgulu S, Chandwaney R, Jaffer FA, Khatri JJ, Davies R, Benton S, Choi JW, Karmpaliotis D, Poommipanit P, Nicholson W, Jaber W, Rinfret S, Frizzell J, Patel T, Jefferson B, Aygul N, Goktekin O, ElGuindy A, Abi-Rafeh N, Rangan BV, Murad B, Burke MN, Sandoval Y, and Brilakis ES. Racial disparities in chronic total occlusion percutaneous coronary interventions: insights from the PROGRESS-CTO registry. *J Invasive Cardiol* 2024; 36(2). PMID: 38441989. Request Article

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Emory University Hospital Midtown, Atlanta, Georgia, USA.
Christ Hospital, Cincinnati, Ohio, USA.
HonorHealth Heart Group Shea, Scottsdale, Arizona, USA.
Selcuk University, Konya, Turkey.

Memorial Bahcelievler Hospital, Istanbul, Turkey.
Aswan Heart Center, Magdi Yacoub Foundation, Cairo, Egypt.
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OBJECTIVES: There is limited data on race and outcomes of chronic total occlusion (CTO) percutaneous coronary intervention (PCI). The authors sought to evaluate CTO PCI techniques and outcomes in different racial groups. METHODS: We examined the baseline characteristics and procedural outcomes of 11 806 CTO PCIs performed at 44 US and non-US centers between 2012 and March 2023. In-hospital major adverse cardiac events (MACE) included death, myocardial infarction, repeat target-vessel revascularization, pericardiocentesis, cardiac surgery, and stroke prior to discharge. RESULTS: The most common racial group was White (84.5%), followed by Black (5.7%), "Other" (3.9%), Hispanic (2.9%), Asian (2.4%), and Native American (0.7%). There were significant differences in the baseline characteristics between different racial groups. When compared with non-White patients, the retrograde approach and antegrade dissection re-entry were more likely to be the successful crossing strategies in White patients without any significant differences in technical success (86.4% vs 86.4%; P = .93), procedural success (84.8% vs 85.0%; P = .79), and in-hospital MACE (2.0% vs 1.5%; P = .15) between the 2 groups. The technical success rate was significantly higher in the "Other" racial group (91.0% vs 86.4% in White, 86.9% in Asian, 84.5% in Black, 84.5% in Hispanic, and 83.3% in Native American; P = .03) without any significant differences in procedural success or in-hospital MACE rates between the groups. CONCLUSIONS: Despite differences in baseline characteristics and procedural techniques, the procedural success and in-hospital MACE of CTO PCI were not significantly different between most racial groups.

Cardiology/Cardiovascular Research
Aurora L, **Grafton G**, and **Cowger J**. Going With the Flow: Device Therapy for Heart Failure Complicated by Cardiorenal Syndrome. *J Card Fail* 2024; Epub ahead of print. PMID: 38447637. Full Text

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Cardiology/Cardiovascular Research
Basir MB, **Gorgis S**, and **Aurora L**. Defining the problem, the first step to making progress in acute myocardial infarction and cardiogenic shock care. *Cardiovasc Revasc Med* 2024; Epub ahead of print. PMID: 38555189. Full Text

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Cardiology/Cardiovascular Research
Bauer TM, Fliegner M, Hou H, Daramola T, McCullough JS, Fu W, Pagani FD, Likosky DS, **Keteyian SJ**, and Thompson MP. The Relationship Between Discharge Location and Cardiac Rehabilitation Use After Cardiac Surgery. *J Thorac Cardiovasc Surg* 2024; Epub ahead of print. PMID: 38522574. Full Text

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BACKGROUND: Cardiac rehabilitation (CR) is a guideline-recommended risk reduction program offered to cardiac surgical patients. Despite CR's association with better outcomes, attendance remains poor. The relationship between discharge location and CR use is poorly understood. METHODS: This study was a nationwide, retrospective cohort analysis of Medicare fee-for-service claims for beneficiaries undergoing coronary artery bypass grafting and/or surgical aortic valve repair between 07/01/2016 and 12/31/2018. The primary outcome was attendance of any CR session. Discharge location was categorized as home discharge or discharge to extended care facility (ECF) [including skilled nursing facility (SNF), inpatient rehabilitation (IPR), and long-term acute care (LTAC)]. Multivariable logistic regression models evaluated the association between discharge location, CR attendance and one-year mortality. RESULTS: Of the 167,966 patients who met inclusion criteria, 34.1% discharged to an ECF. Overall CR usage rate was 53.9%. Unadjusted and adjusted CR usage was lower among patients discharged ECFs versus those discharged home (42.1% vs 60.0%; OR(adj): 0.67; p<0.001). Patients discharged to LTAC were less likely to use CR than those discharged to SNF or IPR (ref: home, OR(adj) LTAC=0.34, OR(ad) SNF=0.67, OR(ad) IPR=0.71, p<0.001). CR attendance was associated with a greater reduction in adjusted one-year mortality in patients discharged to ECFs (9.7% reduction) vs those discharged home (4.3% reduction). CONCLUSIONS: In this national analysis of Medicare beneficiaries, discharge to ECF was associated with lower CR use, despite a greater association with improved 1-year mortality. Interventions aimed at increasing CR enrollment at ECFs may improve CR use and advance surgical quality.

Cardiology/Cardiovascular Research

Buda KG, Hryniewicz K, Eckman PM, **Basir MB**, **Cowger JA**, **Alaswad K**, Mukundan S, Sandoval Y, Elliott A, Brilakis ES, and Megaly MS. Early vs. Delayed Mechanical Circulatory Support in Patients with Acute Myocardial Infarction and Cardiogenic Shock. *Eur Heart J Acute Cardiovasc Care* 2024; Epub ahead of print. PMID: 38502888. Full Text

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BACKGROUND: Despite increased temporary mechanical circulatory support (tMCS) utilization for acute myocardial infarction complicated by cardiogenic shock (AMI-CS), data regarding efficacy and optimal timing for tMCS support are limited. This study aimed to describe outcomes based on tMCS timing in AMI-CS and to identify predictors of 30-day mortality and readmission. METHODS: Patients with AMI-CS identified in the National Readmissions Database were grouped according to the use of tMCS and early (<24 hours) vs. delayed (≥24 hours) tMCS. The correlation between tMCS timing and inpatient outcomes was evaluated using linear regression. Multivariate logistic regression was used to identify variables associated with 30-day mortality and readmission. RESULTS: Of 294,839 patients with AMI-CS, 109,148 patients were supported with tMCS (8,067 veno-arterial extracorporeal membrane oxygenation, 33,577 Impella, and 79,161 intra-aortic balloon pump). Of patients requiring tMCS, patients who received early tMCS (n = 79,906) had shorter lengths of stay (7 days vs. 15 days, p < 0.001) and lower rates of ischemic and bleeding complications than those with delayed tMCS (n = 32,241). Patients requiring tMCS had higher in-hospital mortality (OR [95% CI]) (1.7 [1.7-1.8], p < 0.001). Among patients requiring tMCS, early support was associated with fewer complications, lower mortality (0.90 [0.85-0.94], p < 0.001), and fewer 30-day readmissions (0.91 [0.85-0.97], p = 0.005) compared to patients with delayed tMCS. CONCLUSION: Among patients receiving tMCS for AMI-CS, early tMCS was associated with fewer complications, shorter lengths of stay, lower hospital costs, and fewer deaths and readmissions at 30 days.

Cardiology/Cardiovascular Research
Chiang M, Wong I, Chui SF, Wong CYE, **Villablanca PA**, and Lee MK. First-in-Asia native valve modified-BASILICA TAVR with CT fusion, complicated by annular rupture rescued with coil embolisation. *AsiaIntervention* 2024; 10(1):60-61. PMID: 38425808. Full Text

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Cardiology/Cardiovascular Research
Dual SA, **Cowger J**, Roche E, and Nayak A. The Future of Durable Mechanical Circulatory Support: Emerging Technological Innovations and Considerations to Enable Evolution of the Field. *J Card Fail* 2024; Epub ahead of print. PMID: 38431185. Full Text

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The field of durable mechanical circulatory support (MCS) has undergone an incredible evolution over the past few decades, resulting in significant improvements in longevity and quality of life for patients with advanced heart failure. Despite these successes, substantial opportunities for further improvements remain, including in pump design and ancillary technology, perioperative and postoperative management, and the overall patient experience. Ideally, durable MCS devices would be fully implantable, automatically controlled, and minimize the need for anticoagulation. Reliable and long-term total artificial hearts for biventricular support would be available; and surgical, perioperative, and postoperative management would be informed by the individual patient phenotype along with computational simulations. In this review, we summarize emerging technological innovations in these areas, focusing primarily on innovations in late preclinical or early clinical phases of study. We highlight important considerations that the MCS community of clinicians, engineers, industry partners, and venture capital investors should consider to sustain the evolution of the field.

Cardiology/Cardiovascular Research
Fadel R, **Khan E**, and **Maskoun W**. Deployment of left atrial appendage occlusion device in large aneurysmal left atrial appendage: a case report. *Eur Heart J Case Rep* 2024; 8(3):ytae117. PMID: 38496797. Full Text

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Cardiology/Cardiovascular Research
Fang JX, **Giustino G**, **Wang DD**, **O'Neill BP**, **Gonzalez PE**, **Lee JC**, **Frisoli TM**, **O'Neill WW**, and **Villablanca PA**. Minimalistic Transcaval TAVR for a Patient With a Small Aorta. *JACC Cardiovasc Interv* 2024; Epub ahead of print. PMID: 38520453. Full Text

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Cardiology/Cardiovascular Research
Faza NN, Harb SC, **Wang DD**, van den Dorpel MMP, Van Mieghem N, and Little SH. Physical and Computational Modeling for Transcatheter Structural Heart Interventions. *JACC Cardiovasc Imaging* 2024; 17(4):428-440. PMID: Not assigned. Full Text

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Structural heart disease interventions rely heavily on preprocedural planning and simulation to improve procedural outcomes and predict and prevent potential procedural complications. Modeling technologies, namely 3-dimensional (3D) printing and computational modeling, are nowadays increasingly used to predict the interaction between cardiac anatomy and implantable devices. Such models play a role in patient education, operator training, procedural simulation, and appropriate device selection. However, current modeling is often limited by the replication of a single static configuration within a dynamic cardiac cycle. Recognizing that health systems may face technical and economic limitations to the creation of "in-house" 3D-printed models, structural heart teams are pivoting to the use of computational software for modeling purposes.

Cardiology/Cardiovascular Research
Giustino G, **O'Neill BP**, **Wang DD**, **Fang JX**, **Frisoli TM**, **Lee JC**, **Engel P**, **O'Neill WW**, and **Villablanca PA**. Redo Transcaval Access and Closure for Redo Transcatheter Aortic Valve Replacement. *JACC Cardiovasc Interv* 2024; Epub ahead of print. PMID: 38520455. Full Text

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Cardiology/Cardiovascular Research
Gornik HL, Kolluri R, **Aronow H**, Gray B, Merli G, Weinberg I, and Beckman JA. The time is now for vascular medicine. *Vasc Med* 2024; Epub ahead of print. PMID: 38487902. Full Text

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Cardiology/Cardiovascular Research
Haberman D, Estévez-Loureiro R, Czarnecki A, Denti P, **Villablanca P**, Spargias K, Sudarsky D, Perl L, Fefer P, Manevich L, Masiero G, Nombela-Franco L, Poles L, Caneiro-Queija B, Bowers N, Schiavi D, Tarantini G, Melillo F, Chrissoheris M, Dvir D, Maisano F, Taramasso M, and Shuvy M. Transcatheter edge-to-edge repair in papillary muscle injury complicating acute myocardial infarction. *ESC Heart Fail* 2024; 11(2):1218-1227. PMID: 38303542. Full Text

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AIMS: Acute mitral regurgitation (MR) in the setting of myocardial infarction (MI) may be the result of papillary muscle rupture (PMR). This condition is associated with high morbidity and mortality. We aim to evaluate the feasibility of transcatheter edge-to-edge mitral valve repair (TEER) in this acute setting. METHODS AND RESULTS: We analysed data from the International Registry of MitraClip in Acute Mitral Regurgitation following acute Myocardial Infarction (IREMMI) of 30 centres in Europe, North America, and the middle east. We included patients with post-MI PMR treated with TEER as a salvage procedure, and we evaluated immediate and 30-day outcomes. Twenty-three patients were included in this analysis (9 patients suffered complete papillary muscle rupture, 9 partial and 5 chordal rupture). The patients' mean age was 68 ± 14 years. Patients were at high surgical risk with median EuroSCORE II 27% (IQR 16, 28) and 20 out of 23 (87% were in cardiogenic shock). All patients were treated with vasopressors, and 17 out of 23 patients required mechanical support. TEER procedure was performed on the median 6 days after the index MI date IQR (3, 11). Procedural success was achieved in 87% of patients. The grade of MR was significantly decreased after the procedure. MR reduction to 0 or 1 + was achieved in 13 patients (57%), to 2 + in 7 patients (30%), P < 0.01. V-Wave was reduced from 49 ± 8 mmHg to 26 ± 10 mmHg post-procedure, P < 0.01. Sixteen out of 23 patients (70%) were discharged from hospital and 5 of them required reintervention with surgical mitral valve replacement. No additional death at 1 year was documented. CONCLUSIONS: TEER is a feasible therapy in critically ill patients with PMR due to a recent MI. TEER may have a role as salvage treatment or bridge to surgery in this population.

Cardiology/Cardiovascular Research

Ketterer MW. Emotional Distress (ED) & Clinical Outcomes in Cardiac Patients: Cause, Effect, or Confound? *Am J Cardiol* 2024; 216:102-104. PMID: 38423158. Full Text

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Cardiology/Cardiovascular Research

Krittanawong C, **Qadeer YK**, Ang SP, Wang Z, Alam M, Sharma S, and Jneid H. Clinical Outcomes of Cardiogenic Shock due to Spontaneous Coronary Artery Dissection versus Cardiogenic Shock due to Coronary Artery Disease. *Crit Pathw Cardiol* 2024; Epub ahead of print. PMID: 38467033. Full Text

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Spontaneous coronary artery dissection (SCAD) can be treated conservatively. However, some SCAD patients can develop cardiogenic shock (CS). We evaluated the outcomes of SCAD-related CS using data from a national population-based cohort study from January 1, 2016, to December 30, 2019. In our study of 32,640 patients with SCAD, about 10.6% of patients presented with cardiogenic shock. We found that SCAD patients with cardiogenic shock had higher mortality as well as greater complications including use of mechanical circulatory devices, arrythmias, respiratory support, and acute heart failure compared to those without cardiogenic shock. When comparing cardiogenic shock due to SCAD with that due to coronary artery disease (CAD), we found that while mortality rates were similar, those with cardiogenic shock due to SCAD were associated with higher risk of use of mechanical circulatory support, major bleeding, blood transfusion and respiratory failure.

Cardiology/Cardiovascular Research
Maraj D, **Ahmed O**, **Qureshi M**, and **Othman H**. Traumatic Right Atrium Perforation Causing a Pneumothorax and Pneumopericardium, Treated Conservatively. *Cureus* 2024; 16(2):e54566. PMID: 38516485. Full Text

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Pacemaker insertion is a daily occurrence in the United States of America, and it is a relatively common procedure; however, complications can occur. One common complication includes the development of a pneumothorax; however, there are rare instances where patients can develop a pneumopericardium as well. We present a case of a patient who underwent dual chamber pacemaker implantation complicated by a pneumothorax and left-sided pneumopericardium, which is a rare finding. This patient initially presented with syncopal episodes and a dual chamber pacemaker was inserted; however, not long after, the patient developed pericarditis and was found to have a pneumothorax and a pneumopericardium. In these cases, patients can be treated with chest tube insertion, lead extraction, or even conservatively, depending on the patient's clinical status. Various reasons exist for the development of a pneumothorax and pneumopericardium; however, the guidelines on management are still unclear and require further study. In our patient, his pneumothorax and contralateral pneumopericardium were treated conservatively with stable follow-up post-hospitalization.

Cardiology/Cardiovascular Research
McCord J. Identification and definition of type 2 myocardial infarction: Where do we go from here? *Int J Cardiol* 2024; Epub ahead of print. PMID: 38460733. Full Text

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Cardiology/Cardiovascular Research
Millard MJ, Ashburn NP, Snavely AC, Hashemian T, Supples M, Allen B, Christenson R, Madsen T, **McCord J**, Mumma B, Stopyra J, Wilkerson RG, and Mahler SA. European Society of Cardiology 0/1-hour algorithm (high-sensitivity cardiac troponin T) performance across distinct age groups. *Heart* 2024; Epub ahead of print. PMID: 38471727. Full Text

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BACKGROUND: To determine if the European Society of Cardiology 0/1-hour (ESC 0/1-h) algorithm with high-sensitivity cardiac troponin T (hs-cTnT) meets the ≥99% negative predictive value (NPV) safety threshold for 30-day cardiac death or myocardial infarction (MI) in older, middle-aged and young subgroups. METHODS: We conducted a subgroup analysis of adult emergency department patients with chest pain prospectively enrolled from eight US sites (January 2017 to September 2018). Patients were stratified into rule-out, observation and rule-in zones using the hs-cTnT ESC 0/1-h algorithm and classified as older (≥65 years), middle aged (46-64 years) or young (21-45 years). Patients had 0-hour and 1-hour hs-cTnT measures (Roche Diagnostics) and a History, ECG, Age, Risk factor and Troponin (HEART) score. Fisher's exact tests compared rule-out and 30-day cardiac death or MI rates between ages. NPVs with 95% CIs were calculated for the ESC 0/1-h algorithm with and without the HEART score. RESULTS: Of 1430 participants, 26.9% (385/1430) were older, 57.4% (821/1430) middle aged and 15.7% (224/1430) young. Cardiac death or MI at 30 days occurred in 12.8% (183/1430). ESC 0/1-h algorithm ruled out 35.6% (137/385) of older, 62.1% (510/821) of middle-aged and 79.9% of (179/224) young patients (p<0.001). NPV for 30-day cardiac death or MI was 97.1% (95% CI 92.7% to 99.2%) among older patients, 98.4% (95% CI 96.9% to 99.3%) in middle-aged patients and 99.4% (95% CI 96.9% to 100%) among young patients. Adding a HEART score increased NPV to 100% (95% CI 87.7% to 100%) for older, 99.2% (95% CI 97.2% to 99.9%) for middle-aged and 99.4% (95% CI 96.6% to 100%) for young patients. CONCLUSIONS: In older and middle-aged adults, the hs-cTnT ESC 0/1-h algorithm was unable to reach a 99% NPV for 30-day cardiac death or MI unless combined with a HEART score. TRIAL REGISTRATION NUMBER: NCT02984436.

Cardiology/Cardiovascular Research

Moroni F, Seth M, Changezi HU, Karve M, Arora DS, Sharma M, **Pielsticker E**, Berman AD, Lee D, Qureshi MI, Azzalini L, Sukul D, and Gurm HS. Cause and preventability of in-hospital mortality after PCI: A statewide root-cause analysis of 1,163 deaths. *PLoS One* 2024; 19(3):e0297596. PMID: 38536790. Full Text

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BACKGROUND: Mortality is the most devastating complication of percutaneous coronary interventions (PCI). Identifying the most common causes and mechanisms of death after PCI in contemporary practice is an important step in further reducing periprocedural mortality. OBJECTIVES: To systematically analyze

the cause and circumstances of in-hospital mortality in a large, multi-center, statewide cohort. METHODS: In-hospital deaths after PCI occurring at 39 hospitals included in the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2) between 2012 and 2014 were retrospectively reviewed using validated methods. A priori PCI-related mortality risk was estimated using the validated BMC2 model. RESULTS: A total of 1,163 deaths after PCI were included in the study. Mean age was 71±13 years, and 507 (44%) were women. Left ventricular failure was the most common cause of death (52% of cases). The circumstance of death was most commonly related to prior acute cardiovascular condition (61% of cases). Procedural complications were considered contributing to mortality in 235 (20%) cases. Death was rated as not preventable or slightly preventable in 1,045 (89.9%) cases. The majority of the deaths occurred in intermediate or high-risk patients, but 328 (28.2%) deaths occurred in low-risk patients (<5% predicted risk of mortality). PCI was considered rarely appropriate in 30% of preventable deaths. CONCLUSIONS: In-hospital mortality after PCI is rare, and primarily related to pre-existing critical acute cardiovascular condition. However, approximately 10% of deaths were preventable. Further research is needed to characterize preventable deaths, in order to develop strategies to improve procedural safety.

Cardiology/Cardiovascular Research
Moscardelli S, Masoomi R, **Villablanca P**, **Jabri A**, Patel AK, Moroni F, and Azzalini L. Mechanical Circulatory Support for High-Risk Percutaneous Coronary Intervention. *Curr Cardiol Rep* 2024; Epub ahead of print. PMID: 38407792. Full Text

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PURPOSE OF REVIEW: This review will focus on the indications of mechanical circulatory support (MCS) for high-risk percutaneous coronary intervention (PCI) and then analyze in detail all MCS devices available to the operator, evaluating their mechanisms of action, pros and cons, contraindications, and clinical data supporting their use. RECENT FINDINGS: Over the last decade, the interventional cardiology arena has witnessed an increase in the complexity profile of the patients and lesions treated in the catheterization laboratory. Patients with significant comorbidity burden, left ventricular dysfunction, impaired hemodynamics, and/or complex coronary anatomy often cannot tolerate extensive percutaneous revascularization. Therefore, a variety of MCS devices have been developed and adopted for high-risk PCI. Despite the variety of MCS available to date, a detailed characterization of the patient requiring MCS is still lacking. A precise selection of patients who can benefit from MCS support during high-risk PCI and the choice of the most appropriate MCS device in each case are imperative to provide extensive revascularization and improve patient outcomes. Several new devices are being tested in early feasibility studies and randomized clinical trials and the experience gained in this context will allow us to provide precise answers to these questions in the coming years.

Cardiology/Cardiovascular Research
Mutlu D, Rempakos A, Alexandrou M, Al-Ogaili A, Jaffer FA, **Alaswad K**, Khatri JJ, Young L, **Basir MB**, Krestyaninov O, Khelimskii D, Gorguluu S, Goktekin O, Choi JW, Chandwaney RH, Potluri S, Poommipanit P, Uretsky B, Kandzari DE, Aygul N, Azzalini L, Rangan BV, Mastrodemos OC, Sandoval Y, Burke MN, and Brilakis ES. Use of plaque modification microcatheters during percutaneous coronary interventions for chronic total occlusion: insights from the PROGRESS-CTO Registry. *J Invasive Cardiol* 2024; Epub ahead of print. PMID: 38471154. Request Article

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Plaque modification microcatheters (PM) (Tornus [Asahi] and Turnpike Gold [Teleflex]) are devices that are mainly used to modify the cap or lesion and maintain good support in chronic total occlusion (CTO) percutaneous coronary artery intervention (PCI). We evaluated the frequency of use and outcomes of plaque modification microcatheters in an international multicenter registry. Plaque modification microcatheters were utilized in 242 cases (1.6%: Tornus in 51% and Turnpike Gold in 49%) with decreasing frequency over time (P-for-trend: 0.007 and 0.035, respectively). Technical and procedural success and the incidence of major cardiac adverse events were similar with Tornus and Turnpike Gold use. PM are infrequently utilized in CTO-PCI and are associated with high success and acceptable complication rates.

Cardiology/Cardiovascular Research

Mutlu D, Rempakos A, Alexandrou M, Al-Ogaili A, Khatri JJ, **Alaswad K**, Gorgulu S, Sandoval Y, Burke MN, and Brilakis ES. Validation of the J-Channel Score for retrograde channel crossing in the PROGRESS-CTO registry. *J Invasive Cardiol* 2024; Epub ahead of print. PMID: 38422527. Request Article

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Successful collateral channel (CC) crossing is essential for the success of retrograde chronic total occlusion (CTO) percutaneous coronary intervention (PCI). Based on the Japanese CTO PCI expert registry, the J-Channel score was developed to predict CC crossing. We examined the performance of the J-Channel score in patients who underwent retrograde CTO-PCI at 31 centers between 2013-2023 as part of the Prospective Global Registry for the Study of CTO Intervention (PROGRESS-CTO). We observed an association between successful CC crossing and the J-Channel score, its predictive efficacy was modest for both wire and microcatheter crossing.

Cardiology/Cardiovascular Research

Mutlu D, Rempakos A, Alexandrou M, Al-Ogaili A, Yamane M, **Alaswad K**, **Basir M**, Davies R, Choi J, Gagnor A, Garbo R, Goktekin O, Gorgulu S, Khatri JJ, Nicholson W, Rinfret S, Jaber W, Egred M, Milkas A, Di Mario C, Mashayekhi K, Sandoval Y, Burke MN, and Brilakis ES. Update on chronic total occlusion percutaneous coronary intervention. *J Invasive Cardiol* 2024; 36(3). PMID: 38441986. Request Article

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Chronic total occlusion (CTO) percutaneous coronary intervention (PCI) continues to evolve. This review summarizes recent publications categorized by outcomes, techniques, complications, and ongoing studies in this rapidly growing area.

Cardiology/Cardiovascular Research

Rempakos A, Alexandrou M, Mutlu D, Choi JW, Poommipanit P, Khatri JJ, Young L, Dattilo P, Sadek Y, Davies R, Gorgulu S, Jaffer FA, Chandwaney R, Jefferson B, Elbarouni B, Azzalini L, Kearney KE, **Alaswad K**, **Basir MB**, Krestyaninov O, Khelimskii D, Aygul N, Abi-Rafeh N, Elguindy A, Goktekin O, Rangan BV, Mastrodemos OC, Al-Ogaili A, Sandoval Y, Burke MN, Brilakis ES, and Kalyanasundaram A. Predictors of successful primary antegrade wiring in chronic total occlusion percutaneous coronary intervention. *J Invasive Cardiol* 2024; Epub ahead of print. PMID: 38446022. Request Article

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BACKGROUND: Antegrade wiring is the most commonly used chronic total occlusion (CTO) crossing technique. METHODS: Using data from the PROGRESS CTO registry (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; Clinicaltrials.gov identifier: NCT02061436), we examined the clinical and angiographic characteristics and procedural outcomes of CTO percutaneous coronary interventions (PCIs) performed using a primary antegrade wiring strategy. RESULTS: Of the 13 563 CTO PCIs performed at 46 centers between 2012 and 2023, a primary antegrade wiring strategy was used in 11 332 (83.6%). Upon multivariable logistic regression analysis, proximal cap ambiguity (odds ratio [OR]: 0.52; 95% CI, 0.46-0.59), side branch at the proximal cap (OR: 0.85; 95% CI, 0.77-0.95), blunt/no stump (OR: 0.52; 95% CI: 0.47-0.59), increasing lesion length (OR [per 10 mm increase]: 0.79; 95% CI, 0.76-0.81), moderate to severe calcification (OR: 0.73; 95% CI, 0.66-0.81), moderate to severe proximal tortuosity (OR: 0.67; 95% CI, 0.59-0.75), bifurcation at the distal cap (OR: 0.66; 95% CI, 0.59-0.73), left anterior descending artery CTO (OR [vs right coronary artery]: 1.44; 95% CI, 1.28-1.62) and left circumflex CTO (OR [vs right coronary artery]: 1.22; 95% CI, 1.07-1.40), non-in-stent restenosis lesion (OR: 0.56; 95% CI, 0.49-0.65), and good distal landing zone (OR: 1.18; 95% CI, 1.06-1.32) were independently associated with primary antegrade wiring crossing success. CONCLUSIONS: The use of antegrade wiring as the initial strategy was high (83.6%) in our registry. We identified several parameters associated with primary antegrade wiring success.

Cardiology/Cardiovascular Research
Sebastian J, **Dawdy J**, Ala C, Zehr K, Gupta P, and Afonso L. Role of Transesophageal Echocardiography in the Diagnosis of Coronary Ischemia in a Patient with History of Ross Procedure. *CASE (Phila)* 2024; 8(3Part A):109-116. PMID: 38524985. Full Text

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• Multidisciplinary management is essential for complications post–Ross procedure. • Symptomatic coronary ischemia may occur late in Ross procedure patients. • Coronary ostium narrowing is a differential for ischemia post–Ross procedure. • TEE can aid in diagnosing coronary stenosis in a Ross procedure patient. • TTE may miss eccentric AR post–Ross surgery; high suspicion justifies TEE. [Figure: see text]

Center for Health Policy and Health Services Research
Beck DC, Tabb K, Tilea A, **Vance AJ**, Hall S, Schroeder A, and Zivin K. Diagnosed behavioral health conditions during the perinatal period among a commercially insured population by race/ethnicity, 2008-2020. *Front Public Health* 2024; 12:1345442. PMID: 38515598. Full Text

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OBJECTIVE: We sought to examine trends in diagnosed behavioral health (BH) conditions [mental health (MH) disorders or substance use disorders (SUD)] among pregnant and postpartum individuals between 2008-2020. We then explored the relationship between BH conditions and race/ethnicity, acknowledging race/ethnicity as a social construct that influences health disparities. METHODS: This study included delivering individuals, aged 15-44 years, and continuously enrolled in a single commercial health insurance plan for 1 year before and 1 year following delivery between 2008-2020. We used BH

conditions as our outcome based on relevant ICD 9/10 codes documented during pregnancy or the postpartum year. RESULTS: In adjusted analyses, white individuals experienced the highest rates of BH conditions, followed by Black, Hispanic, and Asian individuals, respectively. Asian individuals had the largest increase in BH rates, increasing 292%. White individuals had the smallest increase of 192%. The trend remained unchanged even after adjusting for age and Bateman comorbidity score, the trend remained unchanged. CONCLUSIONS: The prevalence of diagnosed BH conditions among individuals in the perinatal and postpartum periods increased over time. As national efforts continue to work toward improving perinatal BH, solutions must incorporate the needs of diverse populations to avert preventable morbidity and mortality.

Center for Health Policy and Health Services Research

Deshpande N, Hadi M, **Mansour TR**, **Telemi E**, **Hamilton T**, **Hu J**, **Schultz L**, **Nerenz DR**, Khalil JG, Easton R, Perez-Cruet M, Aleem I, Park P, Soo T, Tong D, **Abdulhak M**, **Schwalb JM**, and **Chang V**. The impact of anxiety and depression on lumbar spine surgical outcomes: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2024; 1-10. Epub ahead of print. PMID: 38427985. Full Text

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OBJECTIVE: The presence of depression and anxiety has been associated with negative outcomes in spine surgery patients. While it seems evident that a history of depression or anxiety can negatively influence outcome, the exact additive effect of both has not been extensively studied in a multicenter trial. The purpose of this study was to investigate the relationship between a patient's history of anxiety and depression and their patient-reported outcomes (PROs) after lumbar surgery. METHODS: Patients in the Michigan Spine Surgery Improvement Collaborative registry undergoing lumbar spine surgery between July 2016 and December 2021 were grouped into four cohorts: those with a history of anxiety only, those with a history of depression only, those with both, and those with neither. Primary outcomes were achieving the minimal clinically important difference (MCID) for the Patient-Reported Outcomes Measurement Information System Physical Function 4-item Short Form (PROMIS PF), EQ-5D, and numeric rating scale (NRS) back pain and leg pain, and North American Spine Society patient satisfaction. Secondary outcomes included surgical site infection, hospital readmission, and return to the operating room. Multivariate Poisson generalized estimating equation models were used to report incidence rate ratios (IRRs) from patient baseline variables. RESULTS: Of the 45,565 patients identified, 3941 reported a history of anxiety, 5017 reported a history of depression, 9570 reported both, and 27,037 reported neither. Compared with those who reported having neither, patients with both anxiety and depression had lower patient satisfaction at 90 days ($p = 0.002$) and 1 year ($p = 0.021$); PROMIS PF MCID at 90 days ($p < 0.001$), 1 year ($p < 0.001$), and 2 years ($p = 0.006$); EQ-5D MCID at 90 days ($p < 0.001$), 1 year ($p < 0.001$), and 2 years ($p < 0.001$); NRS back pain MCID at 90 days ($p < 0.001$) and 1 year ($p < 0.001$); and NRS leg pain MCID at 90 days ($p < 0.001$), 1 year ($p = 0.024$), and 2 years ($p = 0.027$). Patients with anxiety only ($p < 0.001$), depression only ($p < 0.001$), or both ($p < 0.001$) were more likely to be readmitted within 90 days. Additionally, patients with anxiety only ($p = 0.015$) and both anxiety and depression ($p = 0.015$) had higher rates of surgical site infection. Patients with anxiety only ($p = 0.006$) and depression only ($p = 0.021$) also had higher rates of return to the operating room. CONCLUSIONS: The authors observed an association between a history of anxiety and depression and negative outcome after lumbar spine surgery. In addition, they found an additive effect of a history of both anxiety and depression with an increased risk of negative outcome when compared with either anxiety or depression alone.

Center for Health Policy and Health Services Research

Hailemariam M, Bustos TE, Montgomery BW, Brown G, Tefera G, Adaji R, Taylor B, Eshetu H, Barajas C, Barajas R, Najjar V, Dennis D, Hudson J, **Felton JW**, and Johnson JE. Mental health interventions for individuals with serious mental illness in the criminal legal system: a systematic review. *BMC Psychiatry* 2024; 24(1):199. PMID: 38475800. Full Text

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BACKGROUND: Globally, individuals with mental illness get in contact with the law at a greater rate than the general population. The goal of this review was to identify and describe: (1) effectiveness of mental health interventions for individuals with serious mental illness (SMI) who have criminal legal involvement; (2) additional outcomes targeted by these interventions; (3) settings/contexts where interventions were delivered; and (4) barriers and facilitating factors for implementing these interventions. METHODS: A systematic review was conducted to summarize the mental health treatment literature for individuals with serious mental illness with criminal legal involvement (i.e., bipolar disorder, schizophrenia, major depressive disorder). Searches were conducted using PsychINFO, Embase, ProQuest, PubMed, and Web of Science. Articles were eligible if they were intervention studies among criminal legal involved populations with a mental health primary outcome and provided description of the intervention. RESULTS: A total of 13 eligible studies were identified. Tested interventions were categorized as cognitive/behavioral, community-based, interpersonal (IPT), psychoeducational, or court-based. Studies that used IPT-based interventions reported clinically significant improvements in mental health symptoms and were also feasible and acceptable. Other interventions demonstrated positive trends favoring the mental health outcomes but did not show statistically and clinically significant changes. All studies reported treatment outcomes, with only 8 studies reporting both treatment and implementation outcomes. CONCLUSION: Our findings highlight a need for more mental health research in this population. Studies with randomized design, larger sample size and studies that utilize non-clinicians are needed.

Center for Health Policy and Health Services Research

Ogunsola O, Linzey JR, Zaki MM, **Chang V**, **Schultz LR**, **Springer K**, **Abdulhak M**, Khalil JG, **Schwalb JM**, Aleem I, **Nerenz DR**, Perez-Cruet M, Easton R, Soo TM, Tong D, and Park P. Risk factors of emergency department visits following elective cervical and lumbar surgical procedures: a multi-institution analysis from the Michigan Spine Surgery Improvement Collaborative. *J Neurosurg Spine* 2024; 1-7. Epub ahead of print. PMID: 38427993. Full Text

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OBJECTIVE: Emergency department visits 90 days after elective spinal surgery are relatively common, with rates ranging from 9% to 29%. Emergency visits are very costly, so their reduction is of importance. This study's objective was to evaluate the reasons for emergency department visits and determine potentially modifiable risk factors. METHODS: This study retrospectively reviewed data queried from the Michigan Spine Surgery Improvement Collaborative (MSSIC) registry from July 2020 to November 2021. MSSIC is a multicenter (28-hospital) registry of patients undergoing cervical and lumbar degenerative spinal surgery. Adult patients treated for elective cervical and/or lumbar spine surgery for degenerative pathology (spondylosis, intervertebral disc disease, low-grade spondylolisthesis) were included. Emergency department visits within 90 days of surgery (outcome measure) were analyzed utilizing univariate and multivariate regression analyses. RESULTS: Of 16,224 patients, 2024 (12.5%) presented to the emergency department during the study period, most commonly for pain related to spinal surgery (31.5%), abdominal problems (15.8%), and pain unrelated to the spinal surgery (12.8%). On multivariate analysis, age (per 5-year increase) (relative risk [RR] 0.94, 95% CI 0.92-0.95), college education (RR 0.82, 95% CI 0.69-0.96), private insurance (RR 0.79, 95% CI 0.70-0.89), and preoperative ambulation status (RR 0.88, 95% CI 0.79-0.97) were associated with decreased emergency visits. Conversely, Black race (RR 1.30, 95% CI 1.13-1.51), current diabetes (RR 1.13, 95% CI 1.01-1.26), history of deep venous thromboembolism (RR 1.28, 95% CI 1.16-1.43), history of depression (RR 1.13, 95% CI 1.03-1.25), history of anxiety (RR 1.32, 95% CI 1.19-1.46), history of osteoporosis (RR 1.21, 95% CI 1.09-1.34), history of chronic obstructive pulmonary disease (RR 1.19, 95% CI 1.06-1.34), American Society of Anesthesiologists class > II (RR 1.18, 95% CI 1.08-1.29), and length of stay > 3 days (RR 1.29, 95% CI 1.16-1.44) were associated with increased emergency visits. CONCLUSIONS: The most common reasons for emergency department visits were surgical pain, abdominal dysfunction, and pain unrelated to index spinal surgery. Increased focus on postoperative pain management and bowel regimen can potentially reduce emergency visits. The risks of diabetes, history of osteoporosis, depression, and anxiety are areas for additional preoperative screening.

Center for Health Policy and Health Services Research

Zivin K, Pangori A, Zhang X, Tilea A, Hall SV, **Vance A**, Dalton VK, Schroeder A, Courant A, and Tabb KM. Perinatal Mood And Anxiety Disorders Rose Among Privately Insured People, 2008-20. *Health Aff (Millwood)* 2024; Epub ahead of print. PMID: 38507649. Full Text

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Nationwide, perinatal mood and anxiety disorder (PMAD) diagnoses among privately insured people increased by 93.3 percent from 2008 to 2020, growing faster in 2015-20 than in 2008-14. Most states and demographic subgroups experienced increases, suggesting worsening morbidity in maternal mental health nationwide. PMAD-associated suicidality and psychotherapy rates also increased nationwide from 2008 to 2020. Relative to 2008-14, psychotherapy rates continued to rise in 2015-20, whereas suicidality rates declined.

Clinical Quality and Safety

Suleyman G, **Shallal A**, **Ruby A**, **Chami E**, **Gubler J**, McNamara S, Miles-Jay A, **Tibbetts R**, and **Alangaden G**. Use of whole genomic sequencing to detect New Delhi metallo-B-lactamase (NDM)-producing Escherichia coli outbreak associated with endoscopic procedures. *Infect Control Hosp Epidemiol* 2024; 1-8. Epub ahead of print. PMID: 38495009. Full Text

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BACKGROUND: Whole-genome sequencing (WGS) has emerged as an alternative genotyping tool for outbreak investigations in the healthcare setting. We describe the investigation and control of a New Delhi metallo-B-lactamase (NDM)-producing Escherichia coli cluster in Southeast Michigan. METHODS: Michigan Bureau of Laboratories identified several closely related NDM-producing E. coli isolates with WGS. An epidemiologic investigation, including case-control study, assessment of infection control practices, and endoscope culturing, was performed to identify source of transmission. Targeted screening of potentially exposed patients was performed following identification of probable source. RESULTS: Between July 2021 and February 2023, nine patients were identified. Phylogenetic analysis confirmed the isolates were closely related with less than 26 single nucleotide polymorphism (SNP) differences between isolates, suggesting an epidemiological link. Eight (89%) patients had a duodenoscope and/or gastroscope exposure. Cases were compared with 23 controls. Cases had significantly higher odds of exposure to duodenoscopes (odds ratio 15.0; 95% CI, 1.8-142.2; P = .015). The mean incubation period, estimated as date of procedure to positive index culture, was 86 days (range, 1-320 days). No lapses in endoscope reprocessing were identified; NDM-producing E. coli was not recovered from reprocessed endoscopes or during targeted screening. No additional cases were identified after removal of implicated gastroscopes and replacement of duodenoscope with disposable end caps. CONCLUSIONS: In this investigation, WGS was utilized to identify transmission of an NDM-producing E. coli outbreak associated with endoscope exposure. Coupled with epidemiologic data, WGS can facilitate outbreak investigations by rapidly identifying linked cases and potential sources to prevent further transmission.

Dermatology

Akl J, Lee S, Ju HJ, Parisi R, Kim JY, Jeon JJ, Heo YW, Eleftheriadou V, **Hamzavi I**, Griffiths CEM, Ashcroft DM, Mysore V, Gupta S, Parsad D, **Lim H**, Bae JM, and Ezzedine K. Estimating the burden of vitiligo: a systematic review and modelling study. *Lancet Public Health* 2024; Epub ahead of print. PMID: 38552651. Full Text

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BACKGROUND: Vitiligo is a chronic autoimmune disease characterised by depigmented skin patches, which can pose substantial psychosocial challenges particularly in individuals with dark skin tones. Despite its impact on quality of life, there is an absence of standardised global epidemiological data. We sought to address this gap with the present study. METHODS: In this study we did a systematic review and modelling analysis to estimate the global, regional, and national prevalence and incidence of vitiligo. We did a comprehensive search of nine digital libraries (PubMed, Embase, Web of Science, Scientific Electronic Library Online, KCI Korean Journal Database, Russian Science Citation Index, Western Pacific Region Index Medicus, Informit, and Health Research and Development Information Network) from inception up to May 25, 2023. We included cross-sectional or cohort studies reporting the incidence rate or prevalence of vitiligo, or data from which incidence rate or prevalence could be calculated, in the general population of a country or area of a country. Summary estimate data were extracted. A main outcome was to estimate the worldwide, regional, and country-specific lifetime prevalence of vitiligo diagnosed by physicians or dermatologists among the general population and in adults and children (as per age groups defined in included studies). We used a Bayesian hierarchical linear mixed model to estimate prevalence, and calculated number of affected individuals using the UN population structure in 2022. In estimating lifetime prevalence, studies reporting point or period prevalence were excluded. Our other main outcome was to estimate incidence rates of vitiligo, but due to a small number of studies, the data on incidence were presented in a descriptive summary. This study was registered on PROSPERO, CRD42023390433. FINDINGS: Our search identified 22 192 records, of which 90 studies met our inclusion criteria. Of these studies, six focused on the incidence of vitiligo, 79 reported on the prevalence of vitiligo, and five provided data on both incidence and prevalence. 71 studies reported on lifetime prevalence. In the most recent years studied, incidence rates in the general population ranged from 24·7 cases (95% CI 24·3-25·2) per 100 000 person-years in South Korea in 2019, to 61·0 cases (60·6-61·4) in the USA in 2017. In individual studies, incidence rates showed an increasing trend over the periods studied. The global lifetime prevalence of vitiligo diagnosed by a physician or dermatologist was estimated at 0·36% (95% credible interval [CrI] 0·24-0·54) in the general population (28·5 million people [95% CrI 18·9-42·6]), 0·67% (0·43-1·07) in the adult population (37·1 million adults [23·9-58·9]), and 0·24% (0·16-0·37) in the child population (5·8 million children [3·8-8·9]). Vitiligo prevalence was higher in adults than in children across all regions. Central Europe and south Asia reported the highest prevalence (0·52% [0·28-1·07] and 0·52% [0·33-0·82], respectively, in the general population). INTERPRETATION: This study highlights the need for standardised epidemiological data collection globally to inform public health policies and improve vitiligo diagnosis and management. Emphasis on the impact on individuals with darker skin tones is crucial to reducing stigma and improving quality of life. Furthermore, our study highlights the need to conduct more research in regions and populations that have been historically under-represented, to effectively address the worldwide burden of vitiligo. FUNDING: None.

Dermatology

Eichenfield LF, **Stein Gold LF**, Lynde C, Guenther L, Greenberger S, Chu CY, Ghodsi Z, Vlahos B, Sanders P, Cha A, and Canosa JM. Maintenance of Investigator's Static Global Assessment Response with Once-Daily Crisaborole in Participants with Mild to Moderate Atopic Dermatitis. *Dermatol Ther (Heidelb)* 2024; Epub ahead of print. PMID: 38546803. Full Text

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INTRODUCTION: Treatments for atopic dermatitis (AD) often fail to achieve lasting disease control. In the CrisADe CONTROL phase III study (ClinicalTrials.gov: NCT04040192), participants aged ≥ 3 months with mild to moderate AD treated with once-daily (QD) crisaborole, following initial treatment success with crisaborole twice daily (BID), had longer periods of flare-free maintenance, a higher number of flare-free days, and a lower number of flares compared with those who received vehicle. The study was an exploratory analysis of data on the maintenance of response per Investigator's Static Global Assessment (ISGA; ISGA score of 0 [clear] or 1 [almost clear]) during the CrisADe CONTROL study through week 52. METHODS: Exploratory endpoints were the time to ISGA response during the open-label run-in period, and the maintenance of ISGA response and the severity and duration of flares during the double-blind maintenance period. Outcomes were stratified by age (participants aged 3 months to < 12 years and ≥ 12 years) and duration of crisaborole BID treatment (< 4 weeks or ≥ 4 weeks) during the open-label run-in period. RESULTS: During the open-label run-in period, the median time to ISGA response was 41.5 days. From week 4 to week 52 of the double-blind maintenance period, the proportion of participants who maintained ISGA response was greater with crisaborole versus vehicle, and this difference was statistically significant up to week 36 ($P < 0.05$). Duration of flare periods during the maintenance period were 54.1 and 54.0 days for the vehicle and crisaborole-treated groups, respectively. Numerically fewer crisaborole-treated participants experienced a flare with an ISGA score of ≥ 2 compared with vehicle-treated participants (64.8% vs. 74.4%, respectively). Findings were comparable across most subgroups. CONCLUSIONS: Adult and pediatric participants with mild to moderate AD at baseline who had achieved responder criteria (treatment success) with crisaborole BID during the run-in period maintained response per ISGA with crisaborole QD during the double-blind maintenance period through week 52. TRIAL REGISTRATION: ClinicalTrials.gov: NCT04040192.

Dermatology

Harvey VM, Alexis A, Okeke CAV, McKinley-Grant L, Taylor SC, Desai SR, Jaleel T, Heath CR, Kang S, Vashi N, Lester J, Vasquez R, Rodrigues M, Elbuluk N, **Hamzavi I**, Kwatra SG, Sundaram H, Cobb C, Brown SG, 3rd, **Kohli I**, and Callender VD. Integrating skin color assessments into clinical practice and research: A review of current approaches. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 38342247. Full Text

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Skin color classification can have importance in skin health, pigmentary disorders, and oncologic condition assessments. It is also critical for evaluating disease course and response to a variety of therapeutic interventions and aids in accurate classification of participants in clinical research studies. A panel of dermatologists conducted a literature review to assess the strengths and limitations of existing classification scales, as well as to compare their preferences and utilities. We identified 17 skin classification systems utilized in dermatologic settings. These systems include a range of parameters such as UV light reactivity, race, ethnicity, and degree of pigmentation. The Fitzpatrick skin type classification is most widely used and validated. However it has numerous limitations including its conflation with race, ethnicity, and skin color. There is a lack of validation data available for the remaining scales. There are significant deficiencies in current skin classification instruments. Consensus-based initiatives to drive the development of validated and reliable tools are critically needed.

Dermatology
Matthews NH, **Hamad J**, Henderson JB, Weinstock MA, and Ellis CN. Projected burden of melanoma clinical surveillance in the United States. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 38462135. Full Text

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Dermatology
Nelson JM, **Young AT**, **Kolli SS**, **Friedman BJ**, and **Kerr HA**. Pancreatic Panniculitis Mimicking Bilateral Cellulitis: A Case Report. *Clin Exp Dermatol* 2024; Epub ahead of print. PMID: 38430108. Full Text

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Dermatology
Novice M, **Novice T**, **Powers M**, and Lo Sicco KI. The financial burden of scalp cooling therapy: A nonprofit organization data analysis. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 38467304. Full Text

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Dermatology
Passeron T, Dreno B, Puig S, Goh CL, Kang HY, Ly F, Morita A, Ocampo Candiani J, Schalka S, Wei L, Demessant-Flavigny AL, Le Floc'h C, Kerob D, **Lim HW**, and Krutmann J. Outdoor workers and sun

exposure: Results of an international survey on sun exposure behaviours and knowledge among 17 countries, the HELIOS project. *J Eur Acad Dermatol Venereol* 2024; Epub ahead of print. PMID: 38553881. Full Text

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Dermatology

Silverberg JI, Gooderham MJ, Paller AS, Deleuran M, Bunick CG, **Gold LFS**, Hijnen D, Calimlim BM, Lee WJ, Teixeira HD, Hu X, Zhang S, Yang Y, Grada A, Platt AM, and Thaçi D. Early and Sustained Improvements in Symptoms and Quality of Life with Upadacitinib in Adults and Adolescents with Moderate-to-Severe Atopic Dermatitis: 52-Week Results from Two Phase III Randomized Clinical Trials (Measure Up 1 and Measure Up 2). *Am J Clin Dermatol* 2024; Epub ahead of print. PMID: 38528257. Full Text

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BACKGROUND: Atopic dermatitis is a chronic inflammatory disease characterized by increased itch, skin pain, poor sleep quality, and other symptoms that negatively affect patient quality of life. Upadacitinib, an oral selective Janus kinase (JAK) inhibitor with greater inhibitory potency for JAK1 than JAK2, JAK3, or tyrosine kinase 2, is approved to treat moderate-to-severe atopic dermatitis. OBJECTIVE: We aimed to evaluate the effect of upadacitinib on patient-reported outcomes over 52 weeks in adults and adolescents with moderate-to-severe atopic dermatitis. METHODS: Data from two phase III monotherapy trials of upadacitinib (Measure Up 1, NCT03569293; Measure Up 2, NCT03607422) were integrated. Changes in pruritus, pain, other skin symptoms, sleep, quality of life, mental health, and patient impression were evaluated. Patient-reported outcome assessments included the Worst Pruritus Numerical Rating Scale, Patient-Oriented Eczema Measure, Dermatology Life Quality Index, Atopic Dermatitis Symptom Scale,

Atopic Dermatitis Impact Scale, Hospital Anxiety and Depression Scale, SCORing Atopic Dermatitis index, Patient Global Impression of Severity, Patient Global Impression of Change, and Patient Global Impression of Treatment. Minimal clinically important differences, achievement of scores representing minimal disease burden, and the change from baseline were evaluated in patients who received upadacitinib through week 52 and in patients who received placebo through week 16. RESULTS: This analysis included 1609 patients (upadacitinib 15 mg, N = 557; upadacitinib 30 mg, N = 567; placebo, N = 485). Baseline demographics and disease characteristics were generally similar across all arms. The proportion of patients treated with upadacitinib reporting improvements in itch increased rapidly by week 1, increased steadily through week 8, and was sustained through week 52. Patients receiving upadacitinib also experienced improvements in pain and other skin symptoms by week 1, which continued through week 16; improvements were maintained through week 52. Patient reports of improved sleep increased rapidly from baseline to week 1, increased steadily through week 32, and were sustained through week 52. Patients experienced quality-of-life improvements through week 8, which were maintained through week 52. By week 1, patients in both upadacitinib groups experienced rapid improvements in emotional state, and by week 12, patients also achieved meaningful improvements in anxiety and depression. Improvements in mental health continued steadily through week 32 and were maintained through week 52. Patients treated with upadacitinib 30 mg generally experienced improvements in patient-reported outcomes earlier than those treated with upadacitinib 15 mg. Through week 16, patients receiving upadacitinib experienced greater improvements versus those receiving placebo in all assessed patient-reported outcomes. CONCLUSIONS: Adults and adolescents with moderate-to-severe atopic dermatitis treated with once-daily upadacitinib 15 or 30 mg experienced early improvements in itch, pain, other skin symptoms, sleep, quality of life, and mental health that were sustained through week 52. CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov identifiers NCT03569293 (13 August 2018) and NCT03607422 (27 July 2018).

Dermatology

Stein Gold L, Adam DN, Albrecht L, Alonso-Llamazares J, Ferris LK, Gooderham MJ, Hong HC, Kempers SE, Kircik LH, Lebwohl M, Loo WJ, Nahm WK, Papp KA, Stewart D, Toth DP, Zirwas M, Krupa D, Snyder S, Burnett P, Higham R, and Berk DR. Long-term safety and effectiveness of roflumilast cream 0.3% in adults with chronic plaque psoriasis: a 52-week, phase 2, open-label trial. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 38556093. Full Text

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BACKGROUND: Efficacy and/or safety profiles limit topical psoriasis treatments. OBJECTIVE: Evaluate long-term effects of once-daily roflumilast cream 0.3% in patients with psoriasis. METHODS: In this open-label phase 2 trial, adult patients (N = 332) with psoriasis who completed the phase 2b parent trial or were newly enrolled applied roflumilast once-daily for 52 weeks. Safety and effectiveness were assessed. RESULTS: Overall, 244 patients (73.5%) completed the trial; 13 patients (3.9%) discontinued due to adverse events (AEs) and 3 (0.9%) due to lack of efficacy. Twelve patients (3.6%) reported treatment-related AEs; none were serious. ≥97% of patients had no irritation. No tachyphylaxis was observed with 44.8% of the patients achieving Investigator Global Assessment (IGA) Clear or Almost Clear at Week 52. LIMITATIONS: Intertriginous-IGA and Psoriasis Area and Severity Index (PASI) were not evaluated in all patients. CONCLUSIONS: In this long-term trial, once-daily roflumilast cream was well-tolerated and efficacious up to 64 weeks in patients in the earlier trial, suggesting it is suitable for chronic treatment, including the face and intertriginous areas.

Emergency Medicine

Borst B, Jovanovic T, House SL, Bruce SE, Harnett NG, Roeckner AR, Ely TD, Lebois LAM, Young D, Beaudoin FL, An X, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Bollen KA, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Hudak LA, Pascual JL, Seamon MJ, Datner EM, Pearson C, Peak DA, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Harte SE, Koenen KC, Kessler RC, McLean SA, Ressler KJ, Stevens JS, and van Rooij SJH. Sex differences in response inhibition-related neural predictors of PTSD in recent trauma-exposed civilians. *Biol Psychiatry Cogn Neurosci Neuroimaging* 2024; Epub ahead of print. PMID: 38522649. Full Text

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BACKGROUND: Females are more likely to develop posttraumatic stress disorder (PTSD) than males. Impaired inhibition has been identified as mechanism for PTSD development, but studies on the potential sex differences of this neurobiological mechanism and how it relates to PTSD severity and progression are sparse. Here we examined sex differences in neural activation during response inhibition and PTSD following recent trauma. METHODS: Participants (N= 205, 138 female sex assigned at birth) were recruited from emergency departments within 72 hours of a traumatic event. PTSD symptoms were assessed 2-weeks and 6-months post-trauma. A Go/NoGo task was performed 2-weeks post-trauma in a 3T MRI scanner to measure neural activity during response inhibition in the ventromedial prefrontal cortex (vmPFC), right inferior frontal gyrus (rIFG), and the bilateral hippocampus. General Linear models were used to examine the interaction effect of sex on the relationship between our regions of interest (ROIs) and the whole brain, and PTSD symptoms at 6-months, and symptom progression between 2-weeks and 6-months. RESULTS: Lower response-inhibition-related vmPFC activation 2-weeks post-trauma predicted more PTSD symptoms at 6-months in females but not in males, while greater response-inhibition-related rIFG activation predicted lower PTSD symptom progression in males but not females. Whole brain interaction effects were observed in the medial temporal gyrus and left precentral gyrus. CONCLUSIONS: There are sex differences in the relationship between inhibition-related brain activation and PTSD symptom severity and progression. These findings suggest that sex differences should be assessed in future PTSD studies and reveal potential targets for sex-specific interventions.

Emergency Medicine

Garrison-Desany HM, Meyers JL, Linnstaedt SD, House SL, Beaudoin FL, An X, Zeng D, Neylan TC, Clifford GD, Jovanovic T, Germine LT, Bollen KA, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Swor RA, Gentile NT, Hudak LA, Pascual JL, Seamon MJ, Harris E, Pearson C, Peak DA, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Bruce SE, Joormann J, Harte SE, McLean SA, Koenen KC, and Denckla CA. Post-traumatic stress and future substance use outcomes: leveraging antecedent factors to stratify risk. *Front Psychiatry* 2024; 15:1249382. PMID: 38525258. Full Text

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BACKGROUND: Post-traumatic stress disorder (PTSD) and substance use (tobacco, alcohol, and cannabis) are highly comorbid. Many factors affect this relationship, including sociodemographic and psychosocial characteristics, other prior traumas, and physical health. However, few prior studies have investigated this prospectively, examining new substance use and the extent to which a wide range of factors may modify the relationship to PTSD. METHODS: The Advancing Understanding of RecOvery afteR traumA (AURORA) study is a prospective cohort of adults presenting at emergency departments (N = 2,943). Participants self-reported PTSD symptoms and the frequency and quantity of tobacco, alcohol, and cannabis use at six total timepoints. We assessed the associations of PTSD and future substance use, lagged by one timepoint, using the Poisson generalized estimating equations. We also stratified by incident and prevalent substance use and generated causal forests to identify the most important effect modifiers of this relationship out of 128 potential variables. RESULTS: At baseline, 37.3% (N = 1,099) of participants reported likely PTSD. PTSD was associated with tobacco frequency (incidence rate ratio (IRR): 1.003, 95% CI: 1.00, 1.01, p = 0.02) and quantity (IRR: 1.01, 95% CI: 1.001, 1.01, p = 0.01), and alcohol frequency (IRR: 1.002, 95% CI: 1.00, 1.004, p = 0.03) and quantity (IRR: 1.003, 95% CI: 1.001, 1.01, p = 0.001), but not with cannabis use. There were slight differences in incident compared to prevalent tobacco frequency and quantity of use; prevalent tobacco frequency and quantity were associated with PTSD symptoms, while incident tobacco frequency and quantity were not. Using causal forests, lifetime worst use of cigarettes, overall self-rated physical health, and prior childhood trauma were major moderators of the relationship between PTSD symptoms and the three substances investigated. CONCLUSION: PTSD symptoms were highly associated with tobacco and alcohol use, while the association with prospective cannabis use is not clear. Findings suggest that understanding the different risk stratification that occurs can aid in tailoring interventions to populations at greatest risk to best mitigate the comorbidity between PTSD symptoms and future substance use outcomes. We demonstrate that this is particularly salient for tobacco use and, to some extent, alcohol use, while cannabis is less likely to be impacted by PTSD symptoms across the strata.

Endocrinology and Metabolism

Das L, Laway BA, Sahoo J, Dhiman V, Singh P, **Rao SD**, Korbonits M, Bhadada SK, and Dutta P. Bone mineral density, turnover, and microarchitecture assessed by second-generation high-resolution

peripheral quantitative computed tomography in patients with Sheehan's syndrome. *Osteoporos Int* 2024; Epub ahead of print. PMID: 38507080. Full Text

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Sheehan's syndrome (SS) is a rare but well-characterized cause of hypopituitarism. Data on skeletal health is limited and on microarchitecture is lacking in SS patients. PURPOSE: We aimed to explore skeletal health in SS with bone mineral density (BMD), turnover, and microarchitecture. METHODS: Thirty-five patients with SS on stable replacement therapy for respective hormone deficiencies and 35 age- and BMI-matched controls were recruited. Hormonal profile and bone turnover markers (BTMs) were measured using electrochemiluminescence assay. Areal BMD and trabecular bone score were evaluated using DXA. Bone microarchitecture was assessed using a second-generation high-resolution peripheral quantitative computed tomography. RESULTS: The mean age of the patients was 45.5 ± 9.3 years with a lag of 8.3 ± 7.2 years prior to diagnosis. Patients were on glucocorticoid (94%), levothyroxine (94%), and estrogen-progestin replacement (58%). None had received prior growth hormone (GH) replacement. BTMs (P1NP and CTX) were not significantly different between patients and controls. Osteoporosis (26% vs. 16%, p = 0.01) and osteopenia (52% vs. 39%, p = 0.007) at the lumbar spine and femoral neck (osteoporosis, 23% vs. 10%, p = 0.001; osteopenia, 58% vs. 29%, p = 0.001) were present in greater proportion in SS patients than matched controls. Bone microarchitecture analysis revealed significantly lower cortical volumetric BMD (vBMD) (p = 0.02) at the tibia, with relative preservation of the other parameters. CONCLUSION: Low areal BMD (aBMD) is highly prevalent in SS as compared to age- and BMI-matched controls. However, there were no significant differences in bone microarchitectural measurements, except for tibial cortical vBMD, which was lower in adequately treated SS patients.

Endocrinology and Metabolism

Kruger DF, Isaacs D, Hughes L, Miller E, and Bailey TS. Opportunities to overcome underutilization of enhanced insulin delivery technologies in people with type 2 diabetes: a narrative review. *Postgrad Med* 2024; 1-9. Epub ahead of print. PMID: 38497381. Full Text

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Use of innovative technologies such as continuous glucose monitoring (CGM) and insulin delivery systems have been shown to be safe and effective in helping patients with diabetes achieve significantly improved glycemic outcomes compared to their previous therapies. However, these technologies are underutilized in many primary care practices. This narrative review discusses some of the clinical and economic benefits of tubeless insulin delivery devices and discusses how this technology can overcome the main obstacles inherent to use of conventional insulin delivery devices.

Endocrinology and Metabolism

Qiu S, Dhaliwal R, **Divine G**, **Warner E**, and **Rao SD**. Differences in bone histomorphometry between white postmenopausal women with and without atypical femoral fracture after long-term bisphosphonate therapy. *J Bone Miner Res* 2024; Epub ahead of print. PMID: 38477744. Full Text

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Bone histomorphometric endpoints in transilial biopsies may be associated with increased risk of atypical femoral fracture (AFF) in patients with osteoporosis who take antiresorptives, including bisphosphonates (BP). One way to test this hypothesis is to evaluate bone histomorphometric endpoints in age-, gender-, and treatment time matched patients who either had AFF or did not have AFF. In this study, we performed trans-iliac bone biopsies in 52 white postmenopausal women with (n = 20) and without (n = 32) AFFs, all of whom had been treated for osteoporosis continuously with alendronate for 4 to 17 years. Despite the matched range of treatment duration (4-17 yrs), AFF patients received alendronate for significantly longer (10.7 yrs) than non-AFF patients (8.0 yrs) (p = 0.014). Bone histomorphometric endpoints reflecting microstructure and turnover were assessed in cancellous, intracortical and endocortical envelopes from transilial biopsy specimens obtained from BP-treated patients 3-6 months after AFF and from non-AFF patients with similar age-, gender-, and range of BP treatment duration. However, in both cancellous and intracortical envelopes, AFF patients had significantly lower wall thickness (W.Th) and higher osteoclast surface (Oc.S/BS) than non-AFF patients. In addition, AFF patients had significantly higher eroded surface (ES/BS) only in the intracortical envelope. None of the dynamic variables related to bone formation and turnover differed significantly between the groups. In conclusion, in the ilium of BP-treated patients with osteoporosis, AFF patients have lower thickness of superficial bone (lower W.Th) of the cancellous and cortical envelopes than non-AFF patients. AFF and non-AFF patients have similar bone turnover rate in the ilium. Furthermore, in this population, as in previous work, AFF is more likely to occur in BP-treated patients with longer treatment duration.

Family Medicine

White Perkins D, **Milan P**, **Miazek K**, Francis A, **Havstadb S**, **Bossick AS**, and **Wegienka G**. Identifying individual social needs during intake for diabetes Self-Management education and support services in the Detroit, Michigan area. *Prev Med Rep* 2024; 40:102671. PMID: 38487337. Full Text

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The American Diabetes Association has recommended that diabetes self-management education and support (DSMES) teams improve diabetes outcomes by identifying and responding to patients' social needs. This study examines demographic patterns in how hemoglobin A1c (A1c) is related to individual social needs, reported urgency of those needs, and interest in obtaining assistance. A total of 1125 unique persons who had been referred for DSMES and had completed a social needs screener via our electronic medical record were included. The majority (51.9 %) had an A1c < 8 % at their most recent assessment and most respondents (52.5 %) reported having at least 1 unmet social need (n = 591), Those who reported having at least 1 social need, tended to have higher A1c levels compared with those who reported no social needs (median of 8.0 % versus 7.7 %; p < 0.05). Among Black individuals the associations were stronger (median A1c of 8.2 % among those with versus 7.2 % among those without a

reported social need; p < 0.05). However, among White individuals, there was no difference in A1c between these two groups. Among those who reported a social need, those who also reported they needed assistance (35.7 %) tended to have higher A1c levels than those who did not (median 8.3 % versus 7.8 %; p < 0.10). This relationship did not vary by race. Ongoing study of the relationship between unmet social needs and glycemic control is warranted to help identify effective clinical workflows to help providers incorporate consideration of social needs into their medical decision making.

Gastroenterology
Garg N, Mo J, **Fitzmaurice MG**, **Warnke S**, and **Jafri SM**. Falsely Elevated Tacrolimus (FK506) Trough Levels in a Liver Transplant Recipient. *Cureus* 2024; 16(2):e54548. PMID: 38516431. Full Text

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Antibody-conjugated magnetic immunoassay (ACMIA) for tacrolimus (FK506) may detect falsely elevated tacrolimus trough levels, a commonly underreported event. We report a case of falsely elevated whole-blood tacrolimus levels in a patient post-orthotopic liver transplantation. A 71-year-old male patient underwent liver transplantation in 2012. Post-transplantation, the patient was immediately started on tacrolimus for maintenance immunosuppression. His most recent dose was 0.5 mg four times weekly. During monitoring, trough levels were at 25.9 ng/mL using ACMIA. After this result, a decision was made to hold tacrolimus. After holding tacrolimus for seven days, detected trough levels were still continually greater than 20 ng/mL. Upon suspicion of falsely elevated results, liquid chromatography with mass spectroscopy (LC-MS) was used to check tacrolimus trough levels. Results showed normal trough levels of 7.6 ng/mL. Because of its narrow therapeutic window, tacrolimus levels need to be carefully monitored throughout treatment. When high tacrolimus levels are detected using ACMIA without a correlating clinical scenario, trough levels should be re-confirmed using LC-MS to prevent clinical decisions from being made based on falsely elevated results.

Gastroenterology
Obri MS, Fahoury AM, **Alhaj Ali S**, **Samad M**, **Alluri S**, Obri AS, **Almajed MR**, **Harris KB**, and **Jafri SM**. Pulmonary Complications of Everolimus in Liver Transplant Patients: A 10-Year Experience. *Cureus* 2024; 16(1):e53334. PMID: 38435956. Full Text

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This retrospective study aims to evaluate the safety of everolimus when used as part of the immunosuppression regimen in patients who underwent liver transplant from 2009 to 2019 at a tertiary liver transplant center. Patients were divided into two groups: those who received everolimus as part of the post-transplant regimen and those who did not. The primary safety outcome measured was the development of new pulmonary complications that had been associated with everolimus use in prior studies. Lung function was determined by pulmonary function tests if available or CT scans of the chest. Secondary outcomes measured included everolimus discontinuation rates and survival rates. During the study period, 450 patients underwent liver transplant; 35% of patients received everolimus (n=156) and 65% of patients did not receive everolimus (n=292). Primary safety outcome of pulmonary complications was seen in 3.9% of patients who received everolimus (n=6) and 6.3% of the control group patients who did not receive everolimus (n=19). The association between everolimus use and new pulmonary complications was not significant with a chi-square statistic of 1.33 (p=0.249). Overall, 51.3% of patients who received everolimus during their post-transplant course discontinued the medication (n=80). Everolimus is safe from a pulmonary toxicity standpoint in liver transplant immunosuppression regimens as there was no significant difference found in pulmonary complications between patients who received the medication and those who did not.

Global Health Initiative

Fromsa A, Willgert K, **Srinivasan S**, Mekonnen G, Bedada W, Gumi B, Lakew M, Tadesse B, Bayissa B, Sirak A, Girma Abdela M, Gebre S, Chibssa T, Veerasami M, Vordermeier HM, Bakker D, Berg S, Ameni G, Juleff N, de Jong MCM, Wood J, Conlan A, and Kapur V. BCG vaccination reduces bovine tuberculosis transmission, improving prospects for elimination. *Science* 2024; 383(6690):eadl3962. PMID: 38547287. Full Text

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Bacillus Calmette-Guérin (BCG) is a routinely used vaccine for protecting children against Mycobacterium tuberculosis that comprises attenuated Mycobacterium bovis. BCG can also be used to protect livestock against M. bovis; however, its effectiveness has not been quantified for this use. We performed a natural transmission experiment to directly estimate the rate of transmission to and from vaccinated and unvaccinated calves over a 1-year exposure period. The results show a higher indirect efficacy of BCG to reduce transmission from vaccinated animals that subsequently become infected [74%; 95% credible interval (CrI): 46 to 98%] compared with direct protection against infection (58%; 95% CrI: 34 to 73%) and an estimated total efficacy of 89% (95% CrI: 74 to 96%). A mechanistic transmission model of bovine tuberculosis (bTB) spread within the Ethiopian dairy sector was developed and showed how the prospects for elimination may be enabled by routine BCG vaccination of cattle.

Global Health Initiative

Joshi S, **Arshad S**, Lindsay A, **Heinonen J**, **Misikir H**, **Zervos J**, **Prentiss T**, **Verkler J**, **Numi M**, Czander B, David RE, Mossing M, Kilgore PE, Rehman N, and **Zervos M**. Control of SARS-CoV-2 infection in skilled nursing facilities in Detroit, Michigan: a model for emerging infectious diseases. *Infect Control Hosp Epidemiol* 2024; 1-3. Epub ahead of print. PMID: 38505952. Full Text

Division of Infectious Diseases, Henry Ford Hospital, Detroit, MI, USA.
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An infection prevention bundle that consisted of the development of a response team, public-academic partnership, daily assessment, regular testing, isolation, and environmental controls was implemented in 26 skilled nursing facilities in Detroit, Michigan (March 2020-April 2021). This intervention was associated with sustained control of severe acute respiratory coronavirus virus 2 infection among residents and staff.

Graduate Medical Education

Agarwal T, Mereuta OM, Ghozy S, **Larco JLA**, Bilgin C, Kadirvel R, Brinjikji W, and Kallmes DF. High thrombin-activatable fibrinolysis inhibitor expression in thrombi from stroke patients in elevated estrogen states. *BMC Neurol* 2024; 24(1):90. PMID: 38454378. Full Text

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BACKGROUND: The risk of acute ischemic stroke (AIS) associated with high estrogen states, including pregnant patients and those using oral contraceptives, has been well documented. We described the histological composition of thrombi collected in these cases. METHODS: From a prospective tissue registry (STRIP registry) of thrombi retrieved during mechanical thrombectomy for AIS, we identified 5 patients with high estrogen states: 1 post-partum patient, 1 undergoing hormone replacement therapy and 3 consuming oral contraceptive pills. Five male control patients were randomly chosen matched by age. Immunohistochemistry for CD42b (platelets), von Willebrand factor (vWF), thrombin-activatable fibrinolysis inhibitor (TAFI), fibrinogen and plasminogen activator inhibitor-1 (PAI-1) was performed. Expression was quantified using Orbit Image Software. Student's t-test was performed as appropriate. RESULTS: Mean TAFI content for the high estrogen state group was higher than controls (25.6 ± 11.9% versus 9.3 ± 9.0%, p = 0.043*). Mean platelet content for the high estrogen state group was lower than controls (41.7 ± 10.6% versus 61.8 ± 12.9%, p = 0.029*). No significant difference was found in vWF, fibrinogen and PAI-1 expression. Mean time to recanalize was higher in the high estrogen state group compared to the control group (57.8 ± 27.6 versus 22.6 ± 11.4 min, p = 0.0351*). The mean number of passes required was higher in the high estrogen group compared to controls 4.6 versus 1.2, p = 0.0261*). CONCLUSIONS: TAFI expression, a powerful driver of thrombosis, was significantly higher in stroke thrombi among patients with high estrogen states compared to controls.

Graduate Medical Education

Koerber S, **Wager SG**, **Zynda AJ**, and **Santa Barbara MT**. A Scoping Review: Reducing Musculoskeletal Injury Risk Factors for Adaptive Sport Athletes through Prevention Programs. *Am J Phys Med Rehabil* 2024; Epub ahead of print. PMID: 38547088. Full Text

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The purpose of this scoping review was to identify existing strategies to reduce modifiable risk factors for musculoskeletal injury in adaptive athletes. Medline, Embase, Web of Science, and CINAHL were searched. Inclusion criteria required studies written in English, samples of adaptive athletes, and evaluation of any injury prevention programs that would reduce risk factors associated with MSK injury. The literature search resulted in 785 unique articles. 32 full text articles were screened for inclusion. Four studies of wheelchair basketball and wheelchair rugby injury prevention programs were included in the final analysis, and these studies demonstrated increase in shoulder range of motion, decreased shoulder pain, and decreased cumulative traumatic disorders; all of which was proposed to reduce risk of shoulder injury. However, these studies were small and did not include control groups. Future research is needed to implement programs that reduce risk factors of MSK injuries and reduce health disparities for adaptive athletes.

Hematology-Oncology

Gadgeel SM, Rai P, Annavarapu S, Alam S, Goldschmidt JH, West HJ, Santorelli M, and Martins RE. Frontline pembrolizumab monotherapy for metastatic non-small cell lung cancer with PD-L1 expression

≥50%: real-world outcomes in a US community oncology setting. *Front Oncol* 2024; 14:1298603. PMID: 38525422. Full Text

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BACKGROUND: This study investigated real-world time on treatment (rwToT) and overall survival (OS) for patients with metastatic non-small cell lung cancer (mNSCLC) who initiated first-line (1L) pembrolizumab monotherapy. We also explored discontinuation reasons and subsequent treatments, stratified by number of cycles among those who completed ≥17 cycles of 1L pembrolizumab. METHODS: Patients with mNSCLC without actionable genetic aberrations, Eastern Cooperative Oncology Group performance status (ECOG PS) 0-2 and unknown, and PD-L1 TPS ≥ 50% starting 1L pembrolizumab monotherapy between 24-Oct-2016 and 31-Dec-2018 within The US Oncology Network were identified retrospectively and evaluated using structured data, with a data cutoff of 30-Sep-2021. Patient characteristics and disposition were summarized using descriptive statistics. OS and rwToT were evaluated using Kaplan-Meier method for all ECOG PS and PS 0-1. A subgroup of patients who completed ≥17 cycles were evaluated using supplemental chart review data to discern reasons for discontinuation. RESULTS: Of the 505 patients with mNSCLC with PD-L1 TPS ≥50%, 61% had ECOG PS 0-1, 23% had ECOG PS 2, and 65% had nonsquamous histology. Median rwToT and OS of pembrolizumab were 7.0 (95% CI, 6.0-8.4) months and 24.5 (95% CI, 20.1-29.3) months, respectively. In the subgroup with ECOG PS 0-1, they were 7.6 months (95% CI, 6.2-9.2) and 28.8 months (95% CI, 22.4-37.5), respectively. Of the 103 patients who completed ≥17 cycles, 57 (55.3%) patients received 17 - 34 cycles and 46 (44.7%) patients received ≥35 cycles. Approximately 7.7% of the study population received pembrolizumab beyond 35 cycles. Most common reasons for discontinuation were disease progression (38.6%) and toxicity (19.3%) among patients who received 17-34 cycles of pembrolizumab, and disease progression (13.0%) and completion of therapy (10.9%) among patients who received ≥35 cycles. CONCLUSION: Consistent with findings from KEYNOTE-024 and other real-world studies, this study demonstrates the long-term effectiveness of pembrolizumab monotherapy as 1L treatment for mNSCLC with PD-L1 TPS ≥50%. Among patients who completed ≥17 cycles, nearly half completed ≥35 cycles. Disease progression and toxicity were the most common reasons for discontinuation among patients who received 17-34 cycles of pembrolizumab. Reasons for discontinuation beyond 35 cycles need further exploration.

Hematology-Oncology

Sadasivan SM, **Loveless IM**, **Chen Y**, **Gupta NS**, **Sanii R**, **Bobbitt KR**, **Chitale DA**, Williamson SR, Rundle AG, and **Rybicki BA**. Patterns of B-cell lymphocyte expression changes in pre- and post-malignant prostate tissue are associated with prostate cancer progression. *Cancer Med* 2024; 13(6):e7118. PMID: 38523528. Full Text

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BACKROUND: Inflammation characterized by the presence of T and B cells is often observed in prostate cancer, but it is unclear how T- and B-cell levels change during carcinogenesis and whether such changes influence disease progression. METHODS: The study used a retrospective sample of 73 prostate cancer cases (45 whites and 28 African Americans) that underwent surgery as their primary

treatment and had a benign prostate biopsy at least 1 year before diagnosis. CD3+, CD4+, and CD20+ lymphocytes were quantified by immunohistochemistry in paired pre- and post-diagnostic benign prostate biopsy and tumor surgical specimens, respectively. Clusters of similar trends of expression across two different timepoints and three distinct prostate regions-benign biopsy glands (BBG), tumor-adjacent benign glands (TAG), and malignant tumor glandular (MTG) regions-were identified using Time-series Anytime Density Peaks Clustering (TADPole). A Cox proportional hazards model was used to estimate the hazard ratio (HR) of time to biochemical recurrence associated with region-specific lymphocyte counts and regional trends. RESULTS: The risk of biochemical recurrence was significantly reduced in men with an elevated CD20+ count in TAG (HR = 0.81, p = 0.01) after adjusting for covariates. Four distinct patterns of expression change across the BBG-TAG-MTG regions were identified for each marker. For CD20+, men with low expression in BBG and higher expression in TAG compared to MTG had an adjusted HR of 3.06 (p = 0.03) compared to the reference group that had nominal differences in CD20+ expression across all three regions. The two CD3+ expression patterns that featured lower CD3+ expression in the BBG compared to the TAG and MTG regions had elevated HRs ranging from 3.03 to 4.82 but did not reach statistical significance. CONCLUSIONS: Longitudinal and spatial expression patterns of both CD3+ and CD20+ suggest that increased expression in benign glands during prostate carcinogenesis is associated with an aggressive disease course.

Hospital Medicine

Schulman S, Arnold DM, Bradbury CA, Broxmeyer L, Connors JM, Falanga A, Iba T, **Kaatz S**, Levy JH, Middeldorp S, Minichiello T, Nazy I, Ramacciotti E, Resnick HE, Samama CM, Sholzberg M, Thachil J, Zarychanski R, and Spyropoulos AC. 2023 ISTH update of the 2022 ISTH guidelines for antithrombotic treatment in COVID-19. *J Thromb Haemost* 2024; Epub ahead of print. PMID: 38503600. Full Text

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Based on emerging evidence from the COVID-19 pandemic, the International Society on Thrombosis and Haemostasis (ISTH) guidelines for antithrombotic treatment in COVID-19 were published in 2022. Since then, at least 16 new randomized controlled trials have contributed additional evidence, which necessitated a modification of most of the previous recommendations. We used again the American College of Cardiology Foundation/American Heart Association methodology for assessment of level of evidence (LOE) and class of recommendation (COR). Five recommendations had the LOE upgraded to A and 2 new recommendations on antithrombotic treatment for patients with COVID-19 were added. Furthermore, a section was added to answer questions about COVID-19 vaccination and vaccine-induced immune thrombotic thrombocytopenia (VITT), for which studies have provided some evidence. We only included recommendations with LOE A or B. Panelists agreed on 19 recommendations, 4 for nonhospitalized, 5 for noncritically ill hospitalized, 3 for critically ill hospitalized, and 2 for postdischarge patients, as well as 5 for vaccination and VITT. A strong recommendation (COR 1) was given for (a) use of prophylactic dose of low-molecular-weight heparin or unfractionated heparin in noncritically ill patients hospitalized for COVID-19, (b) for select patients in this group, use of therapeutic-dose low-molecular-weight heparin/unfractionated heparin in preference to prophylactic dose, and (c) for use of antiplatelet factor 4 enzyme immunoassays for diagnosing VITT. A strong recommendation was given against (COR 3) the addition of an antiplatelet agent in hospitalized, noncritically ill patients. These international guidelines provide recommendations for countries with diverse healthcare resources and COVID-19 vaccine availability.

Hypertension and Vascular Research
Bryson TD, **Bhat SY**, **Moore C**, **Taube D**, **Xu J**, **Peterson E**, and **Harding P**. Targeted Gene Deletion or Antagonism of the Prostaglandin E2 EP3 Receptor Protects Against Cardiac Injury Postmyocardial Infarction. *Circ Heart Fail* 2024; Epub ahead of print. PMID: 38525608. Full Text

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BACKGROUND: Prostaglandin E2 acts through 4 G-protein-coupled receptors (EP1-EP4). We previously reported that activation of the EP3 receptor reduces cardiac contractility, and its expression increases after a myocardial infarction (MI), mediating the reduction in cardiac function. In contrast, cardiac overexpression of the EP4 receptor in MI substantially improves cardiac function. Moreover, we recently reported that mice overexpressing EP3 have heart failure under basal conditions and worsened cardiac function after MI. Thus, the deleterious effects of the prostaglandin E2 EP receptors in the heart are mediated via its EP3 receptor. We, therefore, hypothesized that cardiomyocyte-specific knockout (CM-EP3 KO) or antagonism of the EP3 receptor protects the heart after MI. METHODS: To test our hypothesis, we made the novel CM-EP3 KO mouse and subjected CM-EP3 KO or controls to sham or MI surgery for 2 weeks. In separate experiments, C57BL/6 mice were subjected to 2 weeks of MI and treated with either the EP3 antagonist L798 106 or vehicle starting 3 days post-MI. RESULTS: CM-EP3 KO significantly prevented a decline in cardiac function after MI compared with WT animals and prevented an increase in hypertrophy and fibrosis. Excitingly, mice treated with L798 106 3 days after MI had significantly better cardiac function compared with vehicle-treated mice. CONCLUSIONS: Altogether, these data suggest that EP3 may play a direct role in regulating cardiac function, and pharmaceutical targeting of the EP3 receptor may be a therapeutic option in the treatment of heart failure.

Hypertension and Vascular Research
Bryson TD, **Zurek M**, **Moore C**, **Taube D**, **Datta I**, **Levin A**, and **Harding P**. Prostaglandin E2 affects mitochondrial function in adult mouse cardiomyocytes and hearts. *Prostaglandins Leukot Essent Fatty Acids* 2024; 201:102614. PMID: 38471265. Full Text

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Prostaglandin E2 (PGE2) signals differently through 4 receptor subtypes (EP1-EP4) to elicit diverse physiologic/pathologic effects. We previously reported that PGE2 via its EP3 receptor reduces cardiac contractility and male mice with cardiomyocyte-specific deletion of the EP4 receptor (EP4 KO) develop dilated cardiomyopathy. The aim of this study was to identify pathways responsible for this phenotype. We performed ingenuity pathway analysis (IPA) and found that genes differentiating WT mice and EP4 KO mice were significantly overrepresented in mitochondrial (adj. p value = 6.28 × 10(-26)) and oxidative phosphorylation (adj. p value = 1.58 × 10(-27)) pathways. Electron microscopy from the EP4 KO hearts show substantial mitochondrial disarray and disordered cristae. Not surprisingly, isolated adult mouse cardiomyocytes (AVM) from these mice have reduced ATP levels compared to their WT littermates and reduced expression of key genes involved in the electron transport chain (ETC) in older mice. Moreover, treatment of AVM from C57Bl/6 mice with PGE2 or the EP3 agonist sulprostone resulted in changes of various genes involved in the ETC, measured by the Mitochondrial Energy Metabolism RT(2)-profiler assay. Lastly, the EP4 KO mice have reduced expression of superoxide dismuatse-2 (SOD2), whereas treatment of AVM with PGE2 or sulprostone increase superoxide production, suggesting increased oxidative stress levels in these EP4 KO mice. Altogether the current study supports the premise that PGE2 acting via its EP4 receptor is protective, while signaling through its other receptors, likely EP3, is deleterious.

Hypertension and Vascular Research
Suhail H, **Peng H**, Matrougui K, and **Rhaleb NE**. Ac-SDKP attenuates ER stress-stimulated collagen production in cardiac fibroblasts by inhibiting CHOP-mediated NF-κB expression. *Front Pharmacol* 2024; 15:1352222. PMID: 38495093. Full Text

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Inflammation and cardiac fibrosis are prevalent pathophysiologic conditions associated with hypertension, cardiac remodeling, and heart failure. Endoplasmic reticulum (ER) stress triggers the cells to activate unfolded protein responses (UPRs) and upregulate the ER stress chaperon, enzymes, and downstream transcription factors to restore normal ER function. The mechanisms that link ER stress-induced UPRs upregulation and NF-κB activation that results in cardiac inflammation and collagen production remain elusive. N-Acetyl-Ser-Asp-Lys-Pro (Ac-SDKP), a natural tetrapeptide that negatively regulates inflammation and fibrosis, has been reported. Whether it can inhibit ER stress-induced collagen production in cardiac fibroblasts remains unclear. Thus, we hypothesized that Ac-SDKP attenuates ER stress-stimulated collagen production in cardiac fibroblasts by inhibiting CHOP-mediated NF-κB expression. We aimed to study whether Ac-SDKP inhibits tunicamycin (TM)-induced ER stress signaling, NF-κB signaling, the release of inflammatory cytokine interleukin-6, and collagen production in human cardiac fibroblasts (HCFs). HCFs were pre-treated with Ac-SDKP (10 nM) and then stimulated with TM (0.25 μg/mL). We found that Ac-SDKP inhibits TM-induced collagen production by attenuating ER stress-induced UPRs upregulation and CHOP/NF-κB transcriptional signaling pathways. CHOP deletion by specific shRNA maintains the inhibitory effect of Ac-SDKP on NF-κB and type-1 collagen (Col-1) expression at both protein and mRNA levels. Attenuating ER stress-induced UPR sensor signaling by Ac-SDKP seems a promising therapeutic strategy to combat detrimental cardiac inflammation and fibrosis.

Infectious Diseases
Best JH, Sadeghi M, Sun X, Seetasith A, Albensi L, **Joshi S**, and **Zervos MJ**. Household Influenza Transmission and Healthcare Resource Utilization Among Patients Treated with Baloxavir vs Oseltamivir: A United States Outpatient Prospective Survey. *Infect Dis Ther* 2024; Epub ahead of print. PMID: 38483775. Full Text

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INTRODUCTION: Influenza is a common, seasonal infectious disease with broad medical, economic, and social consequences. Real-world evidence on the effect of influenza treatment on household transmission and healthcare resource utilization is limited in outpatient settings in the USA. This study examined the real-world effectiveness of baloxavir vs oseltamivir in reducing influenza household transmission and healthcare resource utilization. METHODS: This prospective electronic survey on patient-reported outcomes was conducted between October 2022 and May 2023 via CVS Pharmacy in the USA. Adult participants (≥ 18 years old) were eligible if they filled a prescription for baloxavir or oseltamivir at a CVS Pharmacy within 2 days of influenza symptom onset. Participant demographics, household transmission, and all-cause healthcare resource utilization were collected. Transmission and utilization outcomes were assessed using χ(2) and Fisher exact tests. RESULTS: Of 87,871 unique patients contacted, 1346 (1.5%) consented. Of 374 eligible patients, 286 (90 baloxavir- and 196 oseltamivir-treated patients) completed the survey and were included in the analysis. Mean age of participants was 45.4 years, 65.6% were female, and 86.7% were White. Lower household transmission was observed with baloxavir compared with oseltamivir therapy (17.8% vs 26.5%; relative risk = 0.67; 95% CI 0.41-1.11). Healthcare resource utilization, particularly emergency department visits (0.0% vs 4.6%), was also numerically lower in the baloxavir-treated group; no hospitalizations were reported in either cohort. CONCLUSIONS: The findings from this real-world study suggest that antiviral treatment of influenza with baloxavir may decrease household transmission and reduce healthcare resource utilization compared with oseltamivir.

Infectious Diseases
Joshi S, **Arshad S**, Lindsay A, **Heinonen J**, **Misikir H**, **Zervos J**, **Prentiss T**, **Verkler J**, **Numi M**, Czander B, David RE, Mossing M, Kilgore PE, Rehman N, and **Zervos M**. Control of SARS-CoV-2 infection in skilled nursing facilities in Detroit, Michigan: a model for emerging infectious diseases. *Infect Control Hosp Epidemiol* 2024; 1-3. Epub ahead of print. PMID: 38505952. Full Text

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An infection prevention bundle that consisted of the development of a response team, public-academic partnership, daily assessment, regular testing, isolation, and environmental controls was implemented in 26 skilled nursing facilities in Detroit, Michigan (March 2020-April 2021). This intervention was associated with sustained control of severe acute respiratory coronavirus virus 2 infection among residents and staff.

Infectious Diseases
Suleyman G, **Shallal A**, **Ruby A**, **Chami E**, **Gubler J**, McNamara S, Miles-Jay A, **Tibbetts R**, and **Alangaden G**. Use of whole genomic sequencing to detect New Delhi metallo-B-lactamase (NDM)-producing Escherichia coli outbreak associated with endoscopic procedures. *Infect Control Hosp Epidemiol* 2024; 1-8. Epub ahead of print. PMID: 38495009. Full Text

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BACKGROUND: Whole-genome sequencing (WGS) has emerged as an alternative genotyping tool for outbreak investigations in the healthcare setting. We describe the investigation and control of a New Delhi metallo-B-lactamase (NDM)-producing Escherichia coli cluster in Southeast Michigan. METHODS: Michigan Bureau of Laboratories identified several closely related NDM-producing E. coli isolates with WGS. An epidemiologic investigation, including case-control study, assessment of infection control practices, and endoscope culturing, was performed to identify source of transmission. Targeted screening of potentially exposed patients was performed following identification of probable source. RESULTS: Between July 2021 and February 2023, nine patients were identified. Phylogenetic analysis confirmed the isolates were closely related with less than 26 single nucleotide polymorphism (SNP) differences between isolates, suggesting an epidemiological link. Eight (89%) patients had a duodenoscope and/or gastroscope exposure. Cases were compared with 23 controls. Cases had significantly higher odds of exposure to duodenoscopes (odds ratio 15.0; 95% CI, 1.8-142.2; P = .015). The mean incubation period, estimated as date of procedure to positive index culture, was 86 days (range, 1-320 days). No lapses in endoscope reprocessing were identified; NDM-producing E. coli was not recovered from reprocessed endoscopes or during targeted screening. No additional cases were identified after removal of implicated gastroscopes and replacement of duodenoscope with disposable end caps. CONCLUSIONS: In this investigation, WGS was utilized to identify transmission of an NDM-producing E. coli outbreak associated with endoscope exposure. Coupled with epidemiologic data, WGS can facilitate outbreak investigations by rapidly identifying linked cases and potential sources to prevent further transmission.

Internal Medicine

El Ayoubi LW, Mahmoud O, **Zakhour J**, and Kanj SS. Recent advances in the treatment of Ebola disease: A brief overview. *PLoS Pathog* 2024; 20(3):e1012038. PMID: 38489257. Full Text

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Ebola disease (EBOD) remains a significant and ongoing threat to African countries, characterized by a mortality rate of 25% to 90% in patients with high viral load and significant transmissibility. The most recent outbreak, reported in Uganda in September 2022, was declared officially over in January 2023. However, it was caused by the Sudan Ebola virus (SUDV), a culprit species not previously reported for a decade. Since its discovery in 1976, the management of EBOD has primarily relied on supportive care. Following the devastating outbreak in West Africa from 2014 to 2016 secondary to the Zaire Ebola virus (EBOV), where over 28,000 lives were lost, dedicated efforts to find effective therapeutic agents have resulted in considerable progress in treating and preventing disease secondary to EBOV. Notably, 2 monoclonal antibodies-Ebanga and a cocktail of monoclonal antibodies, called Inmazeb-received Food and Drug Administration (FDA) approval in 2020. Additionally, multiple vaccines have been approved for EBOD prevention by various regulatory bodies, with Ervebo, a recombinant vesicular stomatitis virus-vectored vaccine against EBOV being the first vaccine to receive approval by the FDA in 2019. This review covers the key signs and symptoms of EBOD, its modes of transmission, and the principles guiding supportive care. Furthermore, it explores recent advancements in treating and preventing EBOD, highlighting the unique properties of each therapeutic agent and the ongoing progress in discovering new treatments.

Internal Medicine
El Sharu H, Ibarra S, **Chaudhary A**, Hidri S, Khan Z, and Hoo-Fatt D. Gastric sarcoidosis diagnosed with endoscopic ultrasound. *Clin Case Rep* 2024; 12(3):e8623. PMID: 38481933. Full Text

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KEY CLINICAL MESSAGE: Endoscopic ultrasonography (EUS) is crucial in diagnosing gastrointestinal sarcoidosis, especially when patients exhibit refractory abdominal symptoms. Our case highlights the significance of considering sarcoidosis in such cases and emphasizes the utility of EUS for accurate diagnosis and guiding appropriate treatment. ABSTRACT: Gastrointestinal sarcoidosis is a rare and challenging manifestation of sarcoidosis that often presents with nonspecific abdominal symptoms, making diagnosis a complex process. We report the case of a 46-year-old African American female who experienced chronic epigastric abdominal pain, recurrent nausea, vomiting, and diarrhea for 15 years. Despite extensive investigations, including multiple biopsies, she was misdiagnosed with cyclic vomiting syndrome. Subsequently, an endoscopic ultrasound (EUS) revealed prominent lymph nodes and gastric granulomas, leading to a diagnosis of GS. This case underscores the importance of considering sarcoidosis in patients with refractory abdominal symptoms and highlights the utility of EUS in diagnosing this rare condition.

Internal Medicine
Lohana AC, Rahaman Z, Mohammed YN, Samreen SD, Gulati A, Shivani F, Khurana S, **Kumar D**, and Kirshan Kumar S. A Systematic Review of Gender Disparity in the Authorship of Clinical Trials and Clinical Practice Guidelines in Various Medicine Subspecialties. *Cureus* 2024; 16(2):e54165. PMID: 38496166. Full Text

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Authorship in clinical trials and clinical practice guidelines is considered prestigious and is associated with broader peer recognition. This systematic review investigated female representation among studies reporting authorship trends in clinical trials or clinical practice guidelines in different medicine subspecialties. Our search strategy yielded 836 articles, of which 30 met the inclusion criteria. Our findings indicate that females are severely underrepresented in authorship of clinical trials and clinical practice guidelines. Although the proportions of females may have improved in the past decade, the gains are marginal. Notably, studies in this domain predominantly focus on first/last authorship positions, and whether females are underrepresented in other positions as collaborative partners is currently unknown. Also, authorship trends in clinical trials or clinical practice guidelines of most medicine subspecialties besides cardiovascular medicine remain under-researched. Hence, standardizing the methodology for studying gender disparity in research output for comparative analysis between different subspecialties is as urgent as addressing the gender disparity in authorship.

Internal Medicine
Manivannan A, Madani S, Woodall M, McKelvey G, and Kemper S. Propofol Sedation in Pediatric Upper Endoscopy: A Study of Pharmacodynamics and the Effects of Gastroenterologists, Anesthesiologists, and

Supervised Participants on the Procedure Time and Sedation Time. *Cureus* 2024; 16(2):e54841. PMID: 38533143. Full Text

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Anesthesiology, Detroit Medical Center, Detroit, USA.
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Background and aims Propofol combined with fentanyl is a commonly used sedative for pediatric upper endoscopies (UEs). The primary aim was to study the association between propofol dose and procedure and sedation time. The secondary aims were to assess the pharmacodynamics of propofol use with fentanyl and evaluate if gastroenterologists' and anesthesiologists' years of experience or the presence of supervised participants (such as students, residents, and fellows) have any influence on the procedure and sedation time. Methods A retrospective study was performed at the Children's Hospital of Michigan on patients under 18 years who underwent UEs with propofol sedation with fentanyl over a two-year period. Results A correlation was found between the propofol amount used expressed per body mass index (BMI)/body surface area (BSA), procedure time, and sedation time ($p < 0.0001$). Throat pain was the most common post-procedural adverse event (4.48%). The impact of psychoactive drugs on these events was not statistically significant, but attention-deficit/hyperactivity disorder (ADHD) medication use was related to increased post-procedural pain complaints. The use of prescribed psychoactive medications was associated with larger propofol dose usage ($p = 0.007$) without a significant increase in sedation time. Individual gastroenterologists, their years of experience, and the presence of supervised participants were associated with different procedure times ($p <0.0001$, <0.0001, 0.01). Fellow participation was associated with a 1.11-minute procedure time increase ($p = 0.04$). Individual anesthesiologists, their years of experience, and the presence of supervised participants were associated with different sedation times ($p <0.0001$, <0.0001, 0.01). Conclusion We found a novel correlation between propofol dosing expressed by the BMI/BSA and sedation time. The UE procedure time and sedation time are associated with individual gastroenterologists and anesthesiologists, their years of experience, and the presence of supervised participants.

Internal Medicine

Maraj D, **Ahmed O**, **Qureshi M**, and **Othman H**. Traumatic Right Atrium Perforation Causing a Pneumothorax and Pneumopericardium, Treated Conservatively. *Cureus* 2024; 16(2):e54566. PMID: 38516485. Full Text

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Pacemaker insertion is a daily occurrence in the United States of America, and it is a relatively common procedure; however, complications can occur. One common complication includes the development of a pneumothorax; however, there are rare instances where patients can develop a pneumopericardium as well. We present a case of a patient who underwent dual chamber pacemaker implantation complicated by a pneumothorax and left-sided pneumopericardium, which is a rare finding. This patient initially presented with syncopal episodes and a dual chamber pacemaker was inserted; however, not long after, the patient developed pericarditis and was found to have a pneumothorax and a pneumopericardium. In these cases, patients can be treated with chest tube insertion, lead extraction, or even conservatively, depending on the patient's clinical status. Various reasons exist for the development of a pneumothorax and pneumopericardium; however, the guidelines on management are still unclear and require further study. In our patient, his pneumothorax and contralateral pneumopericardium were treated conservatively with stable follow-up post-hospitalization.

Internal Medicine

Obri MS, Fahoury AM, **Alhaj Ali S**, **Samad M**, **Alluri S**, Obri AS, **Almajed MR**, **Harris KB**, and **Jafri SM**. Pulmonary Complications of Everolimus in Liver Transplant Patients: A 10-Year Experience. *Cureus* 2024; 16(1):e53334. PMID: 38435956. Full Text

Internal Medicine, Henry Ford Health System, Detroit, USA.
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This retrospective study aims to evaluate the safety of everolimus when used as part of the immunosuppression regimen in patients who underwent liver transplant from 2009 to 2019 at a tertiary liver transplant center. Patients were divided into two groups: those who received everolimus as part of the post-transplant regimen and those who did not. The primary safety outcome measured was the development of new pulmonary complications that had been associated with everolimus use in prior studies. Lung function was determined by pulmonary function tests if available or CT scans of the chest. Secondary outcomes measured included everolimus discontinuation rates and survival rates. During the study period, 450 patients underwent liver transplant; 35% of patients received everolimus (n=156) and 65% of patients did not receive everolimus (n=292). Primary safety outcome of pulmonary complications was seen in 3.9% of patients who received everolimus (n=6) and 6.3% of the control group patients who did not receive everolimus (n=19). The association between everolimus use and new pulmonary complications was not significant with a chi-square statistic of 1.33 (p=0.249). Overall, 51.3% of patients who received everolimus during their post-transplant course discontinued the medication (n=80). Everolimus is safe from a pulmonary toxicity standpoint in liver transplant immunosuppression regimens as there was no significant difference found in pulmonary complications between patients who received the medication and those who did not.

Internal Medicine
Virk GS, Javed S, Chaudhry R, Moazam MM, **Mahmood A**, Mahmood F, Zaheer M, Khan SM, and Rajasekaran V. Assessing the Safety and Efficacy of Rivaroxaban for Stroke Prevention in Patients With Atrial Fibrillation: A Systemic Review and Meta-Analysis. *Cureus* 2024; 16(2):e54252. PMID: 38496142.
Full Text

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Internal Medicine, Henry Ford Health System, Detroit, USA.
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An effective anticoagulation therapy is required for patients with atrial fibrillation because it presents a significant risk of stroke. The current study evaluates the relative safety as well as efficacy of rivaroxaban in patients who are diagnosed with atrial fibrillation. A thorough literature review of relevant databases was conducted, focusing on academic and clinical studies that were published from 2017 onward. Inclusion criteria comprised randomized controlled trials and other observational studies comparing the incidence of stroke and the safety index of rivaroxaban in atrial fibrillation. We followed the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) for data overview reporting and overview. A total of 21 studies were selected based on the inclusion criteria. A total of 19/21 studies advocated the adoption of rivaroxaban for minimizing stroke incidence. Rivaroxaban also showed superiority in achieving the therapeutic objectives, i.e., reduction in the incidence of stroke. The results for rivaroxaban against warfarin showed an improved safety index and effectiveness of rivaroxaban. The total effect size for the analysis was calculated to be Z=2.62 (p-value=0.009). The individual effect of all studies favored the "rivaroxaban" group. The heterogeneity in the study was as follows: tau(2)=0.10; chi(2)=110.10, df=6; I(2)=95%. The second analysis for risk reduction and incidence of stroke after rivaroxaban therapy also showed a bias towards rivaroxaban therapy. The combined effect for the analysis was found to be as follows: HR=0.73 ((95% CI: 0.50, 1.07). The total effect was calculated to be

Z=1.61 (p-value= 0.10). The heterogeneity was found to be as follows: tau(2)= 0.20, chi(2)=89.97, df=6, I(2)=93%. Standard dosing of rivaroxaban emerges as a preferred strategy for stroke prevention, balancing efficacy and safety. Clinical decision-making should consider individual patient characteristics and future research should delve into specific subpopulations and long-term outcomes to further refine treatment guidelines.

Neurology
Boyd ED, **Kaur J**, **Ding G**, **Chopp M**, and **Jiang Q**. Clinical magnetic resonance imaging evaluation of glymphatic function. *NMR Biomed* 2024; Epub ahead of print. PMID: 38465514. Full Text

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The glymphatic system is a system of specialized perivascular spaces in the brain that facilitates removal of toxic waste solutes from the brain. Evaluation of glymphatic system function by means of magnetic resonance imaging (MRI) has thus far been largely focused on rodents because of the limitations of intrathecal delivery of gadolinium-based contrast agents to humans. This review discusses MRI methods that can be employed clinically for glymphatic-related measurements intended for early diagnosis, prevention, and the treatment of various neurological conditions. Although glymphatic system-based MRI research is in its early stages, recent studies have identified promising noninvasive MRI markers associated with glymphatic system alterations in neurological diseases. However, further optimization in data acquisition, validation, and modeling are needed to investigate the glymphatic system within the clinical setting.

Neurology
Cheng T, Petraglia AL, **Li Z**, Thiyagarajan M, Zhong Z, Wu Z, Liu D, Maggirwar SB, Deane R, Fernández JA, LaRue B, Griffin JH, **Chopp M**, and Zlokovic BV. Editorial Expression of Concern: Activated protein C inhibits tissue plasminogen activator-induced brain hemorrhage. *Nat Med* 2024; Epub ahead of print. PMID: 38509330. Full Text

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Neurology
Espay AJ, Stocchi F, Pahwa R, Albanese A, Ellenbogen A, Ferreira JJ, Giladi N, Gurevich T, Hassin-Baer S, Hernandez-Vara J, Isaacson SH, Kieburtz K, **LeWitt PA**, Lopez-Manzanares L, Olanow CW, Poewe W, Sarva H, Yardeni T, Adar L, Salin L, Lopes N, Sasson N, Case R, and Rascol O. Safety and efficacy of continuous subcutaneous levodopa-carbidopa infusion (ND0612) for Parkinson's disease with motor fluctuations (BouNDless): a phase 3, randomised, double-blind, double-dummy, multicentre trial. *Lancet Neurol* 2024; Epub ahead of print. PMID: 38499015. Full Text

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BACKGROUND: Conventional oral levodopa therapy for the treatment of Parkinson's disease can be associated with variations in plasma concentrations. Levodopa infusion strategies might provide more consistent drug delivery and fewer motor fluctuations. We aimed to assess the safety and efficacy of a continuous 24 h/day subcutaneous infusion of ND0612 (a levodopa-carbidopa solution) compared with oral immediate-release levodopa-carbidopa for the treatment of motor fluctuations in people with Parkinson's disease. METHODS: We conducted a phase 3, randomised, double-blind, double-dummy, active-controlled, multicentre trial at 117 academic and community neurology sites in 16 countries, including in Europe, Israel, and the USA. Eligible participants were men and women aged 30 years or older with a diagnosis of Parkinson's disease (Hoehn and Yahr stage ≤3 in the on state) who experienced at least 2·5 h/day of off time. Participants underwent an open-label run-in phase (<12 weeks), during which time optimal regimens were established for both oral immediate-release levodopa-carbidopa and for 24 h/day subcutaneous ND0612 infusion (levodopa-carbidopa 60·0/7·5 mg/mL), with supplemental oral levodopa-carbidopa if needed. Participants were then randomly assigned (1:1) to 12 weeks of double-blind treatment with their optimised regimen of either subcutaneous ND0612 or oral levodopa-carbidopa, with matching oral or subcutaneous placebo given as required to maintain blinding. Randomisation was done via an interactive web response system, stratified by region, using a permuted block schedule. Participants, study partners, treating investigators, study site personnel, and the sponsor were masked to treatment group allocation. The primary efficacy endpoint was the change from baseline (ie, time of randomisation, when all patients were receiving an optimised open-label ND0612 regimen) to end of the double-blind phase in total daily on time without troublesome dyskinesia, analysed by intention to treat. This trial is registered with ClinicalTrials.gov, NCT04006210, and is complete. FINDINGS: Between Sept 30, 2019, and April 8, 2022, 381 participants were enrolled, of whom 259 (68%) were randomly assigned, 128 (49%) to subcutaneous ND0612 and 131 (51%) to oral levodopa-carbidopa. 243 (94%) participants completed the study. Treatment with subcutaneous ND0612 provided an additional 1·72 h (95% CI 1·08 to 2·36) of on time without troublesome dyskinesia compared with oral levodopa-carbidopa (change from baseline of -0·48 h [-0·94 to -0·02] with subcutaneous ND0612 vs -2·20 h [-2·65 to -1·74] with oral levodopa-carbidopa; p<0·0001). Significant treatment differences favouring subcutaneous ND0612 were also found in the first four of nine prespecified hierarchical outcomes of daily off time (-1·40 h [95% CI -1·99 to -0·80]), Movement Disorders Society-Unified Parkinson's Disease Rating Scale part II scores (-3·05 [-4·28 to -1·81]), Patients Global Impression of Change (odds ratio [OR] 5·31 [2·67 to 10·58]), and Clinical Global Impression of Improvement (OR 7·23 [3·57 to 14·64]).

Hierarchical testing ended after the fourth secondary endpoint. Adverse events were reported by 287 (89%) of 322 participants during open-label ND0612 optimisation, and by 103 (80%) of 128 in the ND0612 group and 97 (74%) of 131 in the oral levodopa-carbidopa group during the double-blind phase. The most common adverse events were infusion-site reactions (266 [83%] participants during open-label ND0612, and 73 [57%] in the ND0612 group vs 56 [43%] in the oral levodopa-carbidopa group during the double-blind phase), most of which were mild. Serious adverse events in four participants in the ND0612 group were related to study treatment (infusion-site cellulitis [n=2], infusion-site abscess and infusion-site ulcer [n=1]; and paraesthesia and peripheral sensorimotor neuropathy [n=1]). One participant in the ND0612 group died during the double-blind phase, but the death was not related to study treatment (fall leading to traumatic brain injury). INTERPRETATION: Results of this phase 3 study showed that subcutaneous ND0612 used in combination with oral immediate-release levodopa-carbidopa increased on time without troublesome dyskinesia and reduced off time, with a favourable benefit-risk profile. ND0612 might offer a safe and efficacious subcutaneous levodopa infusion approach to managing motor fluctuations in people with Parkinson's disease. The ongoing open-label extension phase will provide further information on the long-term efficacy and safety of treatment. FUNDING: NeuroDerm.

Neurology
LeWitt PA. Getting an earful of stimulation: A novel means for neuromodulation of Parkinson disease. *Parkinsonism Relat Disord* 2024; Epub ahead of print. PMID: 38443212. Full Text

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Neurology
Meeker A, Van Gampelaere J, Zhu L, **Luo H**, and Zhang J. Spike Analysis of the Neural Activities Across the Rats' Auditory Brain Structures. *Journal of Engineering and Science in Medical Diagnostics and Therapy* 2024; 7(4). PMID: Not assigned. Request Article

Tinnitus is a health condition that affects a large population. Clinical diagnosis and treatment have been developed for treating tinnitus for years. However, there are still limitations because researchers have yet to elucidate the mechanisms underlying how tinnitus neural signals develop in brain structures. Abnormal neural interactions among the brain areas are considered to play an important role in tinnitus generation. Researchers have been studying neural activities in the auditory brain structures, including the dorsal cochlear nucleus (DCN), inferior colliculus (IC), and auditory cortex (AC), to seek a better understanding of the information flow among these brain regions, especially in comparison with both health and tinnitus conditions. In this project, neural activities from the DCN, IC, and AC were collected and analyzed before and after the animals were noise-exposed and before and after their auditory cortices were electrically stimulated. These conditions in rats were used to estimate healthy animals, noise-trauma-induced tinnitus, and after auditory cortex electrical stimulation (ACES) treatment. The signal processing algorithms started with the raw measurement data and focused on the local field potentials (LFPs) and spikes in the time domain. The firing rate, shape of spikes, and time differences among channels were analyzed in the time domain, and phase–phase correlation was used to test the phase-frequency information. All the analysis results were summarized in plots and color-heat maps and also used to identify if any neural signal differs and cross-channel relation changes at various animal conditions and discussed.

Neurology
Zeidman LA. Alfred A. Strauss (1897-1957). *J Neurol* 2024; Epub ahead of print. PMID: 38532141. Full Text

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Neurosurgery

Deshpande N, Hadi M, **Mansour TR**, **Telemi E**, **Hamilton T**, **Hu J**, **Schultz L**, **Nerenz DR**, Khalil JG, Easton R, Perez-Cruet M, Aleem I, Park P, Soo T, Tong D, **Abdulhak M**, **Schwalb JM**, and **Chang V**. The impact of anxiety and depression on lumbar spine surgical outcomes: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2024; 1-10. Epub ahead of print. PMID: 38427985. Full Text

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OBJECTIVE: The presence of depression and anxiety has been associated with negative outcomes in spine surgery patients. While it seems evident that a history of depression or anxiety can negatively influence outcome, the exact additive effect of both has not been extensively studied in a multicenter trial. The purpose of this study was to investigate the relationship between a patient's history of anxiety and depression and their patient-reported outcomes (PROs) after lumbar surgery. METHODS: Patients in the Michigan Spine Surgery Improvement Collaborative registry undergoing lumbar spine surgery between July 2016 and December 2021 were grouped into four cohorts: those with a history of anxiety only, those with a history of depression only, those with both, and those with neither. Primary outcomes were achieving the minimal clinically important difference (MCID) for the Patient-Reported Outcomes Measurement Information System Physical Function 4-item Short Form (PROMIS PF), EQ-5D, and numeric rating scale (NRS) back pain and leg pain, and North American Spine Society patient satisfaction. Secondary outcomes included surgical site infection, hospital readmission, and return to the operating room. Multivariate Poisson generalized estimating equation models were used to report incidence rate ratios (IRRs) from patient baseline variables. RESULTS: Of the 45,565 patients identified, 3941 reported a history of anxiety, 5017 reported a history of depression, 9570 reported both, and 27,037 reported neither. Compared with those who reported having neither, patients with both anxiety and depression had lower patient satisfaction at 90 days ($p = 0.002$) and 1 year ($p = 0.021$); PROMIS PF MCID at 90 days ($p < 0.001$), 1 year ($p < 0.001$), and 2 years ($p = 0.006$); EQ-5D MCID at 90 days ($p < 0.001$), 1 year ($p < 0.001$), and 2 years ($p < 0.001$); NRS back pain MCID at 90 days ($p < 0.001$) and 1 year ($p < 0.001$); and NRS leg pain MCID at 90 days ($p < 0.001$), 1 year ($p = 0.024$), and 2 years ($p = 0.027$). Patients with anxiety only ($p < 0.001$), depression only ($p < 0.001$), or both ($p < 0.001$) were more likely to be readmitted within 90 days. Additionally, patients with anxiety only ($p = 0.015$) and both anxiety and depression ($p = 0.015$) had higher rates of surgical site infection. Patients with anxiety only ($p = 0.006$) and depression only ($p = 0.021$) also had higher rates of return to the operating room. CONCLUSIONS: The authors observed an association between a history of anxiety and depression and negative outcome after lumbar spine surgery. In addition, they found an additive effect of a history of both anxiety and depression with an increased risk of negative outcome when compared with either anxiety or depression alone.

Neurosurgery

Hunt R, **Scarpace L**, and **Rock J**. Integration of Augmented Reality Into Glioma Resection Surgery: A Case Report. *Cureus* 2024; 16(2):e53573. PMID: 38445166. Full Text

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Augmented reality (AR) is an exciting technology that has garnered considerable attention in the field of neurosurgery. Despite this, clinical use of this technology is still in its infancy. An area of great potential for this technology is the ability to display 3D anatomy overlaid with the patient to assist with presurgical

and intraoperative decision-making. A 39-year-old woman presented with headaches and was experiencing what was described as a whooshing sound. MRI revealed the presence of a large left frontal mass involving the genu of the corpus callosum, with heterogeneous enhancement and central hemorrhagic necrosis, confirmed to be a glioma. She underwent a craniotomy with intraoperative MRI for resection. An augmented reality system was used to superimpose 3D holographic anatomy onto the patient's head for surgical planning. This report highlights a new AR technology and its immediate application to cranial neurosurgery. It is critical to document new uses of this technology as the field continues to integrate AR as well as other next-generation technologies into practice.

Neurosurgery

Malta TM, **Sabedot TS**, **Morosini NS**, **Datta I**, Garofano L, Vallentgoed W, Varn FS, Aldape K, D'Angelo F, Bakas S, Barnholtz-Sloan JS, Gan HK, Hasanain M, Hau AC, Johnson KC, **Cazacu S**, **deCarvalho AC**, Khasraw M, Kocakavuk E, Kouwenhoven MCM, Migliozzi S, Niclou SP, Niers JM, Ormond DR, Paek SH, Reifenberger G, Sillevis Smitt PA, Smits M, Stead LF, van den Bent MJ, Van Meir EG, Walenkamp A, Weiss T, Weller M, Westerman BA, Ylstra B, Wesseling P, Lasorella A, French PJ, **Poisson LM**, Verhaak RGW, Iavarone A, and **Noushmehr H**. The Epigenetic Evolution of Glioma Is Determined by the IDH1 Mutation Status and Treatment Regimen. *Cancer Res* 2024; 84(5):741-756. PMID: 38117484. Full Text

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Tumor adaptation or selection is thought to underlie therapy resistance in glioma. To investigate longitudinal epigenetic evolution of gliomas in response to therapeutic pressure, we performed an epigenomic analysis of 132 matched initial and recurrent tumors from patients with IDH-wildtype (IDHwt) and IDH-mutant (IDHmut) glioma. IDHwt gliomas showed a stable epigenome over time with relatively low levels of global methylation. The epigenome of IDHmut gliomas showed initial high levels of genome-wide DNA methylation that was progressively reduced to levels similar to those of IDHwt tumors. Integration of epigenomics, gene expression, and functional genomics identified HOXD13 as a master regulator of IDHmut astrocytoma evolution. Furthermore, relapse of IDHmut tumors was accompanied by histologic progression that was associated with survival, as validated in an independent cohort. Finally, the initial cell composition of the tumor microenvironment varied between IDHwt and IDHmut tumors and changed differentially following treatment, suggesting increased neoangiogenesis and T-cell infiltration upon treatment of IDHmut gliomas. This study provides one of the largest cohorts of paired longitudinal glioma samples with epigenomic, transcriptomic, and genomic profiling and suggests that treatment of IDHmut glioma is associated with epigenomic evolution toward an IDHwt-like phenotype. SIGNIFICANCE: Standard treatments are related to loss of DNA methylation in IDHmut glioma, resulting in epigenetic activation of genes associated with tumor progression and alterations in the microenvironment that resemble treatment-naïve IDHwt glioma.

Neurosurgery
Ogunsola O, Linzey JR, Zaki MM, **Chang V**, **Schultz LR**, **Springer K**, **Abdulhak M**, Khalil JG, **Schwalb JM**, Aleem I, **Nerenz DR**, Perez-Cruet M, Easton R, Soo TM, Tong D, and Park P. Risk factors of emergency department visits following elective cervical and lumbar surgical procedures: a multi-institution analysis from the Michigan Spine Surgery Improvement Collaborative. *J Neurosurg Spine* 2024; 1-7. Epub ahead of print. PMID: 38427993. Full Text

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OBJECTIVE: Emergency department visits 90 days after elective spinal surgery are relatively common, with rates ranging from 9% to 29%. Emergency visits are very costly, so their reduction is of importance. This study's objective was to evaluate the reasons for emergency department visits and determine potentially modifiable risk factors. METHODS: This study retrospectively reviewed data queried from the Michigan Spine Surgery Improvement Collaborative (MSSIC) registry from July 2020 to November 2021. MSSIC is a multicenter (28-hospital) registry of patients undergoing cervical and lumbar degenerative spinal surgery. Adult patients treated for elective cervical and/or lumbar spine surgery for degenerative pathology (spondylosis, intervertebral disc disease, low-grade spondylolisthesis) were included. Emergency department visits within 90 days of surgery (outcome measure) were analyzed utilizing univariate and multivariate regression analyses. RESULTS: Of 16,224 patients, 2024 (12.5%) presented to the emergency department during the study period, most commonly for pain related to spinal surgery (31.5%), abdominal problems (15.8%), and pain unrelated to the spinal surgery (12.8%). On multivariate analysis, age (per 5-year increase) (relative risk [RR] 0.94, 95% CI 0.92-0.95), college education (RR 0.82, 95% CI 0.69-0.96), private insurance (RR 0.79, 95% CI 0.70-0.89), and preoperative ambulation

status (RR 0.88, 95% CI 0.79-0.97) were associated with decreased emergency visits. Conversely, Black race (RR 1.30, 95% CI 1.13-1.51), current diabetes (RR 1.13, 95% CI 1.01-1.26), history of deep venous thromboembolism (RR 1.28, 95% CI 1.16-1.43), history of depression (RR 1.13, 95% CI 1.03-1.25), history of anxiety (RR 1.32, 95% CI 1.19-1.46), history of osteoporosis (RR 1.21, 95% CI 1.09-1.34), history of chronic obstructive pulmonary disease (RR 1.19, 95% CI 1.06-1.34), American Society of Anesthesiologists class > II (RR 1.18, 95% CI 1.08-1.29), and length of stay > 3 days (RR 1.29, 95% CI 1.16-1.44) were associated with increased emergency visits. CONCLUSIONS: The most common reasons for emergency department visits were surgical pain, abdominal dysfunction, and pain unrelated to index spinal surgery. Increased focus on postoperative pain management and bowel regimen can potentially reduce emergency visits. The risks of diabetes, history of osteoporosis, depression, and anxiety are areas for additional preoperative screening.

Neurosurgery

Peterson D, Van Poppel M, Boling W, Santos P, **Schwalb J**, Eisenberg H, Mehta A, Spader H, Botros J, Vrionis FD, Ko A, Adelson PD, Lega B, Konrad P, Calle G, Vale FL, Bucholz R, and Richardson RM. Clinical safety and feasibility of a novel implantable neuroimmune modulation device for the treatment of rheumatoid arthritis: initial results from the randomized, double-blind, sham-controlled RESET-RA study. *Bioelectron Med* 2024; 10(1):8. PMID: 38475923. Full Text

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BACKGROUND: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease that causes persistent synovitis, bone damage, and progressive joint destruction. Neuroimmune modulation through electrical stimulation of the vagus nerve activates the inflammatory reflex and has been shown to inhibit the production and release of inflammatory cytokines and decrease clinical signs and symptoms in RA. The RESET-RA study was designed to determine the safety and efficacy of an active implantable device for treating RA. METHODS: The RESET-RA study is a randomized, double-blind, sham-controlled, multi-center, two-stage pivotal trial that enrolled patients with moderate-to-severe RA who were incomplete responders or intolerant to at least one biologic or targeted synthetic disease-modifying anti-rheumatic drug. A neuroimmune modulation device (SetPoint Medical, Valencia, CA) was implanted on the left cervical vagus nerve within the carotid sheath in all patients. Following post-surgical clearance, patients were randomly assigned (1:1) to active stimulation or non-active (control) stimulation for 1 min once per day. A predefined blinded interim analysis was performed in patients enrolled in the study's initial stage (Stage 1) that included demographics, enrollment rates, device implantation rates, and safety of the surgical procedure, device, and stimulation over 12 weeks of treatment. RESULTS: Sixty patients were implanted during Stage 1 of the study. All device implant procedures were completed without

intraoperative complications, infections, or surgical revisions. No unanticipated adverse events were reported during the perioperative period and at the end of 12 weeks of follow-up. No study discontinuations were due to adverse events, and no serious adverse events were related to the device or stimulation. Two serious adverse events were related to the implantation procedure: vocal cord paresis and prolonged hoarseness. These were reported in two patients and are known complications of surgical implantation procedures with vagus nerve stimulation devices. The adverse event of vocal cord paresis resolved after vocal cord augmentation injections with filler and speech therapy. The prolonged hoarseness had improved with speech therapy, but mild hoarseness persists. CONCLUSIONS: The surgical procedures for implantation of the novel neuroimmune modulation device for the treatment of RA were safe, and the device and its use were well tolerated. TRIAL REGISTRATION: NCT04539964; August 31, 2020.

Neurosurgery

Rogers JL, Wall T, Acquaye-Mallory AA, Boris L, Kim Y, Aldape K, Quezado MM, Butman JA, Smirniotopoulos JG, Chaudhry H, Tsien CI, Chittiboina P, Zaghloul K, Aboud O, Avgeropoulos NG, Burton EC, Cachia DM, Dixit KS, Drappatz J, Dunbar EM, Forsyth P, Komlodi-Pasztor E, Mandel J, Ozer BH, Lee EQ, Ranjan S, Lukas RV, Raygada M, Salacz ME, Smith-Cohn MA, **Snyder J**, Soldatos A, Theeler BJ, Widemann BC, Camphausen KA, Heiss JD, Armstrong TS, Gilbert MR, and Penas-Prado M. Virtual multi-institutional tumor board: a strategy for personalized diagnoses and management of rare CNS tumors. *J Neurooncol* 2024; Epub ahead of print. PMID: 38427131. Full Text

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PURPOSE: Multidisciplinary tumor boards (MTBs) integrate clinical, molecular, and radiological information and facilitate coordination of neuro-oncology care. During the COVID-19 pandemic, our MTB transitioned to a virtual and multi-institutional format. We hypothesized that this expansion would allow expert review of challenging neuro-oncology cases and contribute to the care of patients with limited access to specialized centers. METHODS: We retrospectively reviewed records from virtual MTBs held between 04/2020-03/2021. Data collected included measures of potential clinical impact, including referrals to observational or therapeutic studies, referrals for specialized neuropathology analysis, and whether molecular findings led to a change in diagnosis and/or guided management suggestions. RESULTS: During 25 meetings, 32 presenters discussed 44 cases. Approximately half (n = 20; 48%) involved a rare central nervous system (CNS) tumor. In 21% (n = 9) the diagnosis was changed or refined based on molecular profiling obtained at the NIH and in 36% (n = 15) molecular findings guided management. Clinical trial suggestions were offered to 31% (n = 13), enrollment in the observational NCI Natural History Study to 21% (n = 9), neuropathology review and molecular testing at the NIH to 17% (n = 7), and all received management suggestions. CONCLUSION: Virtual multi-institutional MTBs enable remote expert review of CNS tumors. We propose them as a strategy to facilitate expert opinions from specialized centers, especially for rare CNS tumors, helping mitigate geographic barriers to patient care and serving as a pre-screening tool for studies. Advanced molecular testing is key to obtaining a precise diagnosis, discovering potentially actionable targets, and guiding management.

Nursing

Joshi S, **Arshad S**, Lindsay A, **Heinonen J**, **Misikir H**, **Zervos J**, **Prentiss T**, **Verkler J**, **Numi M**, Czander B, David RE, Mossing M, Kilgore PE, Rehman N, and **Zervos M**. Control of SARS-CoV-2 infection in skilled nursing facilities in Detroit, Michigan: a model for emerging infectious diseases. *Infect Control Hosp Epidemiol* 2024; 1-3. Epub ahead of print. PMID: 38505952. Full Text

Division of Infectious Diseases, Henry Ford Hospital, Detroit, MI, USA.
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An infection prevention bundle that consisted of the development of a response team, public-academic partnership, daily assessment, regular testing, isolation, and environmental controls was implemented in 26 skilled nursing facilities in Detroit, Michigan (March 2020-April 2021). This intervention was associated with sustained control of severe acute respiratory coronavirus virus 2 infection among residents and staff.

Nursing

Suleyman G, **Shallal A**, **Ruby A**, **Chami E**, **Gubler J**, McNamara S, Miles-Jay A, **Tibbetts R**, and **Alangaden G**. Use of whole genomic sequencing to detect New Delhi metallo-B-lactamase (NDM)-producing Escherichia coli outbreak associated with endoscopic procedures. *Infect Control Hosp Epidemiol* 2024; 1-8. Epub ahead of print. PMID: 38495009. Full Text

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BACKGROUND: Whole-genome sequencing (WGS) has emerged as an alternative genotyping tool for outbreak investigations in the healthcare setting. We describe the investigation and control of a New Delhi metallo-B-lactamase (NDM)-producing Escherichia coli cluster in Southeast Michigan. METHODS: Michigan Bureau of Laboratories identified several closely related NDM-producing E. coli isolates with WGS. An epidemiologic investigation, including case-control study, assessment of infection control practices, and endoscope culturing, was performed to identify source of transmission. Targeted screening of potentially exposed patients was performed following identification of probable source. RESULTS: Between July 2021 and February 2023, nine patients were identified. Phylogenetic analysis confirmed the isolates were closely related with less than 26 single nucleotide polymorphism (SNP) differences between isolates, suggesting an epidemiological link. Eight (89%) patients had a duodenoscope and/or gastroscope exposure. Cases were compared with 23 controls. Cases had significantly higher odds of exposure to duodenoscopes (odds ratio 15.0; 95% CI, 1.8-142.2; P = .015). The mean incubation period, estimated as date of procedure to positive index culture, was 86 days (range, 1-320 days). No lapses in endoscope reprocessing were identified; NDM-producing E. coli was not recovered from reprocessed endoscopes or during targeted screening. No additional cases were identified after removal of implicated gastroscopes and replacement of duodenoscope with disposable end caps. CONCLUSIONS: In this investigation, WGS was utilized to identify transmission of an NDM-producing E. coli outbreak associated with endoscope exposure. Coupled with epidemiologic data, WGS can facilitate outbreak investigations by rapidly identifying linked cases and potential sources to prevent further transmission.

Obstetrics, Gynecology and Women's Health Services

Ayyash M, **Miller M**, **Smith N**, **Espy J**, and **Kim SK**. Management of small bowel obstruction in the third trimester. *BMJ Case Rep* 2024; 17(3). PMID: 38442967. Full Text

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Small bowel obstruction (SBO) in pregnancy is exceedingly rare. Management of SBO in the third trimester may pose particular challenges, as clinicians must determine whether or not the delivery of the fetus is indicated. In this report, we review the case of a patient in her mid-20's with no prior surgical history who presented with nausea and vomiting at 34 weeks of gestation and was ultimately diagnosed with an SBO. Following expectant management during the initial 4 days of inpatient admission, the patient subsequently underwent an exploratory laparotomy at 35 weeks without concurrent delivery. She was monitored for the remainder of her pregnancy with non-stress tests to evaluate fetal status and eventually underwent induction of labour at 39 weeks, resulting in a successful vaginal delivery. Herein, we review the challenges related to the diagnosis and management of SBO in pregnancy, as well as the maternal-fetal outcomes in the setting of SBO in the third trimester.

Obstetrics, Gynecology and Women's Health Services

Beatty JR, Zelenak L, Gillon S, McGoron L, **Goyert G**, and Ondersma SJ. Risk Identification in Perinatal Health Care Settings via Technology-Based Recruitment Methods: Comparative Study. *JMIR Form Res* 2024; 8:e48823. PMID: 38437004. Full Text

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BACKGROUND: Digital screening and intervention tools have shown promise in the identification and reduction of substance use in health care settings. However, research in this area is impeded by challenges in integrating recruitment efforts into ongoing clinical workflows or staffing multiple study clinics with full-time research assistants, as well as by the underreporting of substance use. OBJECTIVE: The aim of the study is to evaluate pragmatic methods for facilitating study recruitment in health care settings by examining recruitment rates and participant characteristics using in-person-based versus flyer approaches. METHODS: This study compared recruitment rates at a Women's Health clinic in the Midwest under 2 different recruitment strategies: in person versus via a flyer with a QR code. We also examined the disclosure of substance use and risk screener positivity for the 2 strategies. We also obtained information about the current use of technology and willingness to use it for study participation. RESULTS: A greater percentage of patients recruited in person participated than those recruited via flyers (57/63, 91% vs 64/377, 17%). However, the final number recruited in each group was roughly equal (n=57 vs n=64). Additionally, participants recruited via flyers were more likely to screen positive for alcohol use risk on the Tolerance, Annoyed, Cut Down, Eye-Opener alcohol screen than those recruited at the clinic (24/64, 38% vs 11/57, 19%; $\chi(2)(1)=4.9$; P=.03). Participants recruited via flyers were also more likely to screen positive for drug use risk on the Wayne Indirect Drug Use Screener than those recruited at the clinic (20/64, 31% vs 9/57, 16%; $\chi(2)(1)=4.0$; P=.05). Furthermore, of the 121 pregnant women, 117 (96.7%) reported owning a smartphone, 111 (91.7%) had an SMS text message plan on their phone, and 94 (77.7%) reported being willing to receive SMS text messages or participate in a study if sent a link to their phone. CONCLUSIONS: The distribution of flyers with a QR code by medical staff appears to be an efficient and cost-effective method of recruitment that also facilitates disclosure while reducing the impact on clinic workflows. This method of recruitment can be useful for data collection at multiple locations and lead to larger samples across and between health systems. Participant recruitment via technology in perinatal health care appears to facilitate disclosure, particularly when participants can learn about the research and complete screening using their own device at a place and time convenient for them. Pregnant women in an urban Midwestern hospital had access to and were comfortable using technology.

Ophthalmology and Eye Care Services

Kasetty VM, **Sethi D**, and **Hamad AE**. Re: Ji et al.: "Plungerless" diagnostic anterior chamber paracentesis technique. (Ophthalmol Retina 2024;8:136). *Ophthalmol Retina* 2024; Epub ahead of print. PMID: 38456876. Request Article

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Orthopedics/Bone and Joint Center

Becker B, **Spadafore S**, Oberle L, Spittler J, and Khodaee M. Epidemiology of Shoulder Dislocation Treated at Emergency Departments in the United States Between 1997 and 2021. *Orthop J Sports Med* 2024; 12(3). PMID: 38482337. Full Text

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BACKGROUND: The exact incidence of shoulder dislocation in the general population of the United States (US) has yet to be well studied. PURPOSE: To establish the current incidence and patterns of shoulder dislocations in the US, especially regarding sports-related activity. STUDY DESIGN: Descriptive epidemiology study. METHODS: This was a retrospective analysis of shoulder dislocations encountered in emergency departments in the US between 1997 and 2021 as recorded in the National Electronic Injury Surveillance System (NEISS). Data were further analyzed according to patient age, sex, and sports participation. Information from the United States Census Bureau was used to determine the overall incidence of dislocations. RESULTS: A total of 46,855 shoulder dislocations were identified in the NEISS database, representing a national estimate of 1,915,975 dislocations (mean 25.2 per 100,000 person-years). The mean patient age was 35.3 years. More than half of the dislocations (52.5%) were sports-related, and basketball (16.4%), American football (15.6%), and cycling (9%) were the sports most commonly associated with dislocation. Most dislocations (72.1%) occurred in men. This disparity by sex was more significant for sports-related dislocations (86.1% in men) than nonsports-related dislocations (56.7% in men; P < .001). With sports-related dislocations, people <21 years experienced a significantly higher proportion versus those >39 years (44.6% vs 14.9%; P < .001), while the opposite distribution was seen with nonsports-related dislocations (<21 years: 12% vs >39 years: 51.7%; P < .001). Women outnumbered men with shoulder dislocation among people >61 years. CONCLUSION: Sports-related shoulder dislocations were more common among younger and male individuals than older and female individuals. Contact sports such as basketball and American football were associated with more shoulder dislocations compared with noncontact sports.

Orthopedics/Bone and Joint Center
Koerber S, **Wager SG**, **Zynda AJ**, and **Santa Barbara MT**. A Scoping Review: Reducing Musculoskeletal Injury Risk Factors for Adaptive Sport Athletes through Prevention Programs. *Am J Phys Med Rehabil* 2024; Epub ahead of print. PMID: 38547088. Full Text

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The purpose of this scoping review was to identify existing strategies to reduce modifiable risk factors for musculoskeletal injury in adaptive athletes. Medline, Embase, Web of Science, and CINAHL were searched. Inclusion criteria required studies written in English, samples of adaptive athletes, and evaluation of any injury prevention programs that would reduce risk factors associated with MSK injury. The literature search resulted in 785 unique articles. 32 full text articles were screened for inclusion. Four studies of wheelchair basketball and wheelchair rugby injury prevention programs were included in the final analysis, and these studies demonstrated increase in shoulder range of motion, decreased shoulder pain, and decreased cumulative traumatic disorders; all of which was proposed to reduce risk of shoulder injury. However, these studies were small and did not include control groups. Future research is needed to implement programs that reduce risk factors of MSK injuries and reduce health disparities for adaptive athletes.

Orthopedics/Bone and Joint Center
Lawrence RL, Richardson LB, Bilodeau HL, Bonath DJ, Dahn DJ, Em MA, Sarkar S, **Braman JP**, and Ludewig PM. Effects of Scapular Angular Deviations on Potential for Rotator Cuff Tendon Mechanical Compression. *Orthop J Sports Med* 2024; 12(3):23259671231219023. PMID: 38435717. Full Text

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BACKGROUND: One proposed mechanism of rotator cuff disease is scapular motion impairments contributing to rotator cuff compression and subsequent degeneration. PURPOSE: To model the effects

of scapular angular deviations on rotator cuff tendon proximity for subacromial and internal mechanical impingement risk during scapular plane abduction. STUDY DESIGN: Descriptive laboratory study. METHODS: Three-dimensional bone models were reconstructed from computed tomography scans obtained from 10 asymptomatic subjects and 9 symptomatic subjects with a clinical presentation of impingement syndrome. Models were rotated to average scapular orientations from a healthy dataset at higher (120°) and lower (subject-specific) humeral elevation angles to investigate internal and subacromial impingement risks, respectively. Incremental deviations in scapular upward/downward rotation, internal/external rotation, and anterior/posterior tilt were imposed on the models to simulate scapular movement impairments. The minimum distance between the rotator cuff insertions and potential impinging structures (eg, glenoid, acromion) was calculated. Two-way mixed-model analyses of variance assessed for effects of scapular deviation and group. RESULTS: At 120° of humerothoracic elevation, minimum distances from the supraspinatus and infraspinatus insertions to the glenoid increased with ≥5° changes in upward rotation (1.6-9.8 mm, P < .001) or external rotation (0.9-5.0 mm, P≤ .048), or with ≥10° changes in anterior tilt (1.1-3.2 mm, P < .001). At lower angles, ≥20° changes in most scapular orientations significantly increased the distance between the supraspinatus and infraspinatus insertions and the acromion or coracoacromial ligament. CONCLUSION: A reduction in scapular upward rotation decreases the distance between the rotator cuff tendon insertions and glenoid at 120° humerothoracic elevation. Interpretation is complicated for lower angles because the humeral elevation angle was defined by the minimum distance. CLINICAL RELEVANCE: These results may assist clinical decision making regarding the effects of scapular movement deviations in patients with rotator cuff pathology and scapular dyskinesia and may help inform the selection of clinical interventions.

Orthopedics/Bone and Joint Center

Noe MC, Link RC, Warren JR, **Goodrich E**, Sinclair M, and Tougas C. Pediatric Type I Open Both Bone Forearm Fractures: Predicting Failure of Nonoperative Management. *J Pediatr Orthop* 2024; Epub ahead of print. PMID: 38477563. Full Text

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BACKGROUND: In recent years, nonoperative treatment of pediatric type I open both bone forearm fractures (OBBFFs) with bedside irrigation, antibiotics, closed reduction, and casting has yielded low infection rates. However, risk factors for failure of type I OBBFF closed reduction have not been well described. Our purpose was to describe management of patients with type I OBBFFs at our institution and determine what factors are associated with failure of closed reduction in this population. METHODS: This was a review of patients between 5 and 15 years of age who received initial nonoperative management for type I OBBFFs at one institution between 2015 and 2021. Primary outcome was success or failure of nonoperative management (defined as progression to surgical management). Secondary outcomes included infections, compartment syndromes, and neuropraxias. Other variables of interest were demographic information, prereduction and postreduction translation and angulation of the radius and ulna, cast index, and antibiotic administration. RESULTS: Sixty-one patients (67.7% male) with 62 type I OBBFFs were included in this study. Following initial nonoperative management, 55 injuries (88.7%) were successfully treated in casts, while the remaining 7 (11.3%) required surgical intervention following loss of acceptable reduction in cast. Median cast index (0.84, IQR 0.8 to 0.9 vs. 0.75, IQR 0.7-0.8, P=0.020) and postreduction radius translation on anteroposterior films (32.0%, IQR 17.0% to 40.0% vs. 5.0%, IQR 0.0% to 26.0%, P=0.020) were higher among those who failed nonoperative management. Multivariable logistic regression models identified increased odds of failure for every SD (0.7) increase in cast index (OR 3.78, P=0.023, 95% CI: 1.4-14.3) and 25% increase in postreduction radius translation on anteroposterior films (OR 7.39, P=0.044, 95% CI 1.2-70.4). No infections or compartment syndromes and 2 transient ulnar neuropraxias occurred. CONCLUSIONS: Closed reduction of type I OBBFFs was successful in 88.7% of cases. There were no infections after nonoperative management. Increases in cast index of 0.7 and postreduction radius translation on anteroposterior radiographs of 25% were associated with increased likelihood of failure, thus requiring surgery; age was not. LEVEL OF EVIDENCE: Level IV-retrospective comparative study.

Orthopedics/Bone and Joint Center

Ramos YFM, Rice SJ, **Ali SA**, Pastrello C, Jurisica I, Rai MF, Collins KH, Lang A, Maerz T, Geurts J, Ruiz-Romero C, June RK, Thomas Appleton C, Rockel JS, and Kapoor M. Evolution and advancements in genomics and epigenomics in OA research: How far we have come. *Osteoarthritis Cartilage* 2024; Epub ahead of print. PMID: 38428513. Full Text

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OBJECTIVE: Osteoarthritis (OA) is the most prevalent musculoskeletal disease affecting articulating joint tissues, resulting in local and systemic changes that contribute to increased pain and reduced function. Diverse technological advancements have culminated in the advent of high throughput "omic" technologies, enabling identification of comprehensive changes in molecular mediators associated with the disease. Amongst these technologies, genomics and epigenomics - including methylomics and miRNomics, have emerged as important tools to aid our biological understanding of disease. DESIGN: In this narrative review, we selected articles discussing advancements and applications of these technologies to OA biology and pathology. We discuss how genomics, deoxyribonucleic acid (DNA) methylomics, and miRNomics have uncovered disease-related molecular markers in the local and systemic tissues or fluids of OA patients. RESULTS: Genomics investigations into the genetic links of OA, including using genome-wide association studies, have evolved to identify 100+ genetic susceptibility markers of OA. Epigenomic investigations of gene methylation status have identified the importance of methylation to OA-related catabolic gene expression. Furthermore, miRNomic studies have identified key microRNA signatures in various tissues and fluids related to OA disease. CONCLUSIONS: Sharing of standardized, well-annotated omic datasets in curated repositories will be key to enhancing statistical power to detect smaller and targetable changes in the biological signatures underlying OA pathogenesis. Additionally, continued technological developments and analysis methods, including using computational molecular and regulatory networks, are likely to facilitate improved detection of disease-relevant targets, in-turn, supporting precision medicine approaches and new treatment strategies for OA.

Orthopedics/Bone and Joint Center

Washnock-Schmid EA, Livingston N, **Latack K**, Wrobel N, and **Day CS**. Orthopaedic Hand Patient Support Systems Have Valuable Insight to Patient Function and Pain. *J Patient Exp* 2024; 11:23743735241240876. PMID: 38524386. Full Text

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Patient-reported outcome measures (PROs) are increasingly used in clinical assessment. Research on how patient support systems contribute to physician understanding of patient condition is limited. Thus, insights from significant others may provide value, especially when concerns exist regarding patient response validity. Patients recruited from the pre-operative environment undergoing orthopaedic hand procedures responded to PROMIS-Pain Interference (PI), PROMIS-Upper Extremity (UE), PROMIS-Depression (D), and QuickDASH. They then selected a significant other (SO) to do the same. Patients and SOs were also asked to complete the West Haven-Yale Multidimensional Pain Inventory (WHYMPI) as a measure of support-related responses. Patient and SO responses were compared, and support-related responses were added in subsequent analyses to examine their effect on SO PRO assessment.

Orthopedics/Bone and Joint Center
Yedulla NR, Mehta N, Bernstein DN, **Cross AG**, **Elhage KG**, **Moutzouros V**, and **Makhni EC**. When Do Patients Achieve PROMIS Milestones After Rotator Cuff Repair? *Orthop J Sports Med* 2024; 12(3):23259671241231608. PMID: 38510320. Full Text

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BACKGROUND: Given the variability of the questions asked, the Patient-Reported Outcomes Measurement Information System (PROMIS) upper extremity (UE) computer adaptive test (CAT) Version 2.0 item bank aids in the evaluation of rotator cuff repair (RCR) rehabilitation by determining when recovery milestones are possible based on the quality of patient responses at certain time points. PURPOSE: To assess the time point at which patients with RCR were able to achieve specific functional milestones, determined as positive responses to the 5 most frequently asked items on the PROMIS UE CAT Version 2.0. STUDY DESIGN: Case series; Level of evidence, 4. METHODS: The postoperative PROMIS UE CAT Version 2.0 scores of patients who underwent RCR between February 16, 2017, and July 30, 2019, were reviewed with respect to individual PROMIS item, response, and timing of response. A functional milestone was considered achieved if the patient response was "without any difficulty" or "with a little difficulty" to any of the 5 most frequently asked PROMIS items. The percentage of patients in each monthlong postoperative interval who answered with either response was recorded. The logit generalized estimating equations method was used to analyze the association between milestone achievement for each PROMIS item and predictor variables (age, sex, body mass index, smoking status, race, ethnicity, and employment status). RESULTS: A total of 1131 responses from 371 patients were included. The majority of patients attained milestone achievement on 4 of the 5 most frequently asked PROMIS items at time points ranging from 1 to 5 months postoperatively: "Are you able to carry a shopping bag or briefcase?" (by 1 month), "Are you able to put on and take off a coat or jacket?" (by 3 months), "Are you able to pour liquid from a bottle into a glass?" (by 3 months), and "Are you able to carry a heavy object (over 10 pounds/5 kg)?" (by 5 months). For the item "Are you able to put on a shirt or blouse?", the majority of patients did not achieve the milestone by 1 year. CONCLUSION: These findings support the application of PROMIS UE CAT Version 2.0 milestone achievement in the shared decision-making process and postoperative monitoring, as patients can use this information to determine when they can return to certain activities and providers can apply these standards to identify patients needing additional clinical support.

Otolaryngology – Head and Neck Surgery
Hutchings H, Behinaein P, Enofe N, Brue K, **Tam S**, **Chang S**, **Movsas B**, **Poisson L**, **Wang A**, and **Okereke I**. Association of Social Determinants with Patient-Reported Outcomes in Patients with Cancer. *Cancers (Basel)* 2024; 16(5). PMID: 38473374. Full Text

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Patient-reported outcome (PRO) scores have been utilized more frequently, but the relationship of PRO scores to determinants of health and social inequities has not been widely studied. Our goal was to determine the association of PRO scores with social determinants. All patients with a new cancer diagnosis who completed a PRO survey from 2020 to 2022 were included. The PRO survey recorded scores for depression, fatigue, pain interference and physical function. Higher depression, fatigue and pain scores indicated more distress. Higher physical condition scores indicated improved functionality. A total of 1090 patients were included. Married patients had significantly better individual PRO scores for each domain. Patients who were able to use the online portal to complete their survey also had better individual scores. Male patients and non-White patients had worse pain scores than female and White patients, respectively. Patients with prostate cancer had the best scores while patients with head and neck and lung cancer had the worst scores. PRO scores varied by cancer disease site and stage. Social support may act in combination with specific patient/tumor factors to influence PRO scores. These findings present opportunities to address patient support at institutional levels.

Pathology and Laboratory Medicine
Jhaveri JK, Dahmen A, Lazarovich A, Nusbaum D, Trinh QD, **Gupta N**, and Agarwal PK. Necrotizing granulomatous epididymo-orchitis post intravesical BCG administration after brachytherapy for prostate cancer. *Urol Case Rep* 2024; 54:102694. PMID: 38516176. Full Text

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Urothelial carcinoma of the bladder remains a challenging disease to treat. Intravesical instillation of BCG has demonstrated tremendous efficacy in preventing recurrence. BCG related necrotizing granulomatous epididymo-orchitis is rare and has not been previously linked to brachytherapy for adenocarcinoma of the prostate. We hypothesize that prior brachytherapy has a deleterious effect on the verumontanum that can result in retrograde transmission of BCG particles leading to granulomatous epididymo-orchitis. This is the first case report of necrotizing granulomatous epididymo-orchitis related to BCG in a patient status post brachytherapy for adenocarcinoma of the prostate.

Pathology and Laboratory Medicine
Ohan H, **Alruwaii FI**, **Montecalvo J**, and **Al-Obaidy KI**. Persistent Paramesonephric (Müllerian) Duct Remnant in Male Patients: Report of 2 Cases Presenting as Pelvic Masses. *Int J Surg Pathol* 2024; Epub ahead of print. PMID: 38509866. Full Text

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Pathology and Laboratory Medicine
Sadasivan SM, **Loveless IM**, **Chen Y**, **Gupta NS**, **Sanii R**, **Bobbitt KR**, **Chitale DA**, Williamson SR, Rundle AG, and **Rybicki BA**. Patterns of B-cell lymphocyte expression changes in pre- and post-malignant prostate tissue are associated with prostate cancer progression. *Cancer Med* 2024; 13(6):e7118. PMID: 38523528. Full Text

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BACKROUND: Inflammation characterized by the presence of T and B cells is often observed in prostate cancer, but it is unclear how T- and B-cell levels change during carcinogenesis and whether such changes influence disease progression. METHODS: The study used a retrospective sample of 73 prostate cancer cases (45 whites and 28 African Americans) that underwent surgery as their primary treatment and had a benign prostate biopsy at least 1 year before diagnosis. CD3+, CD4+, and CD20+ lymphocytes were quantified by immunohistochemistry in paired pre- and post-diagnostic benign prostate biopsy and tumor surgical specimens, respectively. Clusters of similar trends of expression across two different timepoints and three distinct prostate regions-benign biopsy glands (BBG), tumor-adjacent benign glands (TAG), and malignant tumor glandular (MTG) regions-were identified using Time-series Anytime Density Peaks Clustering (TADPole). A Cox proportional hazards model was used to estimate the hazard ratio (HR) of time to biochemical recurrence associated with region-specific lymphocyte counts and regional trends. RESULTS: The risk of biochemical recurrence was significantly reduced in men with an elevated CD20+ count in TAG (HR = 0.81, p = 0.01) after adjusting for covariates. Four distinct patterns of expression change across the BBG-TAG-MTG regions were identified for each marker. For CD20+, men with low expression in BBG and higher expression in TAG compared to MTG had an adjusted HR of 3.06 (p = 0.03) compared to the reference group that had nominal differences in CD20+ expression across all three regions. The two CD3+ expression patterns that featured lower CD3+ expression in the BBG compared to the TAG and MTG regions had elevated HRs ranging from 3.03 to 4.82 but did not reach statistical significance. CONCLUSIONS: Longitudinal and spatial expression patterns of both CD3+ and CD20+ suggest that increased expression in benign glands during prostate carcinogenesis is associated with an aggressive disease course.

Pathology and Laboratory Medicine

Suleyman G, **Shallal A**, **Ruby A**, **Chami E**, **Gubler J**, McNamara S, Miles-Jay A, **Tibbetts R**, and **Alangaden G**. Use of whole genomic sequencing to detect New Delhi metallo-B-lactamase (NDM)-producing Escherichia coli outbreak associated with endoscopic procedures. *Infect Control Hosp Epidemiol* 2024; 1-8. Epub ahead of print. PMID: 38495009. Full Text

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BACKGROUND: Whole-genome sequencing (WGS) has emerged as an alternative genotyping tool for outbreak investigations in the healthcare setting. We describe the investigation and control of a New Delhi metallo-B-lactamase (NDM)-producing Escherichia coli cluster in Southeast Michigan. METHODS: Michigan Bureau of Laboratories identified several closely related NDM-producing E. coli isolates with WGS. An epidemiologic investigation, including case-control study, assessment of infection control practices, and endoscope culturing, was performed to identify source of transmission. Targeted screening of potentially exposed patients was performed following identification of probable source. RESULTS: Between July 2021 and February 2023, nine patients were identified. Phylogenetic analysis confirmed the isolates were closely related with less than 26 single nucleotide polymorphism (SNP) differences between isolates, suggesting an epidemiological link. Eight (89%) patients had a duodenoscope and/or gastroscope exposure. Cases were compared with 23 controls. Cases had significantly higher odds of exposure to duodenoscopes (odds ratio 15.0; 95% CI, 1.8-142.2; P = .015). The mean incubation period, estimated as date of procedure to positive index culture, was 86 days (range, 1-320 days). No lapses in endoscope reprocessing were identified; NDM-producing E. coli was not recovered from reprocessed endoscopes or during targeted screening. No additional cases were identified after removal of implicated gastroscopes and replacement of duodenoscope with disposable end caps. CONCLUSIONS: In this

investigation, WGS was utilized to identify transmission of an NDM-producing E. coli outbreak associated with endoscope exposure. Coupled with epidemiologic data, WGS can facilitate outbreak investigations by rapidly identifying linked cases and potential sources to prevent further transmission.

Pathology and Laboratory Medicine

Winston-Mcpherson G, and Fasanya-Maku H. The What, Why, and How of Gender Cultural Competency: Clinical laboratories should explore the latest resources in training for phlebotomy staff to take the lead in providing equitable care for all of their patients. *Clinical Laboratory News* 2024; 50(2):8-11. PMID: Not assigned. Request Article

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Pediatrics

Ricciuto A, Liu K, El-Matary W, Amin M, Amir AZ, Aumar M, Auth M, Di Guglielmo MD, Druve Tavares Fagundes E, Rodrigues Ferreira A, Furuya KN, Gupta N, Guthery S, Horslen SP, Jensen K, Kamath BM, Kerkar N, Koot BGP, Laborda TJ, Lee CK, Loomes KM, Mack C, Martinez M, Montano-Loza A, Ovchinsky N, Papadopoulou A, Perito ER, Sathya P, Schwarz KB, **Shah U**, Shteyer E, Soufi N, Stevens JP, Taylor A, Tessier ME, Valentino P, Woynarowski M, and Deneau M. Oral vancomycin is associated with improved inflammatory bowel disease clinical outcomes in primary sclerosing cholangitis-associated inflammatory bowel disease (PSC-IBD): A matched analysis from the Paediatric PSC Consortium. *Aliment Pharmacol Ther* 2024; Epub ahead of print. PMID: 38462727. Full Text

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Golisano Children's Hospital, University of Rochester Medical Center, Rochester, New York, USA.
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Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA.
Baylor College of Medicine, Texas Children's Hospital, Houston, Texas, USA.
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BACKGROUND: Data on oral vancomycin for primary sclerosing cholangitis (PSC)-associated inflammatory bowel disease (IBD) are limited. AIMS: Using data from the Paediatric PSC Consortium, to examine the effect of vancomycin on IBD activity. METHODS: In this retrospective multi-centre cohort study, we matched vancomycin-treated and untreated patients (1:3) based on IBD duration at the time of primary outcome assessment. The primary outcome was Physician Global Assessment (PGA) of IBD clinical activity after 1 year (±6 months) of vancomycin. We used generalised estimating equations (GEE) to examine the association between vancomycin and PGA remission, adjusting for IBD type, severity and medication exposures. Secondary outcomes included serum labs and endoscopic remission (global rating of no activity) among those with available data and also analysed with GEE. RESULTS: 113 PSC-IBD patients received vancomycin (median age 12.7 years, 63% male). The matched cohort included 70 vancomycin-treated and 210 untreated patients. Vancomycin was associated with greater odds of IBD clinical remission (odds ratio [OR] 3.52, 95% CI 1.97-6.31; adjusted OR [aOR] 5.24, 95% CI 2.68-10.22). Benefit was maintained in sensitivity analyses restricted to non-transplanted patients and those with baseline moderate-severe PGA. Vancomycin was associated with increased odds of endoscopic remission (aOR 2.76, 95% CI 1.002-7.62; N = 101 with data), and with lower CRP ($p = 0.03$) and higher haemoglobin and albumin (both $p < 0.01$). CONCLUSION: Vancomycin was associated with greater odds of IBD clinical and endoscopic remission. Additional, preferably randomised, controlled studies are needed to characterise efficacy using objective markers of mucosal inflammation, and to examine safety and define optimal dosing.

Pharmacy

Aguero D, Vest MH, and **Tryon J**. The role of the chief pharmacy officer in leading analytics strategy to support the enterprise. *Am J Health Syst Pharm* 2024; Epub ahead of print. PMID: 38469877. Full Text

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Pharmacy

Lobkovich A, Javed S, Hammoud R, Habhab A, and Lipari M. Pharmacist perceptions of delivering patient care through telehealth. *Am J Health Syst Pharm* 2024; Epub ahead of print. PMID: 38297902. Full Text

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version of record and will be replaced with the final article (formatted per AJHP style and proofed by the authors) at a later time. PURPOSE: To evaluate pharmacists' perceptions of the benefits of and barriers to telehealth as experienced in actual telehealth visits with patients. METHODS: This qualitative study used virtual focus groups and a validated questionnaire (the Health Optimum Telemedicine Acceptance [HOTA] survey) to assess telehealth facilitators and barriers. Participants were included if they were licensed pharmacists utilizing telehealth in the outpatient setting. Pharmacist focus group responses were transcribed and analyzed using Miles and Huberman's qualitative data analysis model. RESULTS: Six pharmacists participated in this study. Their responses were placed into 2 categories: clinical effectiveness and patient experience. All participants had performed at least 20 virtual visits, and all agreed that telehealth improved patients' health status. Respondents agreed that telehealth results in more frequent patient interactions and allows for provision of multiple types of care virtually. However, technological difficulties and the inability to provide physical examinations and obtain laboratory values were identified limitations. The surveyed pharmacists agreed that the main benefit that patients gained from telehealth was the elimination of transportation concerns, allowing increased access to care. However, pharmacists voiced their concern for patient privacy and barriers to educating patients on proper use of medical devices. CONCLUSION: Pharmacists felt that telehealth was useful in several clinical scenarios. However, they also identified opportunities to improve its development in clinical practice. Further investigation must be done to better grasp impediments to telehealth in order to provide the most effective patient care.

Pharmacy

Rebold N, Alosaimy S, Pearson JC, Dionne B, Taqi A, Lagnf A, Lucas K, Biagi M, Lombardo N, Eudy J, Anderson DT, Mahoney MV, Kufel WD, D'Antonio JA, Jones BM, Frens JJ, Baumeister T, Geriak M, Sakoulas G, Farmakiotis D, Delaportas D, Larew J, **Veve MP**, and Rybak MJ. Dalbavancin Sequential Therapy for Gram-Positive Bloodstream Infection: A Multicenter Observational Study. *Infect Dis Ther* 2024; 13(3):565-579. PMID: 38427289. Full Text

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INTRODUCTION: Long-acting lipoglycopeptides such as dalbavancin may have utility in patients with Gram-positive bloodstream infections (BSI), particularly in those with barriers to discharge or who require prolonged parenteral antibiotic courses. A retrospective cohort study was performed to provide further multicenter real-world evidence on dalbavancin use as a sequential therapy for Gram-positive BSI. METHODS: One hundred fifteen patients received dalbavancin with Gram-positive BSI, defined as any positive blood culture or diagnosed with infective endocarditis, from 13 centers geographically spread across the United States between July 2015 and July 2021. RESULTS: Patients had a mean (SD) age of 48.5 (17.5) years, the majority were male (54%), with many who injected drugs (40%). The most common infection sources (non-exclusive) were primary BSI (89%), skin and soft tissue infection (SSTI) (25%), infective endocarditis (19%), and bone and joint infection (17%). Staphylococcus aureus accounted for 72% of index cultures, coagulase-negative Staphylococcus accounted for 18%, and Streptococcus species in 16%. Dalbavancin started a median (Q(1)-Q(3)) of 10 (6-19) days after index culture collection. The most common regimen administered was dalbavancin 1500 mg as one dose for 50% of cases. The primary outcome of composite clinical failure occurred at 12.2%, with 90-day mortality at 7.0% and 90-day BSI recurrence at 3.5%. CONCLUSIONS: Dalbavancin may serve as a useful tool in facilitating hospital discharge in patients with Gram-positive BSI. Randomized controlled trials are anticipated to validate dalbavancin as a surrogate to current treatment standards.

Pharmacy

Smythe MA, Koerber JM, **Roberts A**, Hoffman JL, and Batke J. Hospital Acquired Venous Thromboembolism: A Preventability Assessment. *Hosp Pharm* 2024; 59(2):183-187. PMID: 38450351. Full Text

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Background: The American Heart Association has a call to action to reduce hospital acquired venous thromboembolism (HA-VTE) by 20% by the year 2030. There is increasing recognition that quality improvement initiatives for VTE reduction should focus on reducing potentially preventable HA-VTE. The objective of our study was to determine what proportion of HA-VTE events are potentially preventable. Methods: This was a retrospective, single center pilot study of 50 patients with HA-VTE. Seven preventability factors were identified with a focus on VTE prescription and administration. Data were extracted through chart review using a systematic data collection form. The primary endpoint was the proportion of patients with potentially preventable HA-VTE. Descriptive statistics were used. Results: The median age was 66 years with an admission VTE risk level of moderate-high in 94%. Potentially preventable HA-VTE was found in 40% of cases. Missed doses occurred in 29.8% with a median of 2 missed doses and a range of 1 to 20. Patient refusal was the most common reason for missed doses in 71%. Delays in initiation occurred in 12.7%. Sixty percent of those on mechanical prophylaxis only had nonadherence. Conclusion: Forty percent of HA-VTE cases were potentially preventable. Missed doses was the most common preventability factor identified with patient refusal accounting for most missed doses.

Plastic Surgery

Al-Saghir T, **Vraa A**, **Sawar K**, **Jacobsen G**, **Evangelista MS**, and **Atisha D**. Effects of Marijuana Use in Patients Undergoing Abdominal Free Flap Breast Reconstruction. *Plast Reconstr Surg Glob Open* 2024; 12(3):e5657. PMID: 38435459. Full Text

From the Wayne State University School of Medicine, Detroit, Mich.
Department of General Surgery, Henry Ford Hospital, Detroit, Mich.
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BACKGROUND: Marijuana use has been associated with vascular inflammation and clotting, resulting in endothelial damage and arteritis. As marijuana use rises in the United States, few studies have evaluated its impact on surgical outcomes and wound healing in free flap breast reconstruction. METHODS: A retrospective cohort study of patients undergoing abdominal free flap breast reconstruction between 2016 and 2022 at a large metropolitan healthcare system was performed. Patient demographics, comorbidities, procedural details, and complications were analyzed. Minor complications were defined as skin or fat necrosis not requiring intervention, nipple loss, any wound requiring management in the clinic, hematoma, and seroma. Major complications were defined as reoperation, flap loss, cardiac or thromboembolic events, and hospital readmission. Active marijuana users were those with marijuana use within 12 weeks of surgery. RESULTS: In total, 168 patients underwent 276 deep inferior epigastric artery-based flaps for breast reconstruction. There were 21 active marijuana users. There were no significant differences in patient demographics, cancer treatment, or minor and major complications. However, there were higher rates of active nicotine use (P = 0.001) and anxiety/depression amongst active marijuana users (P = 0.002). Active users had higher rates of bilateral breast reconstruction (P = 0.029), but no significant differences in other operative details. CONCLUSIONS: Active marijuana use of unknown frequency may be safe in patients undergoing breast free flap reconstruction. Advising marijuana abstinence preoperatively may not alter patient outcomes. Further studies of greater sample size are needed to evaluate marijuana's impact on outcomes associated with breast reconstruction using free flap.

Public Health Sciences
Al-Saghir T, **Vraa A**, **Sawar K**, **Jacobsen G**, **Evangelista MS**, and **Atisha D**. Effects of Marijuana Use in Patients Undergoing Abdominal Free Flap Breast Reconstruction. *Plast Reconstr Surg Glob Open* 2024; 12(3):e5657. PMID: 38435459. Full Text

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Public Health Sciences

Aris IM, Lin PD, Wu AJ, Dabelea D, Lester BM, Wright RJ, Karagas MR, Kerver JM, Dunlop AL, **Joseph CL**, Camargo CA, Jr., Ganiban JM, Schmidt RJ, Strakovsky RS, McEvoy CT, Hipwell AE, O'Shea TM, McCormack LA, Maldonado LE, Niu Z, Ferrara A, Zhu Y, Chehab RF, Kinsey EW, Bush NR, Nguyen RHN, Carroll KN, Barrett ES, Lyall K, Sims-Taylor LM, Trasande L, Biagini JM, Breton CV, Patti MA, Coull B, Amutah-Onukagha N, Hacker MR, James-Todd T, and Oken E. Birth outcomes in relation to neighborhood food access and individual food insecurity during pregnancy in the Environmental Influences on Child Health Outcomes (ECHO)-wide cohort study. *Am J Clin Nutr* 2024; Epub ahead of print. PMID: 38431121. Full Text

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BACKGROUND: Limited access to healthy foods, resulting from residence in neighborhoods with low-food access or from household food insecurity, is a public health concern. Contributions of these measures during pregnancy to birth outcomes remain understudied. OBJECTIVES: We examined associations between neighborhood food access and individual food insecurity during pregnancy with birth outcomes. METHODS: We used data from 53 cohorts participating in the nationwide Environmental Influences on Child Health Outcomes-Wide Cohort Study. Participant inclusion required a geocoded residential address or response to a food insecurity question during pregnancy and information on birth outcomes. Exposures include low-income-low-food-access (LILA, where the nearest supermarket is >0.5 miles for urban or >10 miles for rural areas) or low-income-low-vehicle-access (LILV, where few households have a vehicle and >0.5 miles from the nearest supermarket) neighborhoods and individual food insecurity. Mixed-effects models estimated associations with birth outcomes, adjusting for socioeconomic and pregnancy characteristics. RESULTS: Among 22,206 pregnant participants (mean age 30.4 y) with neighborhood food access data, 24.1% resided in LILA neighborhoods and 13.6% in LILV neighborhoods. Of 1630 pregnant participants with individual-level food insecurity data (mean age 29.7 y), 8.0% experienced food insecurity. Residence in LILA (compared with non-LILA) neighborhoods was associated with lower birth weight [β -44.3 g; 95% confidence interval (CI): -62.9, -25.6], lower birth weight-for-gestational-age z-score (-0.09 SD units; -0.12, -0.05), higher odds of small-for-gestational-age [odds ratio (OR) 1.15; 95% CI: 1.00, 1.33], and lower odds of large-for-gestational-age (0.85; 95% CI: 0.77, 0.94). Similar findings were observed for residence in LILV neighborhoods. No associations of individual food insecurity with birth outcomes were observed. CONCLUSIONS: Residence in LILA or LILV neighborhoods during pregnancy is associated with adverse birth outcomes. These findings highlight the need for future studies examining whether investing in neighborhood resources to improve food access during pregnancy would promote equitable birth outcomes.

Public Health Sciences

Babatunde OA, Ramkumar SP, Nguyen SA, Okereke OI, Clark FA, Nagar A, Osazuwa-Peters N, and **Adjei Boakye E**. Association between number of Adverse Childhood Experiences and depression among older adults is moderated by race. *Prev Med* 2024; 181:107921. PMID: 38423302. Full Text

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OBJECTIVE: This study aimed to assess the association between number of Adverse Childhood Experiences (ACE) and history of depression among older adults and to explore the interaction by race. METHODS: This study was a cross-sectional analysis of the 2020 Behavioral Risk Factor Surveillance System (BRFSS) data among 60,122 older respondents (≥ 60 years old). The ACE score (zero, one, two-three, ≥four) included questions assessing exposure to eight types of ACEs before age 18. The outcome was the respondent's self-report depression diagnosed (yes/no). Multivariable logistic regression models examined the association between ACEs and depression stratified by race. Each model adjusted for age, smoking status, income, education, marital status, and body mass index. RESULTS: In this sample of older adults, 47%, 23%, 19% and 10% reported having experienced zero, one, two-three, and four or more types of ACEs, respectively. Depression was reported by 16% of survey respondents. There was a significant interaction between ACE score and race and depression (p = 0.038). Respondents who experienced ≥4 ACEs had higher likelihood of reporting depression for all race/ethnicity groups: non-Hispanic Whites (aOR = 3.83; 95% CI: 3.07, 4.79), non-Hispanic Blacks (aOR = 3.39, 95% CI: 1.71, 6.71), or Hispanics (aOR = 12.61; 95% CI: 4.75, 33.43). This translated to a large effect size for non-Hispanic Whites and Hispanics although the magnitude was bigger for Hispanics. CONCLUSION: The association between number of ACEs and depression was strongest for older adults who identify as Hispanic, but weaker and less consistent for adults who identify as White and Black.

Public Health Sciences

Bryson TD, **Bhat SY**, **Moore C**, **Taube D**, **Xu J**, **Peterson E**, and **Harding P**. Targeted Gene Deletion or Antagonism of the Prostaglandin E2 EP3 Receptor Protects Against Cardiac Injury Postmyocardial Infarction. *Circ Heart Fail* 2024; Epub ahead of print. PMID: 38525608. Full Text

Hypertension & Vascular Research Division, Department of Internal Medicine, Henry Ford Health, Detroit, MI. (T.D.B., S.B., C.M., D.T., J.X., P.H.).
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BACKGROUND: Prostaglandin E2 acts through 4 G-protein-coupled receptors (EP1-EP4). We previously reported that activation of the EP3 receptor reduces cardiac contractility, and its expression increases after a myocardial infarction (MI), mediating the reduction in cardiac function. In contrast, cardiac overexpression of the EP4 receptor in MI substantially improves cardiac function. Moreover, we recently reported that mice overexpressing EP3 have heart failure under basal conditions and worsened cardiac function after MI. Thus, the deleterious effects of the prostaglandin E2 EP receptors in the heart are mediated via its EP3 receptor. We, therefore, hypothesized that cardiomyocyte-specific knockout (CM-EP3 KO) or antagonism of the EP3 receptor protects the heart after MI. METHODS: To test our hypothesis, we made the novel CM-EP3 KO mouse and subjected CM-EP3 KO or controls to sham or MI surgery for 2 weeks. In separate experiments, C57BL/6 mice were subjected to 2 weeks of MI and treated with either the EP3 antagonist L798 106 or vehicle starting 3 days post-MI. RESULTS: CM-EP3 KO significantly prevented a decline in cardiac function after MI compared with WT animals and prevented an increase in hypertrophy and fibrosis. Excitingly, mice treated with L798 106 3 days after MI had significantly better cardiac function compared with vehicle-treated mice. CONCLUSIONS: Altogether, these data suggest that EP3 may play a direct role in regulating cardiac function, and pharmaceutical targeting of the EP3 receptor may be a therapeutic option in the treatment of heart failure.

Public Health Sciences

Bryson TD, **Zurek M**, **Moore C**, **Taube D**, **Datta I**, **Levin A**, and **Harding P**. Prostaglandin E2 affects mitochondrial function in adult mouse cardiomyocytes and hearts. *Prostaglandins Leukot Essent Fatty Acids* 2024; 201:102614. PMID: 38471265. Full Text

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Prostaglandin E2 (PGE2) signals differently through 4 receptor subtypes (EP1-EP4) to elicit diverse physiologic/pathologic effects. We previously reported that PGE2 via its EP3 receptor reduces cardiac contractility and male mice with cardiomyocyte-specific deletion of the EP4 receptor (EP4 KO) develop dilated cardiomyopathy. The aim of this study was to identify pathways responsible for this phenotype. We performed ingenuity pathway analysis (IPA) and found that genes differentiating WT mice and EP4 KO mice were significantly overrepresented in mitochondrial (adj. p value = 6.28 × 10(-26)) and oxidative phosphorylation (adj. p value = 1.58 × 10(-27)) pathways. Electron microscopy from the EP4 KO hearts show substantial mitochondrial disarray and disordered cristae. Not surprisingly, isolated adult mouse cardiomyocytes (AVM) from these mice have reduced ATP levels compared to their WT littermates and reduced expression of key genes involved in the electron transport chain (ETC) in older mice. Moreover, treatment of AVM from C57Bl/6 mice with PGE2 or the EP3 agonist sulprostone resulted in changes of various genes involved in the ETC, measured by the Mitochondrial Energy Metabolism RT(2)-profiler assay. Lastly, the EP4 KO mice have reduced expression of superoxide dismuatse-2 (SOD2), whereas treatment of AVM with PGE2 or sulprostone increase superoxide production, suggesting increased oxidative stress levels in these EP4 KO mice. Altogether the current study supports the premise that PGE2 acting via its EP4 receptor is protective, while signaling through its other receptors, likely EP3, is deleterious.

Public Health Sciences

Corsi NJ, **Stephens A**, **Finati M**, Malchow T, Morrison C, **Davis M**, **Hares K**, **Corsi MP**, **Arora S**, **Chiarelli G**, **Cirulli GO**, Autorino R, Sood A, **Rogers C**, and **Abdollah F**. Testing the external validity of the POUT III trial (adjuvant platnium-based chemotherapy in upper tract urothelial carcinoma) in a North American cohort. *Urol Oncol* 2024; Epub ahead of print. PMID: 38522975. Full Text

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OBJECTIVE: The European POUT III randomized controlled trial provided level-one evidence that adjuvant platinum-based chemotherapy is the standard of care following nephroureterectomy (RNU) for

locally invasive or node-positive upper tract urothelial carcinoma. We aim to assess this European randomized controlled trial's generalizability (external validity) to a North American cohort, using a nationwide database. MATERIALS AND METHODS: To compare trial patients with those seen in real-world practice, we simulated the trial inclusion criteria using data from the National Cancer Database (NCDB). We identified patients with histologically confirmed transitional cell carcinoma who underwent RNU. The available demographic characteristics of the NCDB cohort were compared with the POUT III trial cohort using Chi-squared test. RESULTS: The NCDB cohort (n = 3,380) had a significantly higher proportion of older patients (age ≥ 80: 23.5% vs. 5%), and more males (68% vs. 56.2%) than the POUT cohort (Table 1, both $p < 0.001$). Additionally, the rate of advanced nodal disease was higher in the NCDB (N1 9.6%, N2 9.3%) than in the POUT (N1 6%, N2 3%) cohort ($p < 0.001$). A more extensive lymph node dissection was performed in NCDB vs. POUT patients (node≥10 10.9% vs. 3%, $p < 0.001$). Sensitivity analysis removing all subjects with a Charlson Comorbidity Index > 0 did not change the significance of any results. CONCLUSIONS: While the primary disease stage was similar, the rate of advanced nodal disease was significantly higher in NCDB, which might be explained partially by the more extensive lymph node dissection performed in the latter. These differences warrant caution when applying the POUT III findings to North American patients.

Public Health Sciences

DeCuir J, Payne AB, Self WH, Rowley EAK, Dascomb K, DeSilva MB, Irving SA, Grannis SJ, Ong TC, Klein NP, Weber ZA, Reese SE, Ball SW, Barron MA, Naleway AL, Dixon BE, Essien I, Bride D, Natarajan K, Fireman B, Shah AB, Okwuazi E, Wiegand R, Zhu Y, Lauring AS, Martin ET, Gaglani M, Peltan ID, Brown SM, Ginde AA, Mohr NM, Gibbs KW, Hager DN, Prekker M, Mohamed A, Srinivasan V, Steingrub JS, Khan A, Busse LW, Duggal A, Wilson JG, Chang SY, Mallow C, Kwon JH, Exline MC, Columbus C, **Vaughn IA**, Safdar B, Mosier JM, Harris ES, Casey JD, Chappell JD, Grijalva CG, Swan SA, Johnson C, Lewis NM, Ellington S, Adams K, Tenforde MW, Paden CR, Dawood FS, Fleming-Dutra KE, Surie D, and Link-Gelles R. Interim Effectiveness of Updated 2023-2024 (Monovalent XBB.1.5) COVID-19 Vaccines Against COVID-19-Associated Emergency Department and Urgent Care Encounters and Hospitalization Among Immunocompetent Adults Aged ≥18 Years - VISION and IVY Networks, September 2023-January 2024. *MMWR Morb Mortal Wkly Rep* 2024; 73(8):180-188. PMID: 38421945. Full Text

In September 2023, CDC's Advisory Committee on Immunization Practices recommended updated 2023-2024 (monovalent XBB.1.5) COVID-19 vaccination for all persons aged ≥6 months to prevent COVID-19, including severe disease. However, few estimates of updated vaccine effectiveness (VE) against medically attended illness are available. This analysis evaluated VE of an updated COVID-19 vaccine dose against COVID-19-associated emergency department (ED) or urgent care (UC) encounters and hospitalization among immunocompetent adults aged ≥18 years during September 2023-January 2024 using a test-negative, case-control design with data from two CDC VE networks. VE against COVID-19-associated ED/UC encounters was 51% (95% CI = 47%-54%) during the first 7-59 days after an updated dose and 39% (95% CI = 33%-45%) during the 60-119 days after an updated dose. VE estimates against COVID-19-associated hospitalization from two CDC VE networks were 52% (95% CI = 47%-57%) and 43% (95% CI = 27%-56%), with a median interval from updated dose of 42 and 47 days, respectively. Updated COVID-19 vaccine provided increased protection against COVID-19-associated ED/UC encounters and hospitalization among immunocompetent adults. These results support CDC recommendations for updated 2023-2024 COVID-19 vaccination. All persons aged ≥6 months should receive updated 2023-2024 COVID-19 vaccine.

Public Health Sciences

Deshpande N, Hadi M, **Mansour TR**, **Telemi E**, **Hamilton T**, **Hu J**, **Schultz L**, **Nerenz DR**, Khalil JG, Easton R, Perez-Cruet M, Aleem I, Park P, Soo T, Tong D, **Abdulhak M**, **Schwalb JM**, and **Chang V**. The impact of anxiety and depression on lumbar spine surgical outcomes: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2024; 1-10. Epub ahead of print. PMID: 38427985. Full Text

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OBJECTIVE: The presence of depression and anxiety has been associated with negative outcomes in spine surgery patients. While it seems evident that a history of depression or anxiety can negatively influence outcome, the exact additive effect of both has not been extensively studied in a multicenter trial. The purpose of this study was to investigate the relationship between a patient's history of anxiety and depression and their patient-reported outcomes (PROs) after lumbar surgery. METHODS: Patients in the Michigan Spine Surgery Improvement Collaborative registry undergoing lumbar spine surgery between July 2016 and December 2021 were grouped into four cohorts: those with a history of anxiety only, those with a history of depression only, those with both, and those with neither. Primary outcomes were achieving the minimal clinically important difference (MCID) for the Patient-Reported Outcomes Measurement Information System Physical Function 4-item Short Form (PROMIS PF), EQ-5D, and numeric rating scale (NRS) back pain and leg pain, and North American Spine Society patient satisfaction. Secondary outcomes included surgical site infection, hospital readmission, and return to the operating room. Multivariate Poisson generalized estimating equation models were used to report incidence rate ratios (IRRs) from patient baseline variables. RESULTS: Of the 45,565 patients identified, 3941 reported a history of anxiety, 5017 reported a history of depression, 9570 reported both, and 27,037 reported neither. Compared with those who reported having neither, patients with both anxiety and depression had lower patient satisfaction at 90 days ($p = 0.002$) and 1 year ($p = 0.021$); PROMIS PF MCID at 90 days ($p < 0.001$), 1 year ($p < 0.001$), and 2 years ($p = 0.006$); EQ-5D MCID at 90 days ($p < 0.001$), 1 year ($p < 0.001$), and 2 years ($p < 0.001$); NRS back pain MCID at 90 days ($p < 0.001$) and 1 year ($p < 0.001$); and NRS leg pain MCID at 90 days ($p < 0.001$), 1 year ($p = 0.024$), and 2 years ($p = 0.027$). Patients with anxiety only ($p < 0.001$), depression only ($p < 0.001$), or both ($p < 0.001$) were more likely to be readmitted within 90 days. Additionally, patients with anxiety only ($p = 0.015$) and both anxiety and depression ($p = 0.015$) had higher rates of surgical site infection. Patients with anxiety only ($p = 0.006$) and depression only ($p = 0.021$) also had higher rates of return to the operating room. CONCLUSIONS: The authors observed an association between a history of anxiety and depression and negative outcome after lumbar spine surgery. In addition, they found an additive effect of a history of both anxiety and depression with an increased risk of negative outcome when compared with either anxiety or depression alone.

Public Health Sciences

Hutchings H, Behinaein P, Enofe N, Brue K, **Tam S**, **Chang S**, **Movsas B**, **Poisson L**, **Wang A**, and **Okereke I**. Association of Social Determinants with Patient-Reported Outcomes in Patients with Cancer. *Cancers (Basel)* 2024; 16(5). PMID: 38473374. Full Text

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Patient-reported outcome (PRO) scores have been utilized more frequently, but the relationship of PRO scores to determinants of health and social inequities has not been widely studied. Our goal was to determine the association of PRO scores with social determinants. All patients with a new cancer diagnosis who completed a PRO survey from 2020 to 2022 were included. The PRO survey recorded scores for depression, fatigue, pain interference and physical function. Higher depression, fatigue and

pain scores indicated more distress. Higher physical condition scores indicated improved functionality. A total of 1090 patients were included. Married patients had significantly better individual PRO scores for each domain. Patients who were able to use the online portal to complete their survey also had better individual scores. Male patients and non-White patients had worse pain scores than female and White patients, respectively. Patients with prostate cancer had the best scores while patients with head and neck and lung cancer had the worst scores. PRO scores varied by cancer disease site and stage. Social support may act in combination with specific patient/tumor factors to influence PRO scores. These findings present opportunities to address patient support at institutional levels.

Public Health Sciences

Kessler LG, Comstock B, Aiello Bowles EJ, Mou J, Nash MG, Bravo P, Fleckenstein LE, Pflugeisen C, Gao H, Winer RL, Ornelas IJ, Smith C, **Neslund-Dudas C**, and **Shetty P**. Protocol to measure validity and reliability of colorectal, breast, cervical and lung cancer screening questions from the 2021 National Health Interview Survey: Methodology and design. *PLoS One* 2024; 19(3):e0297773. PMID: 38437207. Full Text

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Previous studies demonstrate that self-reports of mammography screening for breast cancer and colonoscopy screening for colorectal cancer demonstrate concordance, based on adherence to screening guidelines, with electronic medical records (EMRs) in over 90% of those interviewed, as well as high sensitivity and specificity, and can be used for monitoring our Healthy People goals. However, for screening tests for cervical and lung cancers, and for various sub-populations, concordance between self-report and EMRs has been noticeably lower with poor sensitivity or specificity. This study aims to test the validity and reliability of lung, colorectal, cervical, and breast cancer screening questions from the 2021 and 2022 National Health Interview Survey (NHIS). We present the protocol for a study designed to measure the validity and reliability of the NHIS cancer screening questions compared to EMRs from four US-based healthcare systems. We planned a randomized trial of a phone- vs web-based survey with NHIS questions that were previously revised based on extensive cognitive interviewing. Our planned sample size will be 1576 validity interviews, and 1260 interviews randomly assigned at 1 or 3 months after the initial interview. We are enrolling people eligible for cancer screening based on age, sex, and smoking history per US Preventive Services Task Force recommendations. We will evaluate question validity using concordance, sensitivity, specificity, positive predictive value, negative predictive value, and report-to-records ratio. We further are randomizing participants to complete a second survey 1 vs 3 months later to assess question reliability. We suggest that typical measures of concordance may need to be reconsidered in evaluating cancer screening questions.

Public Health Sciences

Malta TM, **Sabedot TS**, **Morosini NS**, **Datta I**, Garofano L, Vallentgoed W, Varn FS, Aldape K, D'Angelo F, Bakas S, Barnholtz-Sloan JS, Gan HK, Hasanain M, Hau AC, Johnson KC, **Cazacu S**, **deCarvalho AC**, Khasraw M, Kocakavuk E, Kouwenhoven MCM, Migliozzi S, Niclou SP, Niers JM, Ormond DR, Paek SH, Reifenberger G, Sillevis Smitt PA, Smits M, Stead LF, van den Bent MJ, Van Meir EG, Walenkamp A, Weiss T, Weller M, Westerman BA, Ylstra B, Wesseling P, Lasorella A, French PJ, **Poisson LM**, Verhaak RGW, Iavarone A, and **Noushmehr H**. The Epigenetic Evolution of Glioma Is Determined by the IDH1 Mutation Status and Treatment Regimen. *Cancer Res* 2024; 84(5):741-756. PMID: 38117484. Full Text

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Tumor adaptation or selection is thought to underlie therapy resistance in glioma. To investigate longitudinal epigenetic evolution of gliomas in response to therapeutic pressure, we performed an epigenomic analysis of 132 matched initial and recurrent tumors from patients with IDH-wildtype (IDHwt) and IDH-mutant (IDHmut) glioma. IDHwt gliomas showed a stable epigenome over time with relatively low levels of global methylation. The epigenome of IDHmut gliomas showed initial high levels of genome-wide DNA methylation that was progressively reduced to levels similar to those of IDHwt tumors. Integration of epigenomics, gene expression, and functional genomics identified HOXD13 as a master regulator of IDHmut astrocytoma evolution. Furthermore, relapse of IDHmut tumors was accompanied by histologic progression that was associated with survival, as validated in an independent cohort. Finally, the initial cell composition of the tumor microenvironment varied between IDHwt and IDHmut tumors and changed differentially following treatment, suggesting increased neoangiogenesis and T-cell infiltration upon

treatment of IDHmut gliomas. This study provides one of the largest cohorts of paired longitudinal glioma samples with epigenomic, transcriptomic, and genomic profiling and suggests that treatment of IDHmut glioma is associated with epigenomic evolution toward an IDHwt-like phenotype. SIGNIFICANCE: Standard treatments are related to loss of DNA methylation in IDHmut glioma, resulting in epigenetic activation of genes associated with tumor progression and alterations in the microenvironment that resemble treatment-naïve IDHwt glioma.

Public Health Sciences

Miyake K, **Kim DY**, **Chau LC**, **Trudeau S**, **Kitajima T**, **Wickramaratne N**, **Shimada S**, **Nassar A**, **Yoshida A**, **Abouljoud MS**, and **Nagai S**. Exception Policy Change Increased the Simultaneous Kidney-liver Transplant Probability of Polycystic Disease in the Centers With High Median MELD at Transplantation. *Transplantation* 2024; Epub ahead of print. PMID: 38548699. Full Text

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BACKGROUND: In 2019, Organ Procurement and Transplantation Network/United Network for Organ Sharing changed the exception policy for liver allocation to the median model for end-stage liver disease at transplantation (MMaT). This study evaluated the effects of this change on-waitlist outcomes of simultaneous liver-kidney transplantation (SLKT) for patients with polycystic liver-kidney disease (PLKD). METHODS: Using the Organ Procurement and Transplantation Network/United Network for Organ Sharing registry, 317 patients with PLKD listed for SLKT between January 2016 and December 2021 were evaluated. Waitlist outcomes were compared between prepolicy (Era 1) and postpolicy (Era 2) eras. RESULTS: One-year transplant probability was significantly higher in Era 2 than in Era 1 (55.7% versus 37.9%; P = 0.001), and the positive effect on transplant probability of Era 2 was significant after risk adjustment (adjusted hazard ratio, 1.76; 95% confidence interval, 1.22-2.54; P = 0.002 [ref. Era 1]), whereas waitlist mortality was comparable. Transplant centers were separated into the high and low MMaT groups with a score of 29 (median MMaT) and transplant probability in each group between eras was compared. In the high MMaT transplant centers, the 1-y transplant probability was significantly higher in Era 2 (27.5% versus 52.4%; P = 0.003). The positive effect remained significant in the high MMaT center group (adjusted hazard ratio, 2.79; 95% confidence interval, 1.43-5.46; P = 0.003 [ref. Era 1]) but not in the low MMaT center group. Although there was a difference between center groups in Era 1 (P = 0.006), it became comparable in Era 2 (P = 0.54). CONCLUSIONS: The new policy increased 1-y SLKT probability in patients with PKLD and successfully reduced the disparities based on center location.

Public Health Sciences

Newman LA, **Chen Y**, Martini R, Demaria S, Formenti S, Elemento O, and Davis MB. Tumor-Associated Lymphocytes and Breast Cancer Survival in Black and White Women. *JAMA Surg* 2024; Epub ahead of print. PMID: 38446467. Full Text

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This case series evaluates whether differences in immune filtration are associated with breast cancer risk in Black vs White women.

Public Health Sciences

Ogunsola O, Linzey JR, Zaki MM, **Chang V**, **Schultz LR**, **Springer K**, **Abdulhak M**, Khalil JG, **Schwalb JM**, Aleem I, **Nerenz DR**, Perez-Cruet M, Easton R, Soo TM, Tong D, and Park P. Risk factors of emergency department visits following elective cervical and lumbar surgical procedures: a multi-institution analysis from the Michigan Spine Surgery Improvement Collaborative. *J Neurosurg Spine* 2024; 1-7. Epub ahead of print. PMID: 38427993. Full Text

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OBJECTIVE: Emergency department visits 90 days after elective spinal surgery are relatively common, with rates ranging from 9% to 29%. Emergency visits are very costly, so their reduction is of importance. This study's objective was to evaluate the reasons for emergency department visits and determine potentially modifiable risk factors. METHODS: This study retrospectively reviewed data queried from the Michigan Spine Surgery Improvement Collaborative (MSSIC) registry from July 2020 to November 2021. MSSIC is a multicenter (28-hospital) registry of patients undergoing cervical and lumbar degenerative spinal surgery. Adult patients treated for elective cervical and/or lumbar spine surgery for degenerative pathology (spondylosis, intervertebral disc disease, low-grade spondylolisthesis) were included. Emergency department visits within 90 days of surgery (outcome measure) were analyzed utilizing univariate and multivariate regression analyses. RESULTS: Of 16,224 patients, 2024 (12.5%) presented to the emergency department during the study period, most commonly for pain related to spinal surgery (31.5%), abdominal problems (15.8%), and pain unrelated to the spinal surgery (12.8%). On multivariate analysis, age (per 5-year increase) (relative risk [RR] 0.94, 95% CI 0.92-0.95), college education (RR 0.82, 95% CI 0.69-0.96), private insurance (RR 0.79, 95% CI 0.70-0.89), and preoperative ambulation status (RR 0.88, 95% CI 0.79-0.97) were associated with decreased emergency visits. Conversely, Black race (RR 1.30, 95% CI 1.13-1.51), current diabetes (RR 1.13, 95% CI 1.01-1.26), history of deep venous thromboembolism (RR 1.28, 95% CI 1.16-1.43), history of depression (RR 1.13, 95% CI 1.03-1.25), history of anxiety (RR 1.32, 95% CI 1.19-1.46), history of osteoporosis (RR 1.21, 95% CI 1.09-1.34), history of chronic obstructive pulmonary disease (RR 1.19, 95% CI 1.06-1.34), American Society of Anesthesiologists class > II (RR 1.18, 95% CI 1.08-1.29), and length of stay > 3 days (RR 1.29, 95% CI 1.16-1.44) were associated with increased emergency visits. CONCLUSIONS: The most common reasons for emergency department visits were surgical pain, abdominal dysfunction, and pain unrelated to index spinal surgery. Increased focus on postoperative pain management and bowel regimen can potentially reduce emergency visits. The risks of diabetes, history of osteoporosis, depression, and anxiety are areas for additional preoperative screening.

Public Health Sciences

Qiu S, Dhaliwal R, **Divine G**, **Warner E**, and **Rao SD**. Differences in bone histomorphometry between white postmenopausal women with and without atypical femoral fracture after long-term bisphosphonate therapy. *J Bone Miner Res* 2024; Epub ahead of print. PMID: 38477744. Full Text

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Bone histomorphometric endpoints in transilial biopsies may be associated with increased risk of atypical femoral fracture (AFF) in patients with osteoporosis who take antiresorptives, including bisphosphonates (BP). One way to test this hypothesis is to evaluate bone histomorphometric endpoints in age-, gender-, and treatment time matched patients who either had AFF or did not have AFF. In this study, we performed trans-iliac bone biopsies in 52 white postmenopausal women with (n = 20) and without (n = 32) AFFs, all of whom had been treated for osteoporosis continuously with alendronate for 4 to 17 years. Despite the matched range of treatment duration (4-17 yrs), AFF patients received alendronate for significantly longer (10.7 yrs) than non-AFF patients (8.0 yrs) (p = 0.014). Bone histomorphometric endpoints reflecting microstructure and turnover were assessed in cancellous, intracortical and

endocortical envelopes from transilial biopsy specimens obtained from BP-treated patients 3-6 months after AFF and from non-AFF patients with similar age-, gender-, and range of BP treatment duration. However, in both cancellous and intracortical envelopes, AFF patients had significantly lower wall thickness (W.Th) and higher osteoclast surface (Oc.S/BS) than non-AFF patients. In addition, AFF patients had significantly higher eroded surface (ES/BS) only in the intracortical envelope. None of the dynamic variables related to bone formation and turnover differed significantly between the groups. In conclusion, in the ilium of BP-treated patients with osteoporosis, AFF patients have lower thickness of superficial bone (lower W.Th) of the cancellous and cortical envelopes than non-AFF patients. AFF and non-AFF patients have similar bone turnover rate in the ilium. Furthermore, in this population, as in previous work, AFF is more likely to occur in BP-treated patients with longer treatment duration.

Public Health Sciences

Rincon NL, McDowell KR, Weatherspoon D, Ritchwood TD, Rocke DJ, **Adjei Boakye E**, and Osazuwa-Peters N. Racial and ethnic disparities in human papillomavirus (HPV) vaccine uptake among United States adults, aged 27-45 years. *Hum Vaccin Immunother* 2024; 20(1):2313249. PMID: 38538572. Full Text

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In 2018, the Food and Drug Administration expanded the age of eligibility for the human papillomavirus (HPV) vaccine to 27 to 45 years. However, it is unclear if there are racial/ethnic disparities in HPV vaccine uptake for this age-group following this expanded recommendation. We aimed to identify any disparities in HPV vaccine in 27 to 45 year-olds based on sociodemographic factors. We analyzed nationally representative, cross-sectional data from the 2019 National Health Interview Survey (n = 9440). Logistic regression models estimated the odds of vaccine uptake (receipt of ≥1 vaccine dose) based on sociodemographic factors. Participants were mostly Non-Hispanic Whites (60.7%) and females (50.9%). In adjusted models, females had over three times greater odds of vaccine uptake compared to males (aOR = 3.58; 95% CI 3.03, 4.23). Also, compared to Non-Hispanic Whites, Non-Hispanic Blacks were 36% more likely (aOR = 1.36; 95% CI 1.09, 1.70), and Hispanics were 27% less likely (aOR = 0.73; 95% CI 0.58, 0.92) to receive the vaccine. Additionally, individuals without a usual place of care had lower odds of vaccine uptake (aOR = 0.72; 95% CI 0.57, 0.93), as were those with lower educational levels (aOR(high school) = 0.62; 95% CI 0.50, 0.78; aOR(some college) = 0.83; 95% CI 0.70, 0.98). There are disparities in HPV vaccine uptake among 27 to 45 year-olds, and adult Hispanics have lower odds of receiving the vaccine. Given the vaccine's importance in cancer prevention, it is critical that these disparities are addressed and mitigated.

Public Health Sciences

Sadasivan SM, **Loveless IM**, **Chen Y**, **Gupta NS**, **Sanii R**, **Bobbitt KR**, **Chitale DA**, Williamson SR, Rundle AG, and **Rybicki BA**. Patterns of B-cell lymphocyte expression changes in pre- and post-malignant prostate tissue are associated with prostate cancer progression. *Cancer Med* 2024; 13(6):e7118. PMID: 38523528. Full Text

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BACKROUND: Inflammation characterized by the presence of T and B cells is often observed in prostate cancer, but it is unclear how T- and B-cell levels change during carcinogenesis and whether such changes influence disease progression. METHODS: The study used a retrospective sample of 73 prostate cancer cases (45 whites and 28 African Americans) that underwent surgery as their primary treatment and had a benign prostate biopsy at least 1 year before diagnosis. CD3+, CD4+, and CD20+ lymphocytes were quantified by immunohistochemistry in paired pre- and post-diagnostic benign prostate biopsy and tumor surgical specimens, respectively. Clusters of similar trends of expression across two different timepoints and three distinct prostate regions-benign biopsy glands (BBG), tumor-adjacent benign glands (TAG), and malignant tumor glandular (MTG) regions-were identified using Time-series Anytime Density Peaks Clustering (TADPole). A Cox proportional hazards model was used to estimate the hazard ratio (HR) of time to biochemical recurrence associated with region-specific lymphocyte counts and regional trends. RESULTS: The risk of biochemical recurrence was significantly reduced in men with an elevated CD20+ count in TAG (HR = 0.81, p = 0.01) after adjusting for covariates. Four distinct patterns of expression change across the BBG-TAG-MTG regions were identified for each marker. For CD20+, men with low expression in BBG and higher expression in TAG compared to MTG had an adjusted HR of 3.06 (p = 0.03) compared to the reference group that had nominal differences in CD20+ expression across all three regions. The two CD3+ expression patterns that featured lower CD3+ expression in the BBG compared to the TAG and MTG regions had elevated HRs ranging from 3.03 to 4.82 but did not reach statistical significance. CONCLUSIONS: Longitudinal and spatial expression patterns of both CD3+ and CD20+ suggest that increased expression in benign glands during prostate carcinogenesis is associated with an aggressive disease course.

Public Health Sciences

Straughen JK, **Loveless I**, **Chen Y**, **Burmeister C**, **Lamerato L**, Lemke LD, O'Leary BF, Reiners JJ, Sperone FG, **Levin AM**, and **Cassidy-Bushrow AE**. The Impact of Environmental Benzene, Toluene, Ethylbenzene, and Xylene Exposure on Blood-Based DNA Methylation Profiles in Pregnant African American Women from Detroit. *Int J Environ Res Public Health* 2024; 21(3). PMID: 38541258. Full Text

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African American women in the United States have a high risk of adverse pregnancy outcomes. DNA methylation is a potential mechanism by which exposure to BTEX (benzene, toluene, ethylbenzene, and xylenes) may cause adverse pregnancy outcomes. Data are from the Maternal Stress Study, which recruited African American women in the second trimester of pregnancy from February 2009 to June 2010. DNA methylation was measured in archived DNA from venous blood collected in the second

trimester. Trimester-specific exposure to airshed BTEX was estimated using maternal self-reported addresses and geospatial models of ambient air pollution developed as part of the Geospatial Determinants of Health Outcomes Consortium. Among the 64 women with exposure and outcome data available, 46 differentially methylated regions (DMRs) were associated with BTEX exposure (FDR adjusted p-value < 0.05) using a DMR-based epigenome-wide association study approach. Overall, 89% of DMRs consistently exhibited hypomethylation with increasing BTEX exposure. Biological pathway analysis identified 11 enriched pathways, with the top 3 involving gamma-aminobutyric acid receptor signaling, oxytocin in brain signaling, and the gustation pathway. These findings highlight the potential impact of BTEX on DNA methylation in pregnant women.

Public Health Sciences
Washnock-Schmid EA, Livingston N, **Latack K**, Wrobel N, and **Day CS**. Orthopaedic Hand Patient Support Systems Have Valuable Insight to Patient Function and Pain. *J Patient Exp* 2024; 11:23743735241240876. PMID: 38524386. Full Text

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Patient-reported outcome measures (PROs) are increasingly used in clinical assessment. Research on how patient support systems contribute to physician understanding of patient condition is limited. Thus, insights from significant others may provide value, especially when concerns exist regarding patient response validity. Patients recruited from the pre-operative environment undergoing orthopaedic hand procedures responded to PROMIS-Pain Interference (PI), PROMIS-Upper Extremity (UE), PROMIS-Depression (D), and QuickDASH. They then selected a significant other (SO) to do the same. Patients and SOs were also asked to complete the West Haven-Yale Multidimensional Pain Inventory (WHYMPI) as a measure of support-related responses. Patient and SO responses were compared, and support-related responses were added in subsequent analyses to examine their effect on SO PRO assessment.

Public Health Sciences
White Perkins D, **Milan P**, **Miazek K**, Francis A, **Havstadb S**, **Bossick AS**, and **Wegienka G**. Identifying individual social needs during intake for diabetes Self-Management education and support services in the Detroit, Michigan area. *Prev Med Rep* 2024; 40:102671. PMID: 38487337. Full Text

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The American Diabetes Association has recommended that diabetes self-management education and support (DSMES) teams improve diabetes outcomes by identifying and responding to patients' social needs. This study examines demographic patterns in how hemoglobin A1c (A1c) is related to individual social needs, reported urgency of those needs, and interest in obtaining assistance. A total of 1125 unique persons who had been referred for DSMES and had completed a social needs screener via our electronic medical record were included. The majority (51.9 %) had an A1c < 8 % at their most recent assessment and most respondents (52.5 %) reported having at least 1 unmet social need (n = 591), Those who reported having at least 1 social need, tended to have higher A1c levels compared with those who reported no social needs (median of 8.0 % versus 7.7 %; p < 0.05). Among Black individuals the associations were stronger (median A1c of 8.2 % among those with versus 7.2 % among those without a reported social need; p < 0.05). However, among White individuals, there was no difference in A1c between these two groups. Among those who reported a social need, those who also reported they needed assistance (35.7 %) tended to have higher A1c levels than those who did not (median 8.3 %

versus 7.8 %; p < 0.10). This relationship did not vary by race. Ongoing study of the relationship between unmet social needs and glycemic control is warranted to help identify effective clinical workflows to help providers incorporate consideration of social needs into their medical decision making.

Radiation Oncology

Ben-Arye E, Lopez AM, Daoud N, Zoller L, **Walker E**, Davidescu M, Shulman K, Gressel O, Stein N, Brosh S, Schiff E, and Samuels N. Identifying factors associated with disparities in access to integrative oncology program. *J Pain Symptom Manage* 2024; Epub ahead of print. PMID: 38552747. Full Text

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CONTEXT AND OBJECTIVES: Cancer centers are increasingly providing complementary medicine as part of an emerging discipline termed 'integrative oncology' (IO). The present study explored factors associated with disparities in referral and adherence to a freely-provided IO program. METHODS: The databases of three oncology centers in northern Israel were searched retrospectively for chemotherapy-treated oncology patients eligible for referral by their oncology healthcare professionals to an integrative physician (IP) consultation. Demographic and cancer-related variables associated with the referral, and attendance by patients at the consultation were identified, as was adherence to the 6-week IO treatment program (high adherence, attending ≥4 IO treatment sessions; low adherence, 0-3 sessions). RESULTS: Of 4,988 eligible patients, 1694 (34%) were referred to the IP consultation, with 1331 (78.6%) attending the consultation of which 766 (57.6%) were adherent to IO treatments. Multivariate analysis revealed lower referral rates among patients speaking primarily Arabic and Russian vs. Hebrew (OR=3.0, 95% CI= 2.0-4.6, P<0.0001); males vs. females (OR=1.94, CI=1.3-2.9, p=0.001); those not reporting emotional distress (OR=1.5, CI=1.02-2.16, p=0.037); and older age (OR=1.04, CI=1.03-1.06, P<0.0001). Arabic and Russian-speaking patients were less likely to adhere to IO treatments (OR=0.52, 95% CI=0.32-0.83, P=0.006). CONCLUSION: Patients' ethno-national origin and immigration status (primary language, Arabic and Russian), male gender and older age were associated with lower rates of referral to and attendance of the IP consultation, with reduced adherence to weekly IO treatments. These findings require further study to identify barriers toward diversity, equity and inclusion in IO care, increasing awareness among healthcare professionals regarding the benefits of these services for improving patient wellbeing.

Radiation Oncology

Hutchings H, Behinaein P, Enofe N, Brue K, **Tam S**, **Chang S**, **Movsas B**, **Poisson L**, **Wang A**, and **Okereke I**. Association of Social Determinants with Patient-Reported Outcomes in Patients with Cancer. *Cancers (Basel)* 2024; 16(5). PMID: 38473374. Full Text

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Patient-reported outcome (PRO) scores have been utilized more frequently, but the relationship of PRO scores to determinants of health and social inequities has not been widely studied. Our goal was to determine the association of PRO scores with social determinants. All patients with a new cancer diagnosis who completed a PRO survey from 2020 to 2022 were included. The PRO survey recorded scores for depression, fatigue, pain interference and physical function. Higher depression, fatigue and pain scores indicated more distress. Higher physical condition scores indicated improved functionality. A total of 1090 patients were included. Married patients had significantly better individual PRO scores for each domain. Patients who were able to use the online portal to complete their survey also had better individual scores. Male patients and non-White patients had worse pain scores than female and White patients, respectively. Patients with prostate cancer had the best scores while patients with head and neck and lung cancer had the worst scores. PRO scores varied by cancer disease site and stage. Social support may act in combination with specific patient/tumor factors to influence PRO scores. These findings present opportunities to address patient support at institutional levels.

Radiation Oncology
Mao W, **Kim J**, and **Chetty IJ**. Association of Internal and External Motion Based on Cine MR Images Acquired During Real-Time Treatment on MRI-Guided Linear Accelerator for Patients With Lung Cancer. *Adv Radiat Oncol* 2024; 9(1):101271. PMID: 38033355. Full Text

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PURPOSE: With the recent clinical implementation of magnetic resonance imaging (MRI)-guided linear accelerators, a large number of real-time planar MR images has been acquired during lung cancer treatment as a standard of care. In this study, associations among lung tumor, diaphragm, and external skin movement were studied based on MR cine imaging during the entire duration of each treatment fraction. METHODS AND MATERIALS: This retrospective study used 181,798 planar MRI frames acquired over 55 treatment/imaging sessions of 13 patients with lung cancer treated on 2 MRI-guided linear accelerators. From each planar MR image frame, in-house software automatically extracted 9 features: the superior-interior (SI) and posterior-anterior (PA) positions of a lung tumor; the area of the lung (Lung_Area); the posterior (Dia_Post), dome/apex (Dia_Dome), and anterior (Dia_Ant) points of a diaphragmatic curve; the diaphragm curve point (Dia_Max); and the chest (Chest) and belly (Belly) skin points experienced the maximum range of motions. Correlation analyses were performed among the 9 features for every session. Lung tumor motion range and standard deviations were calculated based on positions obtained in cine images and compared with motion ranges obtained from 4-dimensional computed tomography images. RESULTS: In the study, 177,009 frames of images were successfully analyzed. For all patients, correlation coefficients were as follows: 0.91 ± 0.10 between any 2 features among Lung_Area, Dia_Post, Dia_Dome, and Dia_Max; 0.82 ± 0.21 between SI and any feature among Lung_Area, Dia_Post, Dia_Dome, and Dia_Max; 0.75 ± 0.24 between SI and Belly. Six of 13 patients were considered large amplitude motion (patients with lung tumor SI motion standard deviation >5 mm). Furthermore, 92,956 frames of images were analyzed for the 6 large-amplitude motion patients. For this set, correlation coefficients were 0.93 ± 0.07 between any 2 features among Lung_Area, Dia_Post, Dia_Dome, and Dia_Max; 0.94 ± 0.06 between SI and any feature among Lung_Area, Dia_Post, Dia_Dome, and Dia_Max; and 0.90 ± 0.09 between SI and Belly. CONCLUSIONS: Both belly and diaphragmatic motions as assessed by cine MRI are highly correlated with large amplitude lung tumor motion in the longitudinal axis.

Research Administration
Montgomery J, Lybbert D, Sana S, El-Zawahry A, **Peabody J**, **Pearce T**, **Adams N**, **Deebajah M**, Dynda D, Babaian K, Crabtree J, Delfino K, McVary K, Robinson K, Rao K, and Alanee S. Urinary bother,

Urinalysis, and Two-Year Efficacy Follow-Up Results of Phase I Trial of Intravesical Bacillus Calmette-Guérin Combined with Intravenous Pembrolizumab in Recurrent or Persistent High-Grade Non-Muscle-Invasive Bladder Cancer after Previous Bacillus Calmette-Guérin Treatment. *Clin Genitourin Cancer* 2024; 22(3):102059. PMID: 38554570. Full Text

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OBJECTIVE: To report urinary bother, urinalysis changes, disease-free survival (DFS), and overall survival (OS) over 2 years for subjects enrolled in a phase I dose-escalation trial (NCT02324582) of intravesical Bacillus Calmette-Guérin (BCG) in combination with systemic pembrolizumab for recurrent or persistent high-grade non-muscle invasive bladder cancer (HGNMIBC). METHODS: Eighteen patients consented to the study. Five were screen failures. Clinical activity was determined using cystoscopy and cytology with a biopsy of suspicious lesions. Urinalysis and International Prostate symptom score were assessed at pre-treatment, Week 10 (during combined BCG and pembrolizumab treatment), and 3 and 6 months from treatment completion. IPSS was analyzed using a mixed-model repeated measures analysis. A Chi-square test was used to compare urinalysis results at each interval. RESULTS: The pathologic disease stage after restaging transurethral resection and before treatment was pTa in 6 (46.2%), CIS in 6 (46.2%), and pT1 in 1 (7.7%). There was no increase in reported urinary bother throughout treatment. Quality of life measurements demonstrated no change in subjective burden. On urinalysis, we did not observe significant differences at 3 months compared to baseline evaluation. At 12 months, the DFS and OS were 69.23% and 92.31%, respectively. At 24 months, the DFS and OS were 38.46% and 92.31%, respectively. CONCLUSIONS: Treatment with BCG combined with intravenous pembrolizumab is not showing increased urinary bother or adverse urinalysis changes. Two-year response data is promising and await confirmation in the phase III study (Keynote 676).

Surgery

Hutchings H, Behinaein P, Enofe N, Brue K, **Tam S**, **Chang S**, **Movsas B**, **Poisson L**, **Wang A**, and **Okereke I**. Association of Social Determinants with Patient-Reported Outcomes in Patients with Cancer. *Cancers (Basel)* 2024; 16(5). PMID: 38473374. Full Text

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Patient-reported outcome (PRO) scores have been utilized more frequently, but the relationship of PRO scores to determinants of health and social inequities has not been widely studied. Our goal was to determine the association of PRO scores with social determinants. All patients with a new cancer diagnosis who completed a PRO survey from 2020 to 2022 were included. The PRO survey recorded scores for depression, fatigue, pain interference and physical function. Higher depression, fatigue and pain scores indicated more distress. Higher physical condition scores indicated improved functionality. A total of 1090 patients were included. Married patients had significantly better individual PRO scores for each domain. Patients who were able to use the online portal to complete their survey also had better individual scores. Male patients and non-White patients had worse pain scores than female and White patients, respectively. Patients with prostate cancer had the best scores while patients with head and neck and lung cancer had the worst scores. PRO scores varied by cancer disease site and stage. Social support may act in combination with specific patient/tumor factors to influence PRO scores. These findings present opportunities to address patient support at institutional levels.

Surgery

Itenberg ER, and **Lozano AM**. Surgical and Interventional Management of Liver Metastasis. *Clin Colon Rectal Surg* 2024; 37(2):80-84. PMID: 38322597. Full Text

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Colorectal cancer is one of the most common cancers diagnosed worldwide. While the incidence of colorectal cancer has been declining since the adoption of screening colonoscopy, the findings of liver metastasis are still found in up to 25% of patients at diagnosis. The management of liver metastasis has evolved over the past two to three decades, and survival rates have improved secondary to improved systemic therapy, surgical options, and local therapies. In this article, we aim to review the available surgical and ablative options for management of colorectal liver metastasis, as well as appropriate imaging and patient selection.

Surgery

Miyake K, **Kim DY**, **Chau LC**, **Trudeau S**, **Kitajima T**, **Wickramaratne N**, **Shimada S**, **Nassar A**, **Yoshida A**, **Abouljoud MS**, and **Nagai S**. Exception Policy Change Increased the Simultaneous Kidney-liver Transplant Probability of Polycystic Disease in the Centers With High Median MELD at Transplantation. *Transplantation* 2024; Epub ahead of print. PMID: 38548699. Full Text

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BACKGROUND: In 2019, Organ Procurement and Transplantation Network/United Network for Organ Sharing changed the exception policy for liver allocation to the median model for end-stage liver disease at transplantation (MMaT). This study evaluated the effects of this change on-waitlist outcomes of simultaneous liver-kidney transplantation (SLKT) for patients with polycystic liver-kidney disease (PLKD). METHODS: Using the Organ Procurement and Transplantation Network/United Network for Organ Sharing registry, 317 patients with PLKD listed for SLKT between January 2016 and December 2021 were evaluated. Waitlist outcomes were compared between prepolicy (Era 1) and postpolicy (Era 2) eras. RESULTS: One-year transplant probability was significantly higher in Era 2 than in Era 1 (55.7% versus 37.9%; P = 0.001), and the positive effect on transplant probability of Era 2 was significant after risk adjustment (adjusted hazard ratio, 1.76; 95% confidence interval, 1.22-2.54; P = 0.002 [ref. Era 1]), whereas waitlist mortality was comparable. Transplant centers were separated into the high and low MMaT groups with a score of 29 (median MMaT) and transplant probability in each group between eras was compared. In the high MMaT transplant centers, the 1-y transplant probability was significantly higher in Era 2 (27.5% versus 52.4%; P = 0.003). The positive effect remained significant in the high MMaT center group (adjusted hazard ratio, 2.79; 95% confidence interval, 1.43-5.46; P = 0.003 [ref. Era 1]) but not in the low MMaT center group. Although there was a difference between center groups in Era 1 (P = 0.006), it became comparable in Era 2 (P = 0.54). CONCLUSIONS: The new policy increased 1-y SLKT probability in patients with PKLD and successfully reduced the disparities based on center location.

Surgery

Parsons RF, Lentine KL, Doshi M, Dunn TB, Forbes R, Fridell JA, **Jesse MT**, Pavlakis M, Sawinski D, Singh N, Axelrod DA, and Cooper M. Generating Strategies for a National Comeback in Pancreas Transplantation: A Delphi Survey and U.S. Conference Report. *Am J Transplant* 2024; Epub ahead of print. PMID: 38499089. Full Text

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In the United States, potential transplant candidates with insulin-dependent diabetes mellitus are inconsistently offered pancreas transplantation, contributing to a dramatic decline in pancreas allograft utilization over the past two decades. The American Society of Transplantation (AST) organized a workshop to identify barriers inhibiting pancreas transplantation and to develop strategies for a national comeback. The two-day workshop focused on four main topics: (1) referral/candidate selection, (2) organ recovery/utilization, (3) program performance/patient outcomes, (4) enhanced education/research. Topics were explored through expert presentations, patient testimonials, breakout sessions, and strategic planning, including identification of tasks for immediate focus. Additionally, a modified Delphi survey was conducted among workshop members to develop and rate the importance of barriers, and the impact and feasibility of workgroup-identified improvement strategies. The panelists identified 16 barriers to progress and 44 strategies for consideration. The steps for a national comeback in pancreas transplantation involve greater emphasis on efficient referral and candidate selection, better donor pancreas utilization practices, eliminating financial barriers to procurement and transplant, improving collaboration between transplant and diabetes societies and professionals, and increasing focus on pancreas transplantation training, education, and research. Partnership between national societies, patient advocacy groups, and professionals will be essential to realizing this critical agenda.

Surgery

Wojack CA, **Smith MC**, and Casida J. Acute Care Nurse Practitioner: Collaboration in a Postpandemic World. *AACN Adv Crit Care* 2024; 35(1):49-54. PMID: 38457621. Full Text

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Meghan C. Smith is Nurse Practitioner, Department of Surgery, Henry Ford Health, Detroit, Michigan.
Jesus Casida is Endowed Professor and Executive Director, Eleanor Mann School of Nursing, University of Arkansas, Fayetteville, Arkansas.

Urology

Barayan GA, **Majdalany S**, **Butaney M**, **Dalela D**, **Peabody JO**, **Abdollah F**, **Menon M**, and **Jeong W**. Intermediate-Term Oncological Outcome Assessment for Robotic Assisted Radical Prostatectomy Comparing Retzius Sparing to Standard Approach in a Randomized Control Cohort. *J Endourol* 2024; Epub ahead of print. PMID: 38429913. Full Text

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INTRODUCTION: Retzius sparing prostatectomy was promoted with the early continence result. The long-term oncological outcome is still unknown. In this study, we aimed to compare the Intermediate-term oncologic outcomes of these two approaches in patient's cohort who was treated as part of a randomized controlled trial. METHODS: A total of 120 patients were previously randomized equally to receive retzius sparing (RS-RARP) versus standard robotic assisted laparoscopic radical prostatectomy (S-RARP) between January 2015 to April 2016. Baseline, surgical, and pathological characteristics as well as oncologic outcomes were assessed. The analysis was done based on the treatment received. RESULT: Sixty-three patients underwent S-RARP while 57 patients underwent RS-RARP. There was no statistically significant difference in the baseline nor surgical characteristics. The median follow up was 71.24 (IQR 59.75 - 75.75). There were more pathological T3 diseases in RS-RARP. There was no significant difference in the positive margin status nor the biochemical recurrence rate among both groups. After S-RARP and RS-RARP, 6 and 10 patients had biochemical recurrence and the 5-years biochemical recurrence free survival were 91% and 85%, respectively. (p= 0.21) Conclusion: In this cohort, there was no difference in biochemical recurrence in the patients who received either technique. Further mutli-institutional studies with a larger sample size and longer follow up are required.

Urology
Becker REN, Dibianco JM, Higgins A, Konheim J, Kleer E, **Leavitt DA**, King A, **Kachroo N**, **Majdalany S**, Gandham D, Fernandez Moncaleano G, Conrado B, Shoemaker E, Daignault S, Dauw CA, and Ghani KR. Daily Ecological Momentary Assessments of Pain and Ability to Work after Ureteroscopy and Stenting. *J Endourol* 2024; Epub ahead of print. PMID: 38545762. Full Text

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Introduction Ureteral stents can cause significant patient discomfort, yet the temporal dynamics and impact on activities remain poorly characterized. We employed an automated tool to collect daily ecological momentary assessments (EMA) regarding pain and ability to work following ureteroscopy with stenting. Our aim was to assess feasability, and better characterize the postoperative patient experience. Methods As an exploratory endpoint within an ongoing clinical trial, patients undergoing ureteroscopy with stenting were asked to complete daily EMAs for 10 days postoperatively, or until the stent was removed. Questionnaires were distributed via text message and included a pain scale (0-10) and a single item from the validated PROMIS Ability to Participate in Social Roles and Activities instrument, as well as days

missed from work or school. Results Among the first 65 trial participants, 59 completed at least 1 EMA (overall response rate 91%). Response rates were >85% for each timepoint through POD10. Median respondent age was 58 years (IQR 50-67), 56% were female. Stones were 54% renal and 46% ureteric, with median diameter 9 mm (IQR 7-10). Median stent dwell time was 7 days (IQR 6-8). Pain scores were highest on POD1 (median score 4) and declined with each subsequent day, reaching median score 2 on POD5. 63% of patients on POD1 reported they had trouble performing their usual work at least sometimes, but by POD5 this was <50% of patients. Patients who work or attend school reported a median of 1 day missed (IQR 0-2). Conclusions An automated daily EMA system for capturing patient-reported outcomes was demonstrated to be feasible with sustained excellent engagement. Patients with stents reported the worst pain and interference with work on POD1 with steady improvements thereafter, and by POD5 the majority of patients had minimal pain or trouble performing their usual work.

Urology

Corsi NJ, **Stephens A**, **Finati M**, Malchow T, Morrison C, **Davis M**, **Hares K**, **Corsi MP**, **Arora S**, **Chiarelli G**, **Cirulli GO**, Autorino R, Sood A, **Rogers C**, and **Abdollah F**. Testing the external validity of the POUT III trial (adjuvant platnium-based chemotherapy in upper tract urothelial carcinoma) in a North American cohort. *Urol Oncol* 2024; Epub ahead of print. PMID: 38522975. Full Text

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OBJECTIVE: The European POUT III randomized controlled trial provided level-one evidence that adjuvant platinum-based chemotherapy is the standard of care following nephroureterectomy (RNU) for locally invasive or node-positive upper tract urothelial carcinoma. We aim to assess this European randomized controlled trial's generalizability (external validity) to a North American cohort, using a nationwide database. MATERIALS AND METHODS: To compare trial patients with those seen in real-world practice, we simulated the trial inclusion criteria using data from the National Cancer Database (NCDB). We identified patients with histologically confirmed transitional cell carcinoma who underwent RNU. The available demographic characteristics of the NCDB cohort were compared with the POUT III trial cohort using Chi-squared test. RESULTS: The NCDB cohort (n = 3,380) had a significantly higher proportion of older patients (age ≥ 80: 23.5% vs. 5%), and more males (68% vs. 56.2%) than the POUT cohort (Table 1, both $p < 0.001$). Additionally, the rate of advanced nodal disease was higher in the NCDB (N1 9.6%, N2 9.3%) than in the POUT (N1 6%, N2 3%) cohort ($p < 0.001$). A more extensive lymph node dissection was performed in NCDB vs. POUT patients (node≥10 10.9% vs. 3%, $p < 0.001$). Sensitivity analysis removing all subjects with a Charlson Comorbidity Index > 0 did not change the significance of any results. CONCLUSIONS: While the primary disease stage was similar, the rate of advanced nodal disease was significantly higher in NCDB, which might be explained partially by the more extensive lymph node dissection performed in the latter. These differences warrant caution when applying the POUT III findings to North American patients.

Urology
Jhaveri JK, Dahmen A, Lazarovich A, Nusbaum D, Trinh QD, **Gupta N**, and Agarwal PK. Necrotizing granulomatous epididymo-orchitis post intravesical BCG administration after brachytherapy for prostate cancer. *Urol Case Rep* 2024; 54:102694. PMID: 38516176. Full Text

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Urothelial carcinoma of the bladder remains a challenging disease to treat. Intravesical instillation of BCG has demonstrated tremendous efficacy in preventing recurrence. BCG related necrotizing granulomatous epididymo-orchitis is rare and has not been previously linked to brachytherapy for adenocarcinoma of the prostate. We hypothesize that prior brachytherapy has a deleterious effect on the verumontanum that can result in retrograde transmission of BCG particles leading to granulomatous epididymo-orchitis. This is the first case report of necrotizing granulomatous epididymo-orchitis related to BCG in a patient status post brachytherapy for adenocarcinoma of the prostate.

Urology
Kunitsky KD, **Almajedi M**, Snajdar E, Adams P, and **Nelson R**. Single-Port Robotic-Assisted Excision of the Urachal Remnant in an Adult Female: A Case Report. *Cureus* 2024; 16(1):e53235. PMID: 38425617. Full Text

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Urachal anomalies and their associated disease processes are quite rare in pediatric populations and even rarer in adults. Although often asymptomatic, patients with symptoms can be treated with a combination of surveillance, antibiotics, and sometimes surgical resection. In this case, we describe our experience using the single-port robotic approach for the excision of a symptomatic urachal remnant. The patient presented with a chief complaint of urinary frequency, dysuria, intermittent hematuria, and right flank pain. A CT scan of the abdomen and pelvis revealed a bladder wall thickening at the dome of the bladder measuring 2.6 x 3.6 x 1.5 cm with concerns for adenocarcinoma. The patient subsequently underwent a biopsy, which was benign. The patient's symptoms persisted, and she elected to undergo surgical resection. Postoperatively, her symptoms resolved, and she was satisfied with her treatment outcome. This case exemplifies the feasibility of the single-port robotic approach to urachal remnant excision, with further applicability to simple transabdominal robotic bladder surgery.

Urology
Montgomery J, Lybbert D, Sana S, El-Zawahry A, **Peabody J**, **Pearce T**, **Adams N**, **Deebajah M**, Dynda D, Babaian K, Crabtree J, Delfino K, McVary K, Robinson K, Rao K, and Alanee S. Urinary bother, Urinalysis, and Two-Year Efficacy Follow-Up Results of Phase I Trial of Intravesical Bacillus Calmette-Guérin Combined with Intravenous Pembrolizumab in Recurrent or Persistent High-Grade Non-Muscle-Invasive Bladder Cancer after Previous Bacillus Calmette-Guérin Treatment. *Clin Genitourin Cancer* 2024; 22(3):102059. PMID: 38554570. Full Text

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OBJECTIVE: To report urinary bother, urinalysis changes, disease-free survival (DFS), and overall survival (OS) over 2 years for subjects enrolled in a phase I dose-escalation trial (NCT02324582) of

intravesical Bacillus Calmette-Guérin (BCG) in combination with systemic pembrolizumab for recurrent or persistent high-grade non-muscle invasive bladder cancer (HGNMIBC). METHODS: Eighteen patients consented to the study. Five were screen failures. Clinical activity was determined using cystoscopy and cytology with a biopsy of suspicious lesions. Urinalysis and International Prostate symptom score were assessed at pre-treatment, Week 10 (during combined BCG and pembrolizumab treatment), and 3 and 6 months from treatment completion. IPSS was analyzed using a mixed-model repeated measures analysis. A Chi-square test was used to compare urinalysis results at each interval. RESULTS: The pathologic disease stage after restaging transurethral resection and before treatment was pTa in 6 (46.2%), CIS in 6 (46.2%), and pT1 in 1 (7.7%). There was no increase in reported urinary bother throughout treatment. Quality of life measurements demonstrated no change in subjective burden. On urinalysis, we did not observe significant differences at 3 months compared to baseline evaluation. At 12 months, the DFS and OS were 69.23% and 92.31%, respectively. At 24 months, the DFS and OS were 38.46% and 92.31%, respectively. CONCLUSIONS: Treatment with BCG combined with intravenous pembrolizumab is not showing increased urinary bother or adverse urinalysis changes. Two-year response data is promising and await confirmation in the phase III study (Keynote 676).

Urology

Qian Z, Alexander J, Daniels D, **Abdollah F**, Cole AP, Iyer HS, and Trinh QD. Racial differences in postpandemic trends in prostate-specific antigen screening. *JNCI Cancer Spectr* 2024; 8(2). PMID: 38546486. Full Text

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Our study investigates the trends in prostate cancer screening amid the COVID-19 pandemic, particularly focusing on racial disparities between Black and White men. Utilizing data from the Behavioral Risk Factor Surveillance System from 2018, 2020, and 2022, we analyzed prostate-specific antigen screening rates in men aged 45-75 years. Our findings reveal initial declines in screening rates for both groups during the pandemic, with subsequent recovery; however, the pace of rebound differed statistically significantly between races. Whereas White men showed a notable increase in screening rates postpandemic, Black men's rates recovered more slowly. This disparity underscores the impact of socioeconomic factors, health-care access, and possibly systemic biases affecting health-care delivery. Our study highlights the need for targeted interventions to address these inequalities and ensure equitable access to prostate cancer preventive care in the aftermath of COVID-19.

Behavioral Health Services/Psychiatry/Neuropsychology

Jan A, **Morisetty S**, and **Boore-Clor L**. Reimagining Management of Behavioral Disturbances in Patients with End-Stage Parkinson's Disease in Outpatient Community Hospice Settings. *Am J Geriatr Psychiatry* 2024; 32(4):S69-S70. Full Text

Introduction: Parkinson's disease (PD) is the fastest growing cause of death and disability among neurologic disorders. As the global population ages and individuals with neurodegenerative disorders survive longer, demand for neurologic care and other healthcare resources will continue to rise. Parkinson's disease and related disorders (PDRD) are the second most common neurodegenerative disease and a leading cause of death. However, patients with PDRD receive less end-of-life care (hospice) than other illnesses, including other neurologic illnesses. Health care resources are disproportionately expended as the end of life approaches. In the United States (US), care for 6% of Medicare beneficiaries who die each year accounts for nearly 30% of Medicare expenditures. PD is associated with high rates of health care utilization compared with matched controls. How health care resources are used at the end of life in PD and other neurodegenerative movement disorders is unknown. Behavioral disturbances complicate clinical management of individuals with PD in outpatient hospice settings, however, outpatient hospice physicians often feel uncomfortable prescribing medications to manage behavioral disturbances of PD patients given (1) unfamiliarity with antipsychotic medications (2) sensitivity of PD patients to centrally acting agents. After conducting our own literature and textbook reviews, we found there exists little consensus and large gaps in how to systematically approach clinical management of behavioral disturbances in patients with end-stage PD. In our poster, we will share themes we observed while conducting our literature review. We also propose next steps for a pilot project to help develop a clinical algorithm for management of behavioral disturbances in patients with end-stage Parkinson's disease in community hospice settings. Methods: We employed a comprehensive search strategy using three main databases: PubMed, Clinical Key, and Cochrane. The following search parameters were used in PubMed: palliative + hospice + parkinson's + 1 year; palliative + hospice + parkinson's + 5 years; palliative + hospice + parkinson's + 10 years; palliative + hospice + parkinson's (with no year filter). A separate search was conducted using the keyword "neuropalliative care," filtered specifically for systematic reviews. In Clinical Key, notable references were retrieved from "Parkinsonism and Other Movement Disorders" and "Palliative Care to Neurological and Neurosurgical Patients". No relevant results were identified in Cochrane using our search criteria. Inclusion and Exclusion Criteria: Studies, reviews, and book chapters were eligible for inclusion if they were written in English and focused on palliative or hospice care for Parkinson's disease patients, specifically addressing behavioral disturbances. The types of literature eligible for inclusion were meta-analyses, systematic reviews, randomized controlled trials (RCTs), and relevant textbook chapters. Papers or chapters that did not discuss behavioral disturbances, solely focused on other neurodegenerative diseases without relevance to Parkinson's disease, focused on inpatient treatment, or lacked depth on the subject were excluded from our review. Screening and Selection: Titles and abstracts of all retrieved records from the searches were initially screened for potential relevance. Full texts of potentially eligible studies were obtained and assessed for eligibility based on the inclusion and exclusion criteria. Any discrepancies regarding study eligibility were resolved through discussion and consensus. Data Extraction: From each included study or book chapter, we extracted data on the study design, population characteristics, interventions, outcomes, and key findings related to the management of behavioral disturbances in end-stage Parkinson's disease. Findings were synthesized and categorized based on themes and gaps identified. Data analysis: Major themes were identified from our literature review and summarized to identify gaps in knowledge and guide our proposal f next steps for research. Results: The comprehensive search yielded a total of 195 articles across all search parameters and databases. The distribution of findings per database is as follows: 1. Pubmed Using the search term "palliative + hospice + parkinson's + 1 year," we retrieved 8 hits. Extending the search to "palliative + hospice + parkinson's + 5 years" resulted in 43 hits. "palliative + hospice + parkinson's + 10 years" produced 66 hits. Using "palliative + hospice + parkinson's" with no year filter gave us 78 hits. 2. Clinical Key Relevant references were obtained from two key sources: "Parkinsonism and Other Movement Disorders" and "Palliative Care to Neurological and Neurosurgical Patients." 3.Cochrane Our search on Cochrane with relevant parameters yielded no results. After the removal of duplicates and initial title and abstract screening, 153 articles remained for full-text evaluation.

Of these, 125 articles were excluded as they did not meet our inclusion criteria, leaving a total of 28 articles for in-depth review. Based upon our analysis of the 28 articles remaining, we identified the following themes in existing literature: 1. Underutilization of Hospice Care: Many patients with Parkinson's Disease and Related Disorders (PDRD) receive less end-of-life care compared to patients with other illnesses, even within the neurologic spectrum. 2. Resource Allocation: Studies highlighted that healthcare resources, especially in the US, are disproportionately spent as the end of life (EOL) approaches. Proper EOL care maximization has shown to lead to a 50% reduction in admissions and a 35% reduction in emergency room visits [https://www.capc.org/about/palliative-care/]. This is also evident in PD patients, who see high rates of healthcare utilization compared to matched controls. 3. Challenges in Behavioral Disturbances Management: Behavioral disturbances in Parkinson's patients in outpatient hospice settings pose a significant challenge for care providers. There exists a hesitancy in prescribing medications due to unfamiliarity with antipsychotic medications and concerns over the sensitivity of PD patients to centrally acting agents. Conclusions: Our review underscored a significant gap in the literature regarding a consensus or systematic approach to managing behavioral disturbances in end-stage Parkinson's disease patients, especially in the outpatient hospice setting. The absence of well-established clinical guidelines further complicates the management of these patients.

Behavioral Health Services/Psychiatry/Neuropsychology

Reffi A, **Kalmbach D**, **Seymour G**, **Solway M**, **Moore D**, **Mahr G**, and **Drake C**. Early identification of patients most vulnerable to acute insomnia after trauma. *Sleep Med* 2024; 115:169. Full Text

Introduction: Acute sleep disturbances are a common, modifiable consequence of trauma that, if left untreated, increase risk of PTSD by nearly two-fold. This suggests acute sleep disturbances after trauma are an important contributor to the etiology of PTSD that could be targeted early to prevent the disorder. Yet, effective strategies to prevent PTSD cannot currently be implemented because we cannot identify who is most at risk of acute sleep disturbances after trauma, thus obstructing the ability to identify high-risk groups in need of early intervention. This study will test sleep reactivity – a trait predisposition to experience sleep disturbances after stress – as a predictor of posttraumatic sleep disturbances within one month following trauma exposure. Materials and Methods: We recruited patients (N = 88, Mage = 39.53 ± 14.31) admitted to Henry Ford Hospital's intensive care unit in Detroit, Michigan for traumatic injury (e.g., gunshot wound). While in the hospital, patients reported their pre-trauma sleep reactivity (Ford Insomnia Response to Stress Test; FIRST) and insomnia symptoms from the past two weeks (Insomnia Severity Index; ISI). Patients then completed the ISI again one month later (n = 48). We tested high sleep reactivity (FIRST ≥ 21) as a prospective predictor of clinically significant posttraumatic sleep disturbances (ISI ≥ 10). Results: Patients were mostly black men (67%), and nearly half reported an annual income ≤ $20,000 (47.7%). Motor vehicle collisions were the most common trauma that precipitated patients' hospital admission (42%), followed by assaults with a weapon (30.7%). While adjusting for age and pre-trauma sleep disturbance, high sleep reactivity predicted increased odds of sleep disturbances one month after trauma (b = 2.08, SE =.98, p =.033, OR = 8.01, CI = 1.19 – 54.15). Conclusions: Individuals with high sleep reactivity are at increased susceptibility of clinically significant sleep disturbances after trauma. The 9-item FIRST is a brief and clinically useful indicator that offers providers the ability to predict the onset of acute sleep disturbances after trauma, which are novel targets for early intervention. This might enable the early identification of potentially vulnerable individuals who might develop PTSD, toward whom sleep-focused preventive efforts can be targeted. Acknowledgements: We are grateful to Henry Ford Hospital's Dept. of Surgery, Division of Acute Care Surgery for supporting our research, and of course, we thank the patients who enrolled in our study during such a stressful time.

Cardiology/Cardiovascular Research

Abu-Much A, Bonnet G, Zhao D, Wollmuth JR, Thompson JB, Moses JW, Redfors B, Bharadwaj AS, Lansky AJ, Falah B, Cohen DJ, Truesdell AG, and **O'Neill WW**. 100.58 Intravascular Imaging or Angiographic Guidance in Patients Undergoing Impella-Supported High-Risk Percutaneous Coronary Intervention. *JACC Cardiovasc Interv* 2024; 17(4):S16. Full Text

Background: Recent randomized trials examining intravascular imaging in complex percutaneous coronary interventions (PCI) have been conflicting. Notably, these trials were focused on anatomic complexity rather than patient (pt.) risk and thus did not include patients who required mechanical

circulatory support during PCI. Therefore, we sought to explore outcomes associated with using intravascular imaging during high-risk PCI (HR-PCI) procedures supported by Impella devices. Methods: We analyzed data from the PROTECT III trial (NCT04136392); a multicenter, observational study of Impella-supported HR-PCI that enrolled patients at 46 U.S. centers from March 2017 to March 2020. Pts were categorized according to the use of intravascular imaging. The primary outcome was the rate of adjudicated major adverse cardiac and cerebrovascular events (MACCE: all-cause death, myocardial infarction, stroke/transient ischemic attack, and revascularization) at 90 d., as well as 1 yr. mortality. Multivariable Cox proportional hazard analysis was conducted with adjustment based on a propensity score (PS). Results: Of 1237 pts enrolled in the cVAD PROTECT III study, 958 had data on intravascular imaging, 477 (50%) of whom underwent intravascular imaging-guided PCI. Baseline characteristics and study outcomes are summarized in Table. After PS adjustment, use of intravascular imaging was not associated with significant reductions in the risk of 90-day MACCE (Adj. HR=0.68 [95% CI 0.44, 1.04], p=0.08) or 1-year mortality (Adj. HR=0.91 [95% CI 0.64, 1.28], p=0.58). Conclusion: Although underpowered to detect statistically significant differences, our study of pts undergoing Impella-supported HRPCI exhibits that the use of intravascular imaging was associated with a trend toward lower 90 d. MACCE, but no notable change in 1 yr. all-cause mortality. [Formula presented]

Cardiology/Cardiovascular Research

Al-Abdouh A, **Jabri A**, Alameh A, Mhanna M, Rmilah AA, **Villablanca P**, and **Alqarqaz M**. 300.1 A Meta-Analysis of Endovascular Therapy for Patients With Large Core Ischemic Stroke. *JACC Cardiovasc Interv* 2024; 17(4):S35. Full Text

Introduction: Endovascular therapy (EVT) is a recommended treatment for stroke patients with large vessel occlusion and an Alberta Stroke Program Early Computed Tomography Score (ASPECTS) ≥6. However, the utility of EVT in patients with large core ischemic stroke has not been well established. Methods: This meta-analysis assesses the efficacy and safety of EVT compared to medical management (MM) in patients with stroke and large ischemic core. The primary endpoint was the mean modified Rankin scale score at 90 days follow-up. We used Mantel-Haenszel method with Paule-Mandel estimator of tau2 and Hartung-Knapp-Sidik-Jonkman adjustment (due to the small number of the included trials) to calculate the standardized mean difference (SMD) for continuous outcomes and the risk ratio (RR) for other outcomes. Results: Five RCTs with a total of 1,547 patients were included in our analysis. EVT as compared with MM was associated with lower mean modified Rankin scale score at 90 days (SMD -0.32; 95% CI -0.46 to -0.18) [Figure]. There was no statistically significant difference in the risk of symptomatic intracranial hemorrhage (RR: 1.73; 95%CI: 0.95 to 3.13] and 90-day mortality (RR: 0.92; 95%CI: 0.77 to 1.11) between the two groups. Conclusion: Our meta-analysis suggests that EVT compared to MM may lead to improved outcomes in stroke patients with large core ischemia. [Formula presented]

Cardiology/Cardiovascular Research

Al-Abdouh A, Sukhon F, **Jabri A**, Alameh A, Khader S, **Villablanca P**, and **Alqarqaz M**. 100.17 Liberal Versus Conservative Transfusion Strategy for Patients With Acute Myocardial Infarction and Anemia: A Systematic Review and Meta-Analysis. *JACC Cardiovasc Interv* 2024; 17(4):S5. Full Text

Background: A goal hemoglobin (Hb) level of 7 or 8 d/dL has been standard of care across the medical field, below which blood transfusion is necessitated. The question of whether patients presenting with acute myocardial infarction (MI) may benefit from a more liberal transfusion strategy has been a topic of debate. We performed a meta-analysis of all trials that have aimed to answer this clinical question. Methods: We conducted a systematic review and meta-analysis including all available RCTs that compared a liberal versus a restrictive transfusion strategy for patient with acute MI presenting with anemia. The primary outcomes were recurrent MI and death or MI. Secondary outcomes included risk of stroke, revascularization, heart failure, and death from any cause. Given the small number of trials, we ran the analysis using the Paul-Mendele method with Hartung Knapp adjustment. Results: Four RCTs were included comprising a total of 2155 patients treated with a liberal transfusion strategy vs 2170 patients treated with a conservative transfusion strategy. Compared with a conservative transfusion strategy, liberal transfusion was not significantly associated with a reduction in MI (relative risk [RR] 0.85; 95% CI 0.72 - 1.02, p = 0.07) or death or MI (relative risk [RR] 0.88; 95% CI 0.45 - 1.71, p = 0.57). It also showed no difference in death from any cause (relative risk [RR] 0.82; 95% CI 0.25 - 2.68, p = 0.63),

stroke (relative risk [RR] 0.89; 95% CI 0.48 - 1.64, p = 0.50), revascularization (relative risk [RR] 0.0.93; 95% CI 0.48 - 1.80, p = 0.68), or heart failure (relative risk [RR] 0.1.14; 95% CI 0.04 - 28.84, p = 0.88). Conclusion: Our meta-analysis further solidifies current medical practices of restricting transfusion of patients with acute MI to those with a Hb level of 7 or 8 g/dL, as more liberal transfusion strategies did not translate into improved clinical outcomes. [Formula presented]

Cardiology/Cardiovascular Research
Almajed MR, **Almajed A**, **El-khatib L**, **Modi K**, **Zweig B**, and **Rao A**. LOEFFLER ENDOCARDITIS PRESENTING AS RECURRENT CARDIOEMBOLIC STROKES. *J Am Coll Cardiol* 2024; 83(13):2990. Full Text

Background Loeffler endocarditis (LE) describes endomyocardial disease due to eosinophilic infiltration in hypereosinophilic syndrome (HES). Rarely, valvular disease occurs, in some cases acting as a nidus for thromboembolism. Case A 77-year-old woman presented with acute right-sided visual loss. History was notable for asthma, rhinosinusitis, and a cryptogenic stroke four months earlier. Laboratory workup showed eosinophilic leukocytosis and elevated inflammatory markers. Infectious workup was unremarkable. Head imaging demonstrated multiple strokes of variable age and distributions, concerning for cardioembolic stroke. Transesophageal echocardiography revealed mitral valve disease consistent with HES causing LE. [Formula presented] Decision-making Our patient met diagnostic criteria for idiopathic HES with persistent eosinophilia and organ involvement. She was managed with steroids and anticoagulation with warfarin to reduce the risk of recurrent stroke. Definitive management in LE with mitral valve disease is surgical valve replacement, biological valves are preferred due to less valve thrombosis. Our patient was deemed not a surgical candidate, she was planned for future reconsideration if recurrent strokes occur. Six months later, she had no further strokes and echocardiography showed stable mitral valve disease. Conclusion LE is managed with eosinophilia suppression, therapeutic anticoagulation for thromboembolism management, and surgical valve replacement for valvular disease.

Cardiology/Cardiovascular Research
Almajed MR, **Almajed A**, **Khan N**, **Major J**, and **Ananthasubramaniam K**. INHERITED PREDILECTION TO SPONTANEOUS CORONARY ARTERY DISSECTION: A CASE ASSOCIATED WITH ALPK3 MUTATION. *J Am Coll Cardiol* 2024; 83(13):3387. Full Text

Background Spontaneous coronary artery dissection (SCAD) is a rare cause of ACS that involves spontaneous separation of the coronary artery walls that is not traumatic or iatrogenic. SCAD results in an intramural hematoma that obstructs the arterial lumen causing myocardial ischemia and infarction. Etiology is multifactorial involving an arteriopathy that is compromised by a pathophysiologic stressor. Young women are more commonly affected. Associations have been drawn with fibromuscular dysplasia, connective tissue disorders, and genetic mutations such as ALPK3. Case A 51-year-old woman with hypertension presented with typical angina. She had no history of CAD, and a Coronary CTA reported a coronary calcium score of zero. HsTnI was 897 ng/L and BNP was 37 pg/mL. Electrocardiogram showed lateral lead ST-segment elevation. Emergent invasive coronary angiography for STEMI demonstrated spontaneous coronary artery dissection of the right posterior descending artery with distal embolization. The coronary arteries were notably tortuous and without atherosclerosis. Echocardiogram revealed an LV EF of 65% with mid-distal apical wall hypokinesis. Decision-making Our was diagnosed with STEMI secondary to SCAD. Coronary artery intervention was not performed. She was medically managed with aspirin, statin, beta-blocker, and angiotensin-converting-enzyme inhibitor therapy with symptom resolution. Further SCAD evaluation was performed with CTA to evaluate for fibromuscular dysplasia which was negative for an arteriopathy. A genetic analysis revealed a significant mutation in the ALPK3 gene which in recent studies has been associated with SCAD. Conclusion We describe a case of SCAD associated with an ALPK3 genetic mutation in the absence of other associations. This highlights the importance of including genetic analysis in the evaluation of patients presenting with SCAD for patients with SCAD to further our understanding of this condition and identify patients who could benefit from monitoring and medical management. Further studies are necessary to assess whether routine genetic screening and vascular imaging of first-degree relatives in gene positive patients is beneficial.

Cardiology/Cardiovascular Research

Almajed MR, **Almajed A**, **Viacava RAC**, **Antishin S**, **Saleem A**, **Wexler B**, and **Hudson MP**. COLLISION CARDIOMYOPATHY: BLUNT CARDIAC INJURY IN THE SETTING OF A MOTOR VEHICLE ACCIDENT. *J Am Coll Cardiol* 2024; 83(13):3233. Full Text

Background Blunt cardiac injury (BCI) encompasses a spectrum of myocardial disease secondary to blunt thoracic trauma (BTT). Patients develop arrhythmias, valvular injury, chamber rupture, and myocardial infarction. BCI can be asymptomatic or present as chest pain, dyspnea, or sudden death. Electrocardiogram is the most sensitive initial testing modality for BCI. Abnormal findings include ectopic beats, conduction defects, atrial fibrillation, and ventricular fibrillation. Further testing including cardiac biomarkers and echocardiography are recommended in patients with an abnormal initial workup. Case A 62-year-old man with hypertension presented after being struck by a vehicle while riding his bicycle. Prior to this, he performed a labor-intensive job and had no symptoms. During the accident, he was ejected off his bicycle causing him to land on the ground with impact to his anterior chest. Trauma evaluation for injuries was notable for lumbar midline and paraspinal back tenderness without other overt signs of trauma. Imaging revealed an acute lumbar spine fracture that did not require surgical intervention. EKG showed a NSR with frequent ectopic ventricular beats; telemetry monitoring revealed a high ectopic burden. Cardiac biomarkers were abnormal with a hsTnI peak of 28 ng/L and high BNP of 178 pg/mL. Echocardiogram was significant for an LV EF of 40%. Decision-making Our patient was found to have cardiac dysfunction in the setting of BTT without overt signs or symptoms of heart failure. His constellation of ventricular ectopy and a reduced LV EF were concerning for BCI. Ischemic evaluation with a Coronary CTA showed minimal non-obstructive CAD, thereby ruling out ischemia. Medical management for HFrEF with GDMT including a beta-blocker resulted in a significant decrease in ventricular ectopy. He was discharged with plans for ambulatory cardiac monitoring and Cardiac MRI for further cardiomyopathy evaluation. Conclusion BCI is a clinical diagnosis made in patients with newly identified cardiac dysfunction in the setting of BTT. Since no diagnostic criteria exists, high clinical suspicion and extensive workup is necessary in this population to exclude alternative etiologies.

Cardiology/Cardiovascular Research

Almajed MR, **Chao S**, **Rothstein-Costris A**, **Patton J**, and **Rao A**. INVADING THE VENTRICLE: MASSIVE RIGHT VENTRICULAR METASTASIS FROM RENAL CELL CARCINOMA. *J Am Coll Cardiol* 2024; 83(13):3512. Full Text

Background Cardiac tumors are rare, the majority of which are secondary metastatic tumors rather than primary cardiac tumors. Cardiac metastases confer a poor prognosis through mass-effect on vital cardiac structures and chambers. Case A 63-year-old woman with clear-cell renal cell carcinoma (RCC) treated with immunotherapy underwent cardiac risk stratification prior to a spinal debulking surgery. She had extensive tumor involvement of the renal vein and inferior vena cava with metastases to the lungs and spine. EKG showed a new RBBB. Echocardiogram was subsequently obtained and revealed significant right ventricular dysfunction with a homogenous hyperechoic echodensity in the mid-apical RV. Chest CT showed a 7 x 3 x 5 cm mass in the RV extending from the tricuspid valve to the apex. Cardiac MRI defined this mass as characteristic of cardiac metastasis with foci of tumor thrombi. [Formula presented] Decision-making Our patient's large metastatic tumor to the RV resulting in cardiac dysfunction necessitated urgent treatment. Evaluation by cardiac surgery deemed the tumor unresectable and she was deemed to have prohibitive risk to undergo surgery for her spinal metastases. Despite several lines of immunotherapy, no curative treatments available and she was recommended a palliative approach which she opted for. Conclusion Cardiac metastases confer a poor prognosis. Curative treatment is typically dependent on systemic therapy with chemotherapy and immunotherapy as surgical resection is often not possible.

Cardiology/Cardiovascular Research

Almajed MR, **Khan N**, **Heil H**, **Wexler B**, **Antishin S**, **Saleem A**, **Mohammed M**, and **Hudson MP**. TICKING TIME BOMB: CORONARY ARTERY ANEURYSM THROMBOSIS IN A PATIENT WITH MARFAN SYNDROME. *J Am Coll Cardiol* 2024; 83(13):2720. Full Text

Background Coronary artery aneurysm (CAA) in adults is associated with Marfan syndrome (MFS), connective tissue disorders, and vasculitides. CAA are at risk for thrombosis which obstructs coronary flow resulting in myocardial infarction. Case A 56-year-old man with MFS and prior aortic-root replacement presented with several hours of typical angina. Workup revealed a hsTnI elevation to 16211 ng/L and inferior lead T-wave inversions. He was medically managed for ACS. Invasive coronary angiography showed diffuse severe aneurysmal disease involving all coronary arteries; the distal-RCA was poorly visualized with contrast pooling in the aneurysmal mid-RCA, suggestive of aneurysm thrombosis causing coronary occlusion. No intervention was performed. Decision-making Our patient's extensive CAA predisposed him to RCA aneurymsla thrombosis, resulting in coronary occlusion. Coronary CTA confirmed CAA up to 2.3 cm in the distal RCA with a thrombosed fusiform aneurysm. Literature on revascularization in such cases is limited. Since our patient's symptoms resolved without intervention, he was managed for NSTEMI and maintained on therapeutic anticoagulation with a Vitamin K Antagonist to reduce the risk of coronary artery thrombosis. [Formula presented] Conclusion CAA is a lesser-known complication of MFS. It confers high morbidity and mortality due to the risk of aneurysm thrombosis. Dedicated imaging to screen for and monitor CAA in this patient population could be useful to prevent disease progression.

Cardiology/Cardiovascular Research
Almajed MR, **Mittal A**, **Ama S**, **Muhammad N**, and **Michaels AT**. SPECTRUM OF SYNTHETASE SHORTAGE: FAMILIAL CARDIOMYOPATHY DUE TO TMEM70 ATP SYNTHASE DEFICIENCY. *J Am Coll Cardiol* 2024; 83(13):3205. Full Text

Background Mitochondrial encephalocardiomyopathy involves mitochondrial degeneration due to genetic mutations in the TMEM70 gene, resulting in ATP synthase deficiency. Initial reports described neonatal presentations with a poor prognosis and short lifespan. However, recent studies describe a spectrum of disease as some patients survive to adulthood with cognitive impairment, hypotonia, and cardiomyopathy. Case A 25-year-old man presented with new-onset decompensated heart failure. Family history was significant for cardiomyopathy with end-stage heart failure in early life. His paternal grandfather died at the age of 40; he had ten children, eight died from heart failure between the ages of 25 to 40. Echocardiogram demonstrated a left ventricular ejection fraction of 15% with diastolic dysfunction and severe aortic insufficiency. Right-heart catheterization revealed elevated filling pressures. Invasive coronary angiography revealed normal coronary arteries. Cardiac magnetic resonance imaging showed severe biventricular dilation and a bicuspid aortic valve, there was no evidence of inflammatory or infiltrative cardiomyopathy. Decision-making Our patient was medically managed for heart failure. Despite this, he developed cardiogenic shock refractory to inotropic therapy and underwent mechanical circulatory support (MCS) with extra-corporeal membrane oxygenation. A heart team determined him to be a candidate for durable MCS implantation with a destination therapy left-ventricular assist device (LVAD). He underwent surgical LVAD implantation and aortic valve replacement (AVR). Genetic testing identified a pathogenic variant in TMEM70 that is associated with autosomal recessive ATP synthase deficiency, a cause of mitochondrial encephalocardiomyopathy. Conclusion We report a case of a 25-year-old man with end-stage heart failure who was managed with LVAD and AVR. Genetic testing identified a mutation in the TMEM70 gene to be the likely cause of his familial cardiomyopathy. This case demonstrates the role of advanced therapies in the treatment of genetic cardiomyopathy and the importance of identifying the etiology to assist with counseling.

Cardiology/Cardiovascular Research
Almajed MR, **Saleem A**, **Wexler B**, **Patton J**, **Villablanca PA**, and **Rabbani B**. RECIPE FOR DISASTER: PROSTHETIC AORTIC VALVE FAILURE, BETA-BLOCKERS, AND CALCIUMCHANNEL BLOCKERS. *J Am Coll Cardiol* 2024; 83(13):2996. Full Text

Background Beta-blocker (BB) therapy is discouraged in patients with AR as negative chronotropy prolongs diastole thereby increasing regurgitant volume. Coadministration of BB and nondihydropyridine calcium channel blocker (CCB) results in profound negative chronotropy causing symptomatic bradycardia and heart block. Treatment of BB and CCB toxicity includes intravenous fluids, atropine, glucagon, vasopressors, and inotropes. Case A 75-year-old man presented with syncope. His history was

notable for CAD for which he underwent LCx stenting two weeks prior and IE for which he underwent SAVR. He had inadvertently taken higher doses of both BB and nondihydropyridine CCB an hour before symptom onset. He was found to be hypothermic, bradycardic, and in undifferentiated shock that did not respond to initial resuscitation. Due to concern for medication overdose, he was treated with atropine, glucagon, and calcium with minimal response; initiation of continuous epinephrine resolved his shock state. Upon reevaluation, he reported exertional dyspnea and was noted to have an early diastolic murmur. Echocardiogram revealed severe insufficiency of the prosthetic aortic valve (AV) with a flail left coronary cusp leaflet and pressure half time of 132 ms. Invasive coronary angiography revealed a patent LCx stent and non-obstructive CAD. Decision-making Our patient's presentation in shock was initially concerning for toxicity associated with the accidental use of both a BB and nondihydropyridine CCB. Further workup revealed that the patient's underlying prosthetic AV failure with severe AI predisposed him to this decompensation. A heart team deemed him high-risk for SAVR, therefore, our patient underwent valve-in-valve TAVR. Conclusion Overdose of BB and nondihydropyridine CCB represents a fatal adverse event involving commonly prescribed medications. Patients with cardiac dysfunction, such as our patient with severe AI, are at increased risk of intolerance of these medications. In our patient with severe symptomatic AI of a prosthetic valve, definitive treatment is aortic valve replacement.

Cardiology/Cardiovascular Research

Andrews TQ, **Bunch C**, **Basir MB**, and **Miller J**. PYOPNEUMOPERICARDITIS SECONDARY TO ENTERO-PERICARDIAL FISTULA: A RARE ETIOLOGY OF DYSPNEA. *J Am Coll Cardiol* 2024; 83(13):4399. Full Text

Background Entero-pericardial fistulae are rare pathophysiologic communications between the gastrointestinal tract and the pericardium, most often a delayed complication of gastroesophageal surgeries. Despite aggressive multidisciplinary action, mortality rate remains >50%. Case An elderly female with remote history of Roux-en-Y gastric bypass and rheumatoid arthritis requiring chronic steroids presented with acute onset dyspnea. CT chest & esophagram demonstrated pneumopericardium (Figure 1). Esophagogastroduodenoscopy confirmed jejunal-pericardial fistula at the site of an ulcer distal to the gastro-jejunal anastomosis. Decision-making A pericardial drain was urgently placed, and subsequent cultures grew methicillin resistant Staphylococcus aureus (MRSA), Streptococcus parasanguinis, and Actinomyces odontolyticus. The patient underwent fistula take-down and was treated with a three-week course of vancomycin for MRSA and S. parasanguinis pericarditis and discharged with a 6-month course of amoxicillinclavulanate for Actinomyces pericarditis. A 3-month course of aspirin and colchicine was chosen for empiric coverage of pericarditis. Conclusion Entero-pericardial fistulas are often complicated by pneumopericardium, tamponade, and pericarditis that require prompt source control, broad spectrum antimicrobial coverage, and cardiovascular support. Despite multidisciplinary action and aggressive surgical and medical management, mortality remains high. [Formula presented]

Cardiology/Cardiovascular Research

Andrews TQ, **Hana A**, **Lee JC**, and **Frisoli TM**. TRANSCATHETER MITRAL VALVE-IN-VALVE IN RING WITH VENTRICULAR SEPTAL DEFECT OCCLUDER ASSIST FOR PERIVALVULAR LEAK. *J Am Coll Cardiol* 2024; 83(13):4233. Full Text

Background Mitral ring annuloplasty failure is uncommon, however, ring dehiscence accounts for 42% of occurrences and allows for detrimental mitral regurgitation (MR). Transcatheter mitral valve replacement (TMVR) has been described as an effective treatment for ring annuloplasty failure with trans-ring and para-ring MR. Case An 86-year-old male with medical history of severe MR post incomplete ring annuloplasty presented with three months of progressive dyspnea. Transesophageal echocardiogram (TEE) demonstrated severe eccentric MR at P2 and originating focally at the site of ring dehiscence from the native mitral annulus. Decision-making Given comorbid conditions and re-do sternotomy status, minimally invasive management was pursued. A transcatheter edge-to-edge repair was aborted due to mitral anatomical limitations. Following, a 29 mm valve was deployed without significant resolution of perivalvular leak (PVL). An additional 29 mm valve was placed with persistent PVL in the posterolateral annulus of the dehisced annuloplasty ring. Ultimately, three ventricular septal defect occluders were placed (8mm and two 10mm) within the dehisced area to completely abolish the PVL. Conclusion TMVR has been described as an effective, minimally invasive option for mitral ring annuloplasty failure.

However, incomplete annular apposition in TMVR remains a procedural complication. Small caliber ventricular septal occluder devices may serve as a sufficient adjuvant implant for persistent PVL. [Formula presented]

Cardiology/Cardiovascular Research
Ayyad A, **Halboni A**, **Al-suraimi A**, and **Peterson K**. TROJAN HEARTBEATS: ACUTE MYELOID LEUKEMIA DISGUISED AS ACUTE CORONARY SYNDROME. *J Am Coll Cardiol* 2024; 83(13):4371. Full Text

Background Leukostasis, a manifestation that affects 15% of acute myeloid leukemia (AML) patients, with rare cardiac involvement including myocardial ischemia, arrhythmias, and pericarditis. We discuss an AML case resembling acute coronary syndrome (ACS) due to leukostasis-induced myocardial ischemia. Case A 52-year-old female, presents to the ED with acute chest pain. EKG indicated t-wave inversions in leads II, V5, V6 and 1 mm ST elevations in leads 1, aVL. Troponins surged to 371 ng/L. Laboratory findings highlighted WBC at 211,000 cell/uL, constituting 83% blasts. Peripheral smear revealed a diagnosis of acute myeloid leukemia (AML) accompanied by pronounced leukocytosis. Decision-making An echocardiogram was performed and revealed a normal left ventricular function without wall motion abnormalities. Furthermore, a coronary angiography showed no evidence of obstructive pathologies or stenotic lesions. In light of the newly established diagnosis of AML, in conjunction with a pristine echocardiogram and a normal coronary angiography, leukostasis was identified as the trigger for the ACS. Immediate leukapheresis and Hydroxyurea administration led to a WBC count reduction to 30,000 cells/μL, subsequently alleviating the angina and EKG changes. [Formula presented] Conclusion ACS can be a rare presentation of AML. Prompt leukapheresis can effectively clear microvascular blockages. Our experience with this patient highlights the importance of recognition of an uncommon presentation of acute leukemia.

Cardiology/Cardiovascular Research
Bashir H, Garcia S, Palmer C, Schmidt C, Yildiz M, Reardon M, **Frisoli TM**, Fam N, Chung E, and Kereiakes DJ. 800.05 Effect of J-Valve on Left Ventricular (LV) Ejection Fraction (EF) and LV Geometry: A Multi-Center Compassionate Use Study in Patients With Aortic Regurgitation. *JACC Cardiovasc Interv* 2024; 17(4):S66. Full Text

Introduction: Severe aortic regurgitation (AR) is the indication for 20-30% of surgical aortic valve replacements and is associated with increased morbidity and mortality. No transcatheter device has received U.S. approval for the treatment of AR. J-valve is a short frame, self-expanding TAVR device specifically designed for treatment of severe AR. Methods: From 2019 through 2023 patients with symptomatic severe AR who were not surgical candidates or excluded from the ALIGN-AR trial were treated as part of the compassionate use program at five North American centers (The Christ Hospital, Henry Ford Hospital, Houston Methodist, St. Michael's Hospital). We report the echocardiographic changes in LVEF and LV geometry of 23 patients treated in the early experience with this novel device. LV geometry was categorized as normal (normal RWT (relative wall thickness), normal LV mass (LVM), CH (increased RWT, increased LVM), EH (normal RWT, increased LVM), or CR (increased RWT, normal LVM). Results: A total of 23 patients (mean age 73.9 ± 16.6 years; 61% male) with symptomatic AR (96% NYHA class III/IV, all with grade 3 or 4 AR) and paired echocardiograms were included. The mean pre-procedural LVEF was 46.3% ± 15.4. Post-procedural AR was none/trivial in all patients, and 22/23 survived to 30 days. Follow-up echocardiograms at 30 days revealed improvement of mean LVEF 47.2 ± 14.1 (p-value 0.24); 1 year echo revealed LVEF 51.9% ± 10.9 (p-value 0.033). LV geometry preprocedural was characterized as 36% CH; 50% EC; and 14% normal. 1 month follow-up, 25% CH; 10% CR; 25% EH; and 40% normal. 1 year follow-up 7% CH; 27% CR; 33% ER; and 33% normal. (Figure 1) Conclusion: Following J-valve placement for symptomatic, severe AR, left ventricular (LV) geometry and ejection fraction often revert toward normal and away from concentric hypertrophy in a large proportion of patients. [Formula presented]

Cardiology/Cardiovascular Research
Bonkowski T, **Foglesong A**, **Jafri S**, Saco RZ, and **Williams CT**. THE TRIPLE THREAT: A RARE CAUSE OF HEART FAILURE. *J Am Coll Cardiol* 2024; 83(13):3228. Full Text

Background L-type transposition of the great vessels (L-TGA) is a congenital anomaly that is associated with anomalous coronary arteries. Here we present a unique case of L-TGA complicated by obstructive CAD and a malignant anomalous coronary artery presenting as new onset heart failure. Case A 66-year-old male presented to the emergency department from his primary care provider's office with chest pain and dyspnea. He was found to have an NSTEMI. Coronary angiography showed anomalous origin of the left coronary system from the right aortic cusp with three-vessel obstructive CAD. Surface echocardiogram showed L-TGA and a dilated systemic ventricle with an ejection fraction of 45%. Coronary CTA confirmed diffuse CAD with anomalous anatomy including a malignant course of the left circumflex artery between the great vessels. Decision-making The patient was transferred to a tertiary care center for advanced therapies. Right heart catheterization showed a low cardiac index. Cardiac MRI showed transmural infarct of the septum with a systemic ventricle ejection fraction of 35%. After a heart team discussion, he was ineligible for CABG due to his anomalous coronaries and a small systemic ventricle excluded him from ventricular assist device implantation. He was then optimized with GDMT and was discharged with plans for heart transplant evaluation. Conclusion This case represents a novel description of anomalous coronary anatomy complicated by a malignant course and severe CAD in an adult patient with L-TGA. [Formula presented]

Cardiology/Cardiovascular Research

Fadel R, **Miller J**, **Cook B**, **Nguyen F**, **Alqarqaz M**, **Fuller B**, **Basir MB**, **Frisoli TM**, **Villablanca PA**, **Jabri A**, **Alaswad K**, **Khandelwal AK**, **Lingam N**, **O'Neill BP**, **Kim HE**, **Pielsticker EJ**, **Koenig GC**, Mills NL, and Mahler SA. THE INCIDENCE OF UNSTABLE ANGINA IN PATIENTS WITH LOW HIGH-SENSITIVITY TROPONIN I VALUES: A SUBGROUP ANALYSIS OF THE RACE-IT TRIAL. *J Am Coll Cardiol* 2024; 83(13):1268. Full Text

Background We sought to identify the incidence of unstable angina in patients with low high-sensitivity cardiac troponin I (hs-cTnI) in Emergency Departments (EDs). Methods This was a preplanned secondary analysis of the Rapid Acute Coronary Syndrome Exclusion using high-sensitivity I cardiac Troponin (RACE-IT) stepped-wedge randomized trial, which compared two rule-out protocols (0/1-hour and 0/3-hour) for myocardial infarction (MI) in 9 EDs from 7/2020-3/2021. A hs-cTnI assay from Beckman Coulter was used (99th percentile 18 ng/L). In the accelerated protocol (AP), MI was excluded if hs-cTnI was <4 ng/L at presentation, or =4 ng/L at presentation with a 1-hour value <8 ng/L. Those that did not rule-out within 1 hour required a 3-hour hs-cTnI ≤18 ng/L to rule-out. In the standard care (SC), MI was excluded if hs-cTnI values were ≤18 ng/L at 0 and 3 hours. Patients were excluded if hs-cTnI was >18 ng/L within 3 hours of presentation. Unstable angina was adjudicated based on the ISCHEMIA trial definition, which required electrocardiographic changes or findings at coronary angiography (ruptured/ulcerated plaque or thrombus). Adjudication was performed by interventional cardiologists for patients undergoing coronary angiography, and by cardiology fellows in patients with hs-cTnI >18 ng/L >3 hours after presentation. Results Of the 32,608 patients in the trial, 58 patients (0.18%) met the definition of unstable angina (35 in the AP and 23 in the SC protocol). In the AP 12/35 (34.3%) patients with unstable angina had a presenting hs-cTnI <4 ng/L. In the AP, among patients who ruledout for MI within 1 hour, 13/10444 (0.12%) had unstable angina vs. 22/8659 (0.25%) among those who did not meet early rule-out criteria (adjusted odds ratio 0.73, 95% CI 0.33 - 1.60, p=0.43). Within 30 days there were 113 (0.35%) patients in the entire cohort who had a revascularization procedure and in the unstable angina group there were 38 (65.5%). Conclusion Unstable angina is rare in patients with a low hs-cTnI values at presentation to the ED and few receive revascularization procedures. However, of those ultimately diagnosed with unstable angina in the AP, a substantial portion had an extremely low hs-cTnI at presentation.

Cardiology/Cardiovascular Research

Fang JX, and **Villablanca PA**. ACUTE CORONARY SYNDROME DURING LITHOTRIPSY-ASSISTED BALLOON MITRAL VALVULOPLASTY. *J Am Coll Cardiol* 2024; 83(13):4479. Full Text

Background Lithotripsy-assissted mitral balloon valvuloplasty is an emerging therapy for mitral stenosis. Complications of the procedure is not well studied. Case A 49 year-old lady with severe mitral stenosis and NYHA class III heart failure was referred for balloon valvuloplasty. Echocardiogram showed severe annular and bileaflet calcification with mean gradient of 15mmHg and valve area of 0.7cm^2. Coronary

arteriogram showed 80% lesion in proximal LAD (A) We performed balloon mitral annuloplasty and lithotripsy with a 2 12mm L6 lithotripsy balloons (B) followed by valvoplasty with 28mm balloon (C) guided by intracardiac ultrasound. (D) We used cerebral embolic protection device. (E) Therapeutic heparinization was maintained. Immediately post valvuloplasty, patient had chest pain and ECG showed peaked precordial T waves. Coronary arteriogram showed occlusion of proximal LAD at the pre-existing lesion. (F) intravascular ultrasound showed plaque rupture with thrombus. (G). Decision-making We performed PCI with a 4.0 x 28mm stent, postdilated with 4.5/5.0 non-compliant balloons and restored TIMI 3 flow (H). No calcium debris was found from the embolic protection device. Echocardiogram showed reduction of mean gradient from 15mmHg to 6mmHg. Conclusion Embolisation is a known complication of PBMV but plaque rupture and thrombosis has not been reported before. A possible mechanism is disruption of calcified plaque from lithotripsy. [Formula presented]

Cardiology/Cardiovascular Research

Gregerson S, **Fang JX**, **O'Neill B**, **Giustino G**, **Wang D**, **Lee J**, **Frisoli T**, **Gonzalez PE**, **O'Neill W**, and **Villablanca P**. 800.67 Feasibility And Periprocedural Outcomes of Transcatheter Mass Extraction in Left Heart and Aortic Arch. *JACC Cardiovasc Interv* 2024; 17(4):S79. Full Text

Background: Transcatheter vacuum-assisted mass extraction (TVME) is an alternative to surgical thrombectomy in high-risk patients especially for right-sided heart chambers. TVME in the left heart is less frequently performed owing to the need for transeptal puncture or alternative access, and the potential need for embolic protection, and the higher risk of blood loss. We report a case series of left-sided TVME at a high-volume center in USA. Methods: We performed left sided TVME in 24 consecutive patients from January 2019 to July 2023 at Henry Ford Hospital, MI, USA. The AngioVAC (Angiodynamics Inc, USA) was used. The preferred placement location for the blood return cannula was into the arterial system. Large bore access and closure were performed with standard techniques. TVME was performed for mass in the left atrium in 3 patients, left atrial appendage in 9 patients, left ventricle in 7 patients, aortic arch in 5 patients. Transeptal puncture was performed in all cases of left atrial and left ventricular masses. Transcaval access was performed in 4 out of 5 cases of aortic arch masses in order to gain enough catheter reach. Embolic protection device was used in 20 out of 24 patients. Concurrent left-atrial appendage occlusion was done in 5 patients with left-atrial appendage thrombus and concurrent balloon mitral valvuloplasty in two patients. Procedural success was defined as debulking of the total mass volume by 70% or more on echocardiogram. Results: The mean age of the patients was 59. Half were male. Mean left ventricular ejection fraction was 45%. The mean diameter of the mass was 3.2 cm. The procedure was completed in 96% (23 out of 24) of cases and aborted in 1 case. Successful debulking was achieved in 79% of cases. The median procedure time was 186 minutes. The mean procedural blood loss was 161 ml. The return cannula was placed on the arterial side in 66.6% (16 out of 24) of cases and on the venous side in 33.3% (8 out of 24) of cases. Periprocedural complications were uncommon. One patient developed stroke. One patient developed retroperitoneal bleeding. One patient developed a right femoral pseudoaneurysm. 2 patients required blood transfusion periprocedurally. The median length of hospitalization was 10 days. All patients were discharged alive from the hospital. Conclusions: TVME is technically feasible and safe for left-sided and aortic arch lesions.

Cardiology/Cardiovascular Research

McBride P, **Gupta K**, **Lemor A**, **Alkhatib A**, **Cowger JA**, **Grafton G**, **Alaswad K**, **O'Neill WW**, **Villablanca PA**, and **Basir MB**. USE OF PERCUTANEOUS MECHANICAL CIRCULATORY SUPPORT FOR RIGHT VENTRICULAR FAILURE. *J Am Coll Cardiol* 2024; 83(13):456. Full Text

Background RV dysfunction is a significant cause of in-hospital morbidity/mortality due to under recognition and lack of experience with right ventricular mechanical circulatory support (RV-MCS). The purpose of this project was to identify if intervention, in addition to timing, impacted outcomes. Methods Single center retrospective cohort study of patients treated with RV-MCS for any indication between 2015-2022. Baseline comorbidities, hemodynamic, and laboratory data were collected. Primary outcome was in-hospital mortality analyzed as a logistic outcome in a multivariable model. Results Among 58 patients, median age was 66 years. 31% of patients were female. 50% of patients were hospitalized for acute on chronic heart failure. 64% were SCAI SHOCK Stage D. Median time from index hospitalization to placement of RV-MCS was 2 days. 50% were treated with Impella RP and 50% received Protek Duo.

Left ventricular mechanical circulatory support (LV-MCS) was used concomitantly with 45% of people. RV-MCS resulted in lower MAP (79.5 vs 67.6, p<0.001), and CVP (20 vs 15 mmHg, p<.002). Additionally, increased CO (3.8 vs 5.8, p <.001), CI (1.9 vs 2.7, p<.001), and RV SWI (8.9 vs 12.7 g*m/m2, p<.006) were observed at 24 hours. Lactate levels were significantly lower at 24 hours (3.5 vs 1.8, p<.05). In-hospital mortality of individuals treated with RV-MCS was 48.3%. In these individuals, median CVP and CVP/PCWP trended towards being increased (24 vs 19, p =.052 and 1.2 vs 1.0, p=.086, respectively). Median serum lactate was also significantly higher (4.1 vs 2.2, p<.007). In the multivariable logistic model, age (OR 1.11 [1.01, 1.22], p<.033), diabetes mellitus (OR 7.7 [1.0, 59.0], p<.048), CVP (OR 1.18 [1.03, 1.35], p<.017) and serum lactate (OR 1.32 [1.06, 1.65], p<.013) prior to placement of RV-MCS were associated with mortality. Conclusion Patients treated with RV-MCS had an in-hospital mortality of 48%. Use of RV-MCS was associated with reduced MAP, and improved CVP, systolic PA pressure, CO, CI, RVSWI, and lactate clearance. Diabetes mellitus, elevated CVP, and elevated lactate at presentation were independently associated with increased mortality.

Cardiology/Cardiovascular Research
Modi K, and **Ananthasubramaniam K**. ALL ABOUT THE FLOW - INSIGHTS INTO HIGH OUTPUT HEART FAILURE. *J Am Coll Cardiol* 2024; 83(13):4191. Full Text

Background High output heart failure (HF) is an uncommon etiology for HF, but an essential one to investigate given its high morbidity. Case A 74-year-old man with ESRD status post renal transplant, allograft nephropathy, HF presented with leg swelling, dyspnea, and respiratory failure. Patient has had multiple similar presentations previously. Physical exam was notable for respiratory distress, soft systolic murmur in the left upper sternal border, pitting lower extremity edema, and warm extremities. Blood work showed known renal dysfunction, minimal BNP and troponin elevations. ECG showed sinus rhythm, and CXR pulmonary congestion. Echocardiogram showed hyperdynamic LV ejection fraction, normal LV cavity size, wall thickness, indeterminate diastology, pulmonary artery pressure (PAP) 63 mmHg, and normal right ventricle (RV) size and function. Transaortic maximum velocity was 3.74 m/s, but valve area suggested mild stenosis. Cardiac output was 11.97 L/min, cardiac index 4.69 L/min/m2. Invasive hemodynamics showed mildly elevated right atrial pressure at 7 mmHg, mean PAP 22 mmHg, capillary wedge pressure 12. Cardiac output and index were 12.49 L/min, and 4.77 L/min/m2, systemic vascular resistance (SVR) 627 dynes/sec/cm2. Decision-making Given elevated cardiac output, patient's HF was thought to be secondary to a high flow state. He had an arteriovenous fistula (AVF) from prior dialysis. Interrogation of the AVF shows elevated flow at 1335 mL/sec. Patient underwent fistula revision with reduction in cephalic vein lumen size. Repeat echocardiogram showed normalized cardiac output and index, measuring 5.4 L/min and 2.24 L/min/m2. Patient has dramatic improvement in symptomatically. HF has numerous etiologies, and high disease burden. High output HF is relatively uncommon and is defined by increased cardiac output (greater than 8 L/min) and reduced SVR. It is secondary to other pathologies, such as obesity, shunts, liver, and lung disease. Persistence of AVF is an uncommon cause of high flow state but needs to be factored in. Conclusion AVF in rare instances contribute to high output heart failure and systemic workup could lead to correct diagnosis and management.

Cardiology/Cardiovascular Research
Muhammad N, **Fadel R**, **Ama S**, and **Ananthasubramaniam K**. UTILITY OF PET CT IN DIAGNOSING CARDIAC SARCOIDOSIS, ESPECIALLY AS A COMPLEMENTARY MODALITY TO CARDIAC MRI. *J Am Coll Cardiol* 2024; 83(13):3506. Full Text

Background Cardiac sarcoidosis (CS) is an infiltrative cardiomyopathy resulting from granulomatous inflammation. Advanced imaging with positron emission tomography (PET) and magnetic resonance imaging (MRI) has the added benefit of detecting active inflammation and fibrosis due to CS, and can guide management. Case A 59-year-old male presented with presyncope for 2 weeks. Electrocardiogram demonstrated complete heart block. Transthoracic echocardiogram demonstrated mildly reduced left ventricular ejection fraction of 50-55%. Cardiac MRI demonstrated late gadolinium enhancement involving the mid myocardial basal septum and subepicardial mid inferior wall of the left ventricle suggestive of CS (figure1). A follow-up FDG-PET demonstrated similar distribution of active myocardial inflammation. The patient was treated with prednisone. Decision-making Utility of advanced imaging is key in the setting of suspected CS. MRI brings high spatial resolution and fibrosis detection, while PET provides myocardial

inflammatory information. Both modalities identify different histopathologic features of CS, hence the complimentary use of both tests in defining the need for treatment and assisting in risk stratification. Conclusion In patients with high suspicion of CS, combination of MRI and PET can help establish the diagnosis as well as identify distribution of active inflammation, and guide treatment options/prognosis. [Formula presented]

Cardiology/Cardiovascular Research
O'Neill WW, Kaki A, Moses J, Holy C, Ruppenkamp JW, Coplan P, and Vetrovec GW. 100.66 Percutaneous Ventricular Assist Device Supported Elective Percutaneous Coronary Intervention Performed in Sicker, More Complex Patients Compared to Intra-Aortic Balloon Pump. *JACC Cardiovasc Interv* 2024; 17(4):S19-S20. Full Text

Background: Observational studies comparing patients undergoing elective percutaneous coronary intervention (PCI) with percutaneous ventricular assist device (pVAD) or intra-aortic balloon pump (IABP) have shown disparate results. We compared patient and procedural characteristics of IABP and pVAD-supported PCI populations. Methods: Patients undergoing elective PCI with pVAD or IABP support in the PREMIER database (2018-2022) were identified. Exclusion criteria included isolated right heart failure, cardiogenic shock and/or STEMI on admission, coronary artery bypass graft surgery at index and pVAD and IABP use within same admission. Propensity scores (PS) were estimated using logistic regression and distributions of PS were compared between pVAD and IABP cohorts to assess baseline comparability on measured covariates. Results: 3,098 and 799 patients with PVAD- and IABP were analyzed. PVAD vs IABP patients had older mean age (72.6 vs 71.1) and significantly more comorbidities: congestive heart failure (73% vs 57%), renal failure (38% vs 32%), chronic total occlusion (24% vs 15%) and ischemic cardiomyopathy (46% vs 28%). For their actual PCI procedure: PVAD vs IABP was more likely to have 2 or more arteries dilated (51% vs 28%), and 3 or more arteries dilated (21% vs 11%). PS distributions showed limited overlap between cohorts. Conclusions: Among elective PCI patients, pVAD cases were older and sicker, with more arteries treated, vs IABP. Most pVAD cases were at the high end of the PS range, where there were relatively few IABP patients, suggesting limited comparability between groups. [Formula presented]

Cardiology/Cardiovascular Research
O'Neill WW, Shah T, Holy C, Coplan P, Almedhychy A, Moses J, Parise H, and Lansky A. 100.63 In-Hospital Safety and Effectiveness of Non-Emergent, MCS-Supported High-Risk PCI Procedures: A Comprehensive Propensity-Score Matched Analysis of Contemporary, Large-Scale Claims Dataset. *JACC Cardiovasc Interv* 2024; 17(4):S18. Full Text

Background: The safety and effectiveness of elective high-risk percutaneous coronary intervention (HRPCI) with microaxial percutaneous ventricular assist device support (v-HRPCI) or intra-aortic balloon pump support (b-HRPCI) are important considerations. Our study compared the safety and effectiveness of v-HRPCI and b-HRPCI in contemporary large-scale dataset. Methods: We identified patients with validated ICD-10 claims in Premier database (2018-22), who had elective v-HRPCI or b-HRPCI in the Premier database between 2018-22. We excluded admissions for right heart failure, cardiogenic shock, STEMI, and CABG procedures concurrent with HRPCI. Propensity score matching (PSM) using logistical regression model was performed on 125 relevant variables to compensate for confounders in history, admission and comorbidities, and pre-existing risks for bleeding. Endpoints included in-hospital (ih) mortality, discharge disposition (home, home health care/HHC, hospice, skilled nursing facility/SNF), length of stay (LOS), hospitalization costs (hosp-$), new-onset in-hospital occurrences of bleeding requiring transfusions (ih-BRT), of kidney failure (ih-KF), of stroke (ih-Strk), and all-cause 30-, and 90-days readmissions (rehosp). Results: After matching, we identified 741 b-HRPCI patients, and 741 v-HRPCI patients. Matching balance was achieved on all 125 variables. In both cohorts, the average age was 71 years, 66% males, ~60% congestive heart failure, and ~34% renal failure. The HRPCI was performed on 1-vessel PCI in 49.9% and 71.5% (p<0.001), while 3-vessel PCI performed in 20.8 vs 11.1% (p<0.001), for v-HRPCI and b-HRPCI, respectively. Atherectomy utilization was 8% in v-HRPCI vs 6% in b-HRPCI (p=0.078). The LOS was 4.60±6.75 days vs 6.25±7.74 days (p<0.001), Mortality 7.3% vs 11.1%, (p=0.015), home discharge 70.6% vs 60.1% (p<0.001), SNF 9.4% vs 15.8% (p=0.015), in-hospital BRT was 1.9% vs 1.8% (p=NS), ih-KF was 10.8 vs 17.1 (p=0.001), In-Strk was 1.5 vs 3.1 (p=0.056), for

v-HRPCI and b-HRPCI, respectively. Readmission rates were similar for both groups. Conclusions: In the present analysis, when matching contemporary patients for cardiovascular history, risks, the patients undergoing v-HRPCI experienced lower LOS, ih-mortality, SNF, ih-KF, and had higher home discharge rates, compared b-HRPCI. The ih-BRT and ih-Strk, as well as 30-, and 90-day readmission rates were similar between groups.

Cardiology/Cardiovascular Research
Obeidat L, **Maki M**, **Jebbawi LA**, **El-khatib L**, **Fram G**, and **Michaels AT**. ISOLATED RIGHT VENTRICULAR FAILURE REQUIRING MECHANICAL CIRCULATORY SUPPORT AS A PRESENTING MANIFESTATION OF RECURRENT VIRAL MYOCARDITIS. *J Am Coll Cardiol* 2024; 83(13):3993. Full Text

Background Myocarditis can manifests in various forms, ranging from asymptomatic to cardiogenic shock (CGS). It is often triggered by viral infections, such as adenovirus. The Human Coxsackievirus and Adenovirus receptor (hCAR), which is localized to the intercalated discs, plays a significant role in the pathogenesis of recurrent viral myocarditis. Case A 20 year old female with a history of Coxsackie B myocarditis presented with CGS following several days of fever and sore throat. She was tachycardic, and hypotensive, requiring vasopressors. Laboratory results indicated lactic acidosis, elevated BNP and high sensitivity troponin, AKI, shock liver, and a respiratory panel positive for adenovirus. An EKG with ST depression in the precordial leads. An echocardiogram revealed a preserved EF of 55-60%, normal left ventricular function, an enlarged severely hypokinetic right ventricle (RV), and a flattened interventricular septum, consistent with acute RV failure. Despite initial resuscitation and inotropic support, she remained in refractory CGS, necessitating the placement of a RV assist device (RVAD). Her symptoms were attributed to a disseminated adenovirus infection, and was started on Cidofovir therapy. She later rapidly improved, and RVAD support was subsequently weaned. Endomyocardial biopsy (EMB) and cardiac MRI (cMRI) performed later during her stay were negative, indicating a positive response to therapy. Decision-making Our patient's case was likely related to the expression of hCAR, explaining her susceptibility to these viruses and the subsequent development of recurrent myocarditis and RV failure. EMB is the gold standard for diagnosis; however, its value can be limited due to presence of areas spared from pathology. cMRI is an alternative diagnostic tool; however, findings can be nonspecific. Conclusion We emphasize the significance of identifying isolated RV failure as a rare yet possible manifestation of myocarditis, particularly in cases of recurrent viral infections. Furthermore, it's crucial to consider an underlying heritable cardiomyopathy, like arrhythmogenic cardiomyopathy in such cases, and discuss the potential need for genetic testing.

Cardiology/Cardiovascular Research
Patel V, **Hana A**, **Modi S**, and **Ananthasubramaniam K**. CARDIAC82RUBIDIUM18F FDG-POSITRON EMISSION TOMOGRAPHY (PET) GUIDED REVASCULARIZATION OF CHRONIC TOTALLY OCCLUDED LESIONS: ISCHEMIA AND VIABILITY ASSESSMENT IS ALIVE AND WELL. *Journal of the American College of Cardiology (JACC)* 2024; 83(13):3821-3821. Full Text

Henry Ford Hospital, Detroit, MI, USA

Cardiology/Cardiovascular Research
Rangavajla G, Ayub MT, Thoma F, Mulukutla S, Zhu J, Jain SK, Saba SF, and Bhonsale A. RECEPTOR AGONISTS AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH ATRIAL FIBRILLATION AND DIABETES. *J Am Coll Cardiol* 2024; 83(13):192. Full Text

Background Glucagon-like peptide-1 receptor agonists (GLP-1 RA) improve glycemic, obesity, and cardiovascular outcomes in patients with diabetes mellitus (DM). Atrial fibrillation (AF) often coexists with DM, but large-scale real-world data on clinical outcomes with GLP-1 RA in AF patients with DM is limited. Methods We extracted clinical data from adult AF patients with DM and no heart failure (HF) from a large tertiary-care system. GLP-1 RA recipients were matched with non-GLP-1 RA controls using propensity score matching with 22 variables (fig. 1A) and caliper size 0.2. Baseline characteristics after matching were assessed with t tests. Differences between GLP-1 RA recipients and controls were evaluated via Kaplan-Meier analyses for all-cause mortality, MACE (death, myocardial infarction, stroke, or major

bleed), and AF hospitalization. Results Of 24862 patients meeting inclusion criteria, 1261 GLP-1 RA recipients and 1261 controls were matched. Of the matching variables, only BMI showed a small but significant difference between groups (fig. 1A). Over a median follow up of 2.3 years (IQR 0.7-3.4), GLP-1 RA use was associated with significantly improved mortality and MACE, but not associated with AF hospitalization (fig. 1B). Conclusion In this large contemporary cohort of patients with AF and diabetes without HF, GLP-1 RA use was associated with improved hard clinical outcomes. While these results should be validated prospectively, they suggest a benefit from GLP-1 RA in this population. [Formula presented]

Cardiology/Cardiovascular Research
Rangavajla G, Newhouse D, Thoma F, Mulukutla S, Jain SK, and Saba SF. LEADLESS PACING VS TVP: ASSOCIATIONS WITH TRICUSPID REGURGITATION AND CARDIOMYOPATHY. *J Am Coll Cardiol* 2024; 83(13):193. Full Text

Background Prior reports suggest leadless pacing (LP) is associated with less de novo cardiomyopathy compared to transvenous pacing (TVP). However, the effect of LP vs TVP on progression of cardiomyopathy (CM) and tricuspid regurgitation (TR) is less clear. Methods We extracted clinical data from adults receiving LP or TVP from 2016-2022 at a large tertiary-care system. Adjusted differences were analyzed between groups for a composite outcome of mortality and heart failure (HF) hospitalization using Kaplan-Meier (KM) analysis. After propensity score matching LP and TVP recipients with 12 variables (fig. 1B), we used Wilcoxon signed-rank tests to evaluate baseline and post-implant (LVEF, new CM, need for biventricular pacing, and TR grade) differences. Results Of 4985 patients, 108 had LP and 4877 TVP with median follow-up 3.1 years (IQR 1.6-5.1). KM analysis showed no significant differences in the composite outcome between groups (fig. 1A). There were no differences in baseline metrics after matching (fig. 1B). Post-implant CM and TR outcomes in the matched subset also showed no significant differences (fig. 1C). Conclusion LP compared to TVP was not associated with improved cardiomyopathy outcomes; this finding differs from prior reports. There was also no significant difference between groups in TR progression. Replication of these results in a large cohort may suggest more limited benefits of LP than previously reported, which can better inform patient selection and counseling. [Formula presented]

Cardiology/Cardiovascular Research
Sabra M, **Al-Darzi W**, **Hannawi B**, **Russell C**, and **Ananthasubramaniam K**. RECOGNITION OF DISEASE ACTIVITY AND TREATMENT MONITORING IN CARDIAC SARCOIDOSIS: INTEGRAL ROLE OF CARDIAC POSITRON EMISSION TOMOGRAPHY (PET). *J Am Coll Cardiol* 2024; 83(13):3504. Full Text

Background 18F-Flourodeoxyglucose (FDG) PET imaging is crucial for diagnosing and monitoring disease activity in cardiac sarcoidosis (CS). However, little is known regarding the utility of follow-up PET scans in managing immunosuppression. Case 49 year old male with history of heart failure with reduced EF, complete heart block s/p CRT-D, atrial fibrillation, underwent a cardiac 82Rubidium 18F FDG PET scan for suspected CS. In the top figure, multifocal FDG uptake was observed, indicating active inflammation in the septum, right ventricle (RV), and right atrium despite normal perfusion. Treatment began with methotrexate and prednisone. After 3 months, follow-up PET scan revealed no inflammation (middle figure), resulting in reduction of prednisone dose with symptomatic improvement. 6 months later, another PET scan revealed recurrent inflammatory pattern of uptake in the septum, anterior wall, and RV prompting initiation of infliximab alongside methotrexate and a gradual prednisone taper until discontinuation. Decision-making Our case highlights the importance of serial 18F-FDG PET imaging in monitoring CS, emphasizing the challenges of immunosuppressive therapy, the recurrence of inflammation, and the value of follow-up cardiac PET scans. Increased RV FDG uptake is linked to higher long term event rates. Conclusion In the absence of specific guidelines, FDG PET may serve as a valuable tool for monitoring inflammation progression and assessing the response to immunosuppressive therapy. [Formula presented]

Cardiology/Cardiovascular Research
Sabra M, **Kabani S**, and **Maskoun W**. ROLE OF CARDIAC EVENT MONITOR IN THE DETECTION OF DELAYED HIGH-GRADE AV BLOCK AFTER NEGATIVE ELECTROPHYSIOLOGY STUDY IN

PATIENTS WITH POST- TRANSCATHETER AORTIC VALVE REPLACEMENT. *J Am Coll Cardiol* 2024; 83(13):2934. Full Text

Background Approximately 15% of transcatheter aortic valve replacement (TAVR) patients require permanent pacemaker (PPM) due to High-grade AV Block (HG AVB) following the procedure. 30-day event monitors are commonly recommended to detect delayed (> 2 days) HG AVB post-TAVR. Electrophysiology study (EPS), the following day post TAVR, has emerged as a potential risk assessment method for earlier detection of HG AVB prior to hospital discharge. Case We present two cases of high-grade atrioventricular block (HG AVB) following TAVR procedures and negative EPS. Case 1: A 94-year-old female with severe aortic stenosis underwent TAVR with a 23 mm SAPIEN Ultra valve. Transient complete heart block occurred during the procedure, followed by new-onset left bundle branch block (LBBB, QRS 142 ms). EPS showed normal AV node and HV intervals, with no infra-Hisian block. She was discharged with a 30 day event monitor. After discharge, she experienced intermittent HG AVB (including 4 to 1 block), leading to the immediate placement of a PPM on day 8 post-TAVR. Case 2: An 87-year-old female with severe aortic stenosis underwent TAVR with a 23 mm SAPIEN Ultra valve. Prior to the procedure, she had first-degree AV block (220 ms) and LBBB (QRS 152 ms) following AV valvuloplasty a few months earlier. A 30-day monitor showed no HG AVB. Following her uneventful TAVR procedure, there was no change to her baseline LBBB and 1st degree AV block. EPS post TAVR confirmed upper normal AH and HV intervals, normal AV nodal Wenckebach, and no infra-Hisian block. She was discharged with an event monitor. However, on day 24 post-TAVR, she developed sustained complete AV block, necessitating an emergent PPM placement during an ICU stay for hypoxic respiratory failure. She was discharged in stable condition. Decision-making HG AVB post TAVR remains one of the most significant complications of TAVR procedures. Our cases highlights the importance of post-discharge rhythm monitoring to detect late onset HG AVB post-TAVR after negative EPS and 24-48 hours of telemetry monitoring. Conclusion A negative EPS might not eliminate the need for 30 day event monitors to detect late onset HG AVB post TAVR, which could necessitate emergent PPM placement.

Cardiology/Cardiovascular Research
Stephan J, **Viacava RAC**, **McClafferty A**, and **Frisoli TM**. A DIAGNOSIS WITHOUT EXCLUSION: REVERSE TAKOTSUBO IN A 26-YEAR-OLD FEMALE. *J Am Coll Cardiol* 2024; 83(13):3582. Full Text

Background Takotsubo cardiomyopathy is a diagnosis of exclusion that typically requires a left heart catheterization. Reverse takotsubo has a prevalence of approximately 2% of all takotsubo cardiomyopathies. Case A 26-year-old female with no past medical history presented for elective bilateral salpingectomy. Intra-operatively, the patient became bradycardic and suffered a cardiac arrest. She was resuscitated but was found to be in shock. CT angiogram of the chest was negative for pulmonary embolism and showed diffuse pulmonary edema. Echocardiogram showed an ejection fraction (EF) of 15-20% with akinesis of the basal-mid anterior, inferior, anteroseptal, inferoseptal and lateral wall (figure 1). The patient improved with inotropic support and diuresis. Repeat echocardiogram, four days later, showed improvement of EF to 45%. She was placed on guideline-directed medical therapy and EF recovered 1 month after presentation. [Formula presented] Decision-making The multiple regions of akinesis with preserved apical contraction seen on echocardiogram do not fit a coronary territory, and thus these findings are incompatible with a coronary pathology. The diagnosis of reverse takotsubo was made without the use of a left heart catheterization given the patient's clinical presentation, characteristic imaging findings, and rapid normalization of wall motion abnormalities. Conclusion We present a case of reverse takotsubo in a 26-year-old female where the diagnosis was made conclusively by echocardiogram.

Cardiology/Cardiovascular Research
Sukhon F, **Jabri A**, Al-Abdouh A, Alameh A, Khader S, **Villablanca P**, and **AlQarqaz M**. 100.72 FFR-Guided Revascularization Versus Non-FFR-Guided Partial or Complete Revascularization in Acute Myocardial Infarction: A Systematic Review and Meta-Analysis. *JACC Cardiovasc Interv* 2024; 17(4):S22. Full Text

Background: Following revascularization of the infarct related artery (IRA) in acute myocardial infarction (MI), the utility of Fractional Flow Reserve (FFR)-guided percutaneous coronary intervention (PCI) of

angiographically severe non-IRAs is controversial. We performed a meta-analysis of all clinical trials involving this clinical question. Methods: We conducted a systematic review and meta-analysis including all available trials that looked at FFR-guided complete revascularization versus IRA-only revascularization or complete revascularization without FFR use. Primary outcomes were major adverse cardiac events (MACE), cardiovascular death, MI, or repeat revascularization. Secondary outcomes were death of all causes, major bleed, stent thrombosis, and stroke risk. Results: Six RCTs were included comprising a total of 2597 patients treated with IRA revascularization or complete revascularization without FFR use vs 2314 patients treated with FFR-guided complete revascularization. Compared with non-FFR use, FFR-guided PCI was significantly favored in terms of MACE (relative risk [RR] 1.65; 95% CI 1.04 - 2.63 p=0.04) and repeat revascularization (relative risk [RR] 1.92; 95% CI 1.18 - 3.11 p=0.02). There was, however, no difference in cardiovascular death (relative risk [RR] 1.67; 95% CI 0.98 - 2.85 p=0.06), MI (relative risk [RR] 1.43; 95% CI 0.78 - 2.61 p=0.19), death from any cause (relative risk [RR] 1.33; 95% CI 0.87 - 2.02 p=0.14), major bleed (relative risk [RR] 1.35; 95% CI 0.21- 8.49 p=0.56), stent thrombosis (relative risk [RR] 1.11; 95% CI 0.52 - 2.38 p=0.72), or stroke (relative risk [RR] 0.62 95% CI 0.26 - 1.44 p=0.19). Conclusion: Our meta-analysis shows that FFR-guided complete revascularization of non-IRAs at the time of MI has a significant benefit in lowering the risk of MACE and repeat revascularization. [Formula presented]

Cardiology/Cardiovascular Research
Thomas M, and **Cowger JA**. WHAT'S BLACK AND WHITE AND STRESSED ALL OVER? A ZEBRA PRESENTATION OF A ZEBRA CASE. *J Am Coll Cardiol* 2024; 83(13):3723. Full Text

Background Pheochromocytomas (PHEOS) are rare catecholamine secreting tumors. Rare cases of stress induced cardiomyopathy (SICM) and cardiogenic shock (CGS) have been reported with PHEOS. The management of PHEO related CGS is not well defined. Case A 34 year old male with no past medical history presented to an outside hospital with 3 days of worsening generalized weakness. He was afebrile, hypertensive, and tachycardic. TTE showed a newly reduced LVEF of 10% with global hypo-kinesis and a hyper contractile base, LV apical thrombus, and bi-ventricular dilation. Hospital course was complicated by a subacute infarct in the right parietal lobe, oliguric renal failure, and acute liver injury. He was then transferred to Henry Ford Hospital. A RHC showed elevated systemic pressures and filling pressures, severely reduced cardiac index, and severely increased systemic vascular resistance. He was started on dobutamine, Nipride, emergent dialysis, and a Swan Ganz Catheter (SGC) was placed. He remained hypertensive with high filling pressures and transitioned to a hyperdynamic state. Inotropes were stopped. Review of imaging showed a hypo-dense 3.1cm cystic nodule in the left adrenal gland. Adrenal adenoma work up revealed elevated plasma metanephrines. He was transitioned to maximally titrated medical therapy for HFrEF. He had a successful left adrenalectomy. Pathology was positive for PHEO. On follow up, LV and renal function had recovered. Decision-making TTE suggested SICM or LM/LAD stenosis. LHC was deferred due to the patient's renal dysfunction and low pretest probability of CAD. Escalation to inotropes with SGC was necessary due to CGS progression. Mechanical circulatory support was not pursued because the patient's hemodynamics favored after load reduction and the presence of an intra-cardiac thrombus. SICM has a variety of proposed mechanisms, including excessive catecholamines. Thus, medical treatment focused on reducing sympathetic tone with HFrEF treatment. Definitive treatment was adrenalectomy. Conclusion In the treatment of CGS, this case emphasizes the need for continuous hemodynamic monitoring, a multi-disciplinary team approach, and etiology focused plan.

Cardiology/Cardiovascular Research
Viacava RAC, **Naimi A**, **Almajed MR**, **Al-Suraimi A**, **Thomas M**, and **Kim HE**. USE OF TANDEM HEART FOR CARDIOGENIC SHOCK AND SEVERE AORTIC INSUFFICIENCY IN BARTONELLA HENSELAE INFECTIVE ENDOCARDITIS. *J Am Coll Cardiol* 2024; 83(13):3177. Full Text

Background Bartonella species infection, especially Bartonella henselae, is an increasingly common cause of culture-negative Infective Endocarditis (IE), which carries an exceedingly high morbidity and mortality. The necessity of valvular intervention for these cases has been found to be higher than on culture positive IE. Case A 53-year-old Hispanic man with no past medical history presented to the with palpitations, exertional dyspnea, orthopnea, and a non-intentional thirty-pound weight loss. His social

history was significant for cohabitating with 20 domestic cats. Initial workup revealed leukocytosis, azotemia and transaminitis. Microbiologic studies showed negative blood cultures. Chest radiograph showed signs of bilateral pulmonary edema. Transthoracic echocardiogram showed preserved ejection fraction, no diastolic dysfunction and signs of bicuspid aortic valve with severe aortic insufficiency (AI). Transesophageal echocardiogram confirmed the previous findings and revealed vegetations on the aortic valve. Blood gases revealed severely low cardiac indices. Due to his rapid clinical deterioration, he was admitted to the Cardiac Intensive Care Unit and started on vasopressors and inotropic agents. Infectious Diseases and Cardiac Surgery were consulted. Decision-making Upon further workup for culture-negative IE, Bartonella antibody titers were found positive. Cardiac Surgery recommended no surgical intervention due to the patient being to hemodynamically unstable and high risk. Despite maximizing inotropic agents and preload management, his course was complicated by SCAI Stage D cardiogenic shock and multiorgan system failure. Due to the severe AI, intraaortic balloon pump was contraindicated; and due to risk of septic embolism, devices such an Impella were contraindicated. Ultimately, a percutaneous Tandem Heart left ventricular assist device was placed and helped to successfully stabilize the patient. Conclusion IE can have several complications such as severe valvular disease leading to refractory cardiogenic shock. The usefulness of MCS in these patients is extremely high as a transient step until a definite valvular intervention.

Cardiology/Cardiovascular Research

Viacava RAC, **Naimi A**, **Almajed MR**, and **Swanson B**. INTERROGATING THE QUESTION: PACEMAKER-INDUCED CARDIOMYOPATHY SECONDARY TO TRANSCATHETER AORTIC VALVE REPLACEMENT-INDUCED HIGH-DEGREE HEART BLOCK. *J Am Coll Cardiol* 2024; 83(13):3176. Full Text

Background Pacemaker-induced cardiomyopathy (PICM) is defined as a drop in the left ventricular ejection fraction (LVEF) in the setting of long-standing high burden right ventricular pacing. The rise in use of implantable cardiac pacemakers has increased patient's quality of life, however complications such as infections, lead malfunction, and cardiomyopathy may arise. Case A 90-year-old white gentleman, with a past medical history of hypertension, coronary artery disease (CAD), sick sinus syndrome (SSS) requiring a dual-chamber permanent pacemaker implantation, severe aortic stenosis requiring a transcatheter aortic valve replacement (TAVR), presented for three weeks of exertional dyspnea, orthopnea, and bilateral leg swelling. He was hemodynamically stable, but hypoxic requiring oxygen supplementation. Initial workup revealed elevated BNP and elevated troponins. Electrocardiogram showed an AV-paced rhythm and no signs of ischemia. Chest radiograph showed bilateral pulmonary edema. Transthoracic echocardiogram showed a new decreased LVEF of 38% (previously 56%), no regional wall motion abnormalities, and a 26 mm Edwards Sapien 3 transcatheter aortic valve prosthesis with mild perivalvular regurgitation and TAPSE of 2.02 cm. Decision-making Device interrogation found an AV-paced rhythm with a right ventricular pacing of 99%. The last one, six months prior to this admission (four months before TAVR) showed a right ventricular pacing of 1%. Upon our discussion, patient was diagnosed with PICM. Electrophysiology was consulted, and upon stabilization of the patient's congestive heart failure, performed a device upgrade to a Cardiac Resynchronization Therapy (CRT), without any complications. Patient's condition improved significantly with this procedure and the use of intravenous loop diuretics. Ultimately, patient was discharged without oxygen supplementation requirements. Conclusion Conduction abnormalities are well-known complications of TAVR that often require pacemaker implantation. Patients with pacemakers require a careful device interrogation and right ventricular pacing assessment to diagnose PICM, for which CRT is a treatment of choice.

Dermatology

Bunick CG, Bhatia N, Del Rosso J, Draelos ZD, Eichenfield LF, Kircik LH, Lebwohl MG, Gooderham M, Green LJ, Hebert AA, Vender RB, Zirwas M, Simpson EL, **Gold LS**, Seal M, Snyder S, Osborne DW, Burnett P, Higham RC, Chu DH, and Berk DR. Investigator- and patient-rated local tolerability in phase 3 trials of topical roflumilast in patients with psoriasis, seborrheic dermatitis, and atopic dermatitis. *Br J Dermatol* 2024; 190:II9-II10. Full Text

Introduction: Formulating a topical medication that does not irritate the skin is an important factor contributing to patient treatment adherence and satisfaction. Many topical prescription products use

penetration enhancers (including propylene glycol, polyethylene glycol, and ethanol) to overcome barrier properties of the skin. However, these excipients may irritate the skin causing tolerability reactions such as burning and stinging, which can reduce patient treatment adherence. Topical roflumilast is a highly potent (Kd~0.7 nM) phosphodiesterase 4 inhibitor formulated as a water-based cream or foam that does not contain penetration enhancers or fragrances. Objectives: We present prospectively assessed investigator- and patient-rated local tolerability from Phase 3 trials of topical roflumilast for patients with psoriasis (DERMIS-1, DERMIS-2, ARRECTOR) seborrheic dermatitis (SD; STRATUM), and atopic dermatitis (AD; INTEGUMENT-1, INTEGUMENT-2). Methods: Patients were randomized to apply topical roflumilast (DERMIS: 0.3% cream; ARRECTOR and STRATUM: 0.3% foam; INTEGUMENT: 0.15% cream) or vehicle once daily for 8 weeks (DERMIS, ARRECTOR, and STRATUM) or 4 weeks (INTEGUMENT). Investigators assessed local tolerability on an 8-point scale (0 [no evidence of irritation] to 7 [strong reaction spreading beyond application site]) in the clinic before investigational product (IP) application. Patients reported local tolerability on a 4-point scale (0 [none: no sensation] to 3 [severe: hot, tingling/stinging sensation that has caused definite discomfort]) in the clinic 10-15 minutes after IP application. Tolerability was also assessed by reviewing documented adverse events. Results:
As assessed by investigators, ≥96.5% of patients in the roflumilast-treated groups had no evidence of irritation at the application site across all trials at all timepoints. Patient-rated local tolerability was favorable and improved with treatment: across all trials, 1% of roflumilast-treated patients reported a score of 3 (severe; defined as a “hot tingling/stinging sensation that has caused definite discomfort”) after the first application (day 1) and <1% at each subsequent assessment. Rates of adverse events, including those at the application site, were low for all trials. Conclusions: Roflumilast cream and foam formulations demonstrated favorable local tolerability based on investigator- and patient-rated assessments in patients with psoriasis, SD, and AD, including application to sensitive areas such as the face and intertriginous areas. ClinicalTrials.gov Identifiers: DERMIS-1: NCT04211363; DERMIS-2: NCT04211389; ARRECTOR: NCT05028582; STRATUM: NCT04973228; INTEGUMENT-1: NCT04773587; INTEGUMENT-2: NCT04773600.

Dermatology
Gooderham MJ, Weidinger S, Simpson EL, Deleuran M, **Gold LFS**, Farooqui SA, Biswas P, Chan G, Güler E, and Koppensteiner H. Treatment efficacy in patients with moderate-to-severe atopic dermatitis who switched from dupilumab to abrocitinib in JADE EXTEND, a phase 3 long-term extension study. *Br J Dermatol* 2024; 190:II32-II33. Full Text

Background: Abrocitinib, an oral, once-daily, Janus kinase 1–selective inhibitor, and dupilumab, an anti–interleukin 4 receptor α monoclonal antibody, have been approved for the treatment of patients with moderate-to-severe atopic dermatitis (AD). The efficacy of abrocitinib and dupilumab as monotherapy or in combination with medicated topical therapy has been demonstrated in multiple phase 3 clinical trials. As is the case with many therapies, some patients with AD may need to discontinue treatment with dupilumab (due to inadequate efficacy, intolerable side-effects, patient choice, or other reasons) and switch to other systemic therapies. Objective: To evaluate the long-term treatment response in patients with moderate-to-severe AD who switched from dupilumab to abrocitinib, as it is valuable information for prescribers and patients to consider when making treatment decisions. Methods: The phase 3 JADE COMPARE trial (NCT03720470) evaluated the efficacy of abrocitinib (100 mg or 200 mg once daily) and dupilumab (300 mg every 2 weeks) versus placebo in combination with topical medicated therapy in patients with moderate-to-severe AD through week 16. After a wash-out period, dupilumab-treated patients from JADE COMPARE who enrolled in the ongoing long-term extension trial JADE EXTEND (NCT03422822; clinical data cutoff: Sept 25, 2021) were randomised to receive double-blinded treatment with abrocitinib 100 mg or 200 mg. This post hoc analysis evaluated the response to dupilumab through week 16 in JADE COMPARE and thereafter in JADE EXTEND following a switch to abrocitinib through week 104 of total treatment duration/week 84 of abrocitinib treatment. Assessments included Investigator’s Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline (IGA 0/1), ≥75% or ≥90% improvement from baseline in Eczema Area and Severity Index (EASI-75 or EASI-90), ≥4-point improvement from baseline in Peak Pruritus Numerical Rating Scale score (PP-NRS4; PP-NRS used with permission from Regeneron Pharmaceuticals, Inc., and Sanofi), and a PP-NRS score of 0 or 1 (PP-NRS 0/1). JADE EXTEND data are presented as observed; patients with missing data at a visit were excluded. Analyses included both dupilumab responders and non-responders. Results:

Overall, 242 patients were treated with dupilumab in JADE COMPARE (mean age: 37 years; IGA score 4: 33%). Of those, 203 enrolled in JADE EXTEND and received abrocitinib 200 mg (n=73) or abrocitinib 100 mg (n=130). After 16 weeks of treatment with dupilumab in JADE COMPARE, the proportion of responders was 39% for IGA 0/1, 66% for EASI-75, 39% for EASI-90, 57% for PP-NRS4, and 24% for PP-NRS 0/1. As early as 2 weeks after switching to abrocitinib (200 mg/100 mg) in JADE EXTEND, the proportion of responders was observed to increase in a dose-dependent manner, respectively, for IGA 0/1 (61%; 51%), EASI-75 (90%; 85%), EASI-90 (60%; 54%), PP-NRS4 (81%; 72%), and PP-NRS 0/1 (47%; 37%). Long-term efficacy was observed out to week 84 (Figure). Conclusions: In patients with moderate-to-severe AD who received prior treatment with dupilumab, switching to abrocitinib resulted in dose-dependent increases in the proportion of responders as early as week 2 after treatment with abrocitinib. This efficacy continued to be observed long-term through week 84 of abrocitinib treatment.

Dermatology

Passeron T, Ezzedine K, **Hamzavi I**, van Geel N, Schlosser BJ, Hu XF, Huang XH, Rosmarin D, Harris JE, Camp HS, and Pandya AG. Efficacy and safety of upadacitinib in a phase 2 randomized, double-blind, dose-ranging study of adults with extensive non-segmental vitiligo. *Br J Dermatol* 2024; 190:II64-II65. Full Text

Introduction & Objectives: Janus kinase (JAK) inhibition is a promising approach for the treatment of vitiligo. Here, we report the clinical efficacy and safety of upadacitinib (UPA), an oral JAK inhibitor, in a phase 2b multicenter, randomized, double-blind, placebo-controlled study of adults with extensive non-segmental vitiligo (NSV). Materials & Methods: Eligible patients were aged 18–65 years with NSV, a Facial Vitiligo Area Scoring Index (F-VASI) of ≥0.5, and a Total Vitiligo Area Scoring Index (T-VASI) of ≥5 at baseline. This 52-week study (NCT04927975) comprised 2 periods. In period 1, patients were randomly assigned to once daily UPA 22 mg (UPA22), UPA 11 mg (UPA11), UPA 6 mg (UPA6), or placebo (PBO) for 24 weeks of treatment. In a 28-week blinded extension (period 2), patients receiving UPA during period 1 continued their respective regimens; patients who received PBO in period 1 were pre-assigned to either UPA11 or UPA22. Clinical efficacy endpoints evaluated through week 36 included percent change from baseline (%CFB) in F-VASI (week 24, primary endpoint), reductions from baseline in F-VASI of ≥50% (F-VASI 50) and ≥75% (F-VASI 75), %CFB in T-VASI, and reduction from baseline in T-VASI of ≥50% (T-VASI 50). Safety data as of January 13, 2023 (data cutoff date) are presented. Results: Of the 185 patients enrolled in period 1, 165 (89.2%) continued to period 2. At baseline, 68% of patients had extensive vitiligo (T-VASI > 10), and 71% had active vitiligo. At week 24, the %CFB in F-VASI was greater with UPA11 (−35.6%) and UPA22 (−34.0%) vs PBO (−14.4%; nominal P = .005 and P = .013, respectively). A greater proportion of patients achieved F-VASI 50 and F-VASI 75 with UPA11 (38.3%, 19.1%) and UPA22 (39.5%, 14.0%) vs PBO (10.9%, 2.2%; nominal P < .05 for both doses and for both endpoints). Likewise, the %CFB in T-VASI was greater with UPA11 (−17.3%) and UPA22 (−20.7%) vs PBO (−6.4%; nominal P = .026 and P = .005, respectively). A higher percentage of patients achieved T-VASI 50 with UPA22 (11.6%) than with PBO (2.2%; nominal P = .027). UPA efficacy continued to improve through week 36, with %CFB in F-VASI for UPA6, UPA11, and UPA22 of −20.8%, −44.9% and −47.7%, respectively. At week 36, F-VASI 50 was achieved with UPA6, UPA11, and UPA22 by 34.2%, 54.3% and 61.5% of patients and F-VASI 75 by 15.8%, 40.0%, and 30.8%, respectively. At week 36, %CFB in T-VASI for UPA6, UPA11 and UPA22 were −24.3%, −32.0% and −37.6%, with 10.5%, 20.0% and 19.2% of patients, respectively, achieving T-VASI 50. Treatment-emergent adverse event (TEAE) rates were generally similar with UPA and PBO in period 1 (most common TEAEs: COVID-19, acne, fatigue, and headache) and were similar across treatment arms in period 2. One death adjudicated as undetermined/unknown cause and deemed by the investigator to have no reasonable possibility of being related to study drug occurred in the UPA22 group (period 1). One adjudicated event of nonfatal ischemic stroke occurred with UPA11 (period 2). There were no adjudicated events of venous thromboembolism, gastrointestinal perforation, or events of opportunistic infection, active tuberculosis, or malignancy. Conclusion: Treatment with UPA for 24 weeks resulted in greater improvements vs PBO in the clinical outcomes of adults with extensive NSV. Observed clinical efficacy continued to improve through week 36 with UPA treatment. UPA was generally well tolerated, with no new safety signals -identified.

Dermatology

Silverberg JI, Eichenfield LF, Hebert AA, Simpson E, **Gold LS**, Bissonnette R, Papp KA, Browning J, Kwong P, Korman NJ, Brown PM, Rubenstein DS, Piscitelli SC, Somerville MC, Tallman AM, and Kircik L. Tapinarof cream 1% once daily: significant efficacy in the treatment of atopic dermatitis in two pivotal phase 3 trials in adults and children down to 2 years of age. *Br J Dermatol* 2024; 190:II17-II18. Full Text

Introduction: Tapinarof cream 1% once daily (QD) demonstrated efficacy versus vehicle and was well tolerated in adults and adolescents with moderate to severe atopic dermatitis (AD) in a previously reported phase 2 trial. Objective: Here, we report pivotal phase 3 efficacy and safety results for tapinarof cream 1% QD in the treatment of adults and children down to 2 years of age with AD. Materials and Methods: ADORING 1 and 2 were two identical phase 3, randomized, double-blind, vehicle-controlled trials. Eligibility criteria included a Validated Investigator Global Assessment for Atopic DermatitisTM (vIGA-ADTM) score of ≥3, Eczema Area and Severity Index (EASI) score of ≥6, and body surface area (BSA) involvement of 5–35%. Patients were randomized 2:1 to receive tapinarof cream 1% or vehicle cream QD for 8 weeks. The primary efficacy endpoint was vIGA-ADTM response, defined as a score of clear (0) or almost clear (1) and ≥2-grade improvement from baseline at Week 8. Secondary efficacy endpoints included ≥75% improvement in EASI score (EASI75) and proportion of patients (aged ≥12 years) with a baseline Peak Pruritus-Numerical Rating Scale (PP-NRS) score of ≥4 who achieved a ≥4-point reduction at Week 8. Adverse events (AEs) included rates of AEs of special interest (AESIs): contact dermatitis, follicular event, and headache. Results: 407 and 406 patients aged 2–81 years were randomized in ADORING 1 and 2, respectively. At baseline, 84.0–89.9% of patients had a vIGA-ADTM score of 3 (moderate), mean EASI score of 12.5–13.3, and mean BSA affected of 16.7–16.9% across trials. At Week 8, both the primary and all secondary efficacy endpoints were met with statistical significance in the tapinarof groups versus vehicle: vIGA-ADTM response rates were 45.4% vs 13.9% and 46.4% vs 18.0% (both P<0.0001); EASI75 response rates were 55.8% vs 22.9% and 59.1% vs 21.2% (both P<0.0001); and a ≥4-point reduction in PP-NRS was achieved by 55.8% vs 34.2% (P=0.0366) and 52.8% vs 24.1% (P=0.0015), in ADORING 1 and 2, respectively. AEs were mostly mild or moderate; the most frequent (≥5% in any group) were folliculitis, headache, and nasopharyngitis. Trial discontinuation rates due to AEs were lower with tapinarof versus vehicle (ADORING 1: 1.9% vs 3.6%; ADORING 2: 1.5% vs 3.0%, respectively). Rates of AESIs with tapinarof versus vehicle were: contact dermatitis 1.5% vs 2.2% and 1.1% vs 1.5%; follicular events 10.0% vs 0.7% and 8.9% vs 1.5%; and headache 7.0% vs 2.2% and 1.5% vs 0%, in each trial, respectively. Conclusions: Tapinarof cream 1% QD demonstrated statistically significant efficacy compared with vehicle for primary and secondary efficacy endpoints in adults and children down to 2 years of age with AD. Tapinarof was well tolerated, with no new safety or tolerability signals. AEs were mostly mild to moderate and led to low rates of trial discontinuation, demonstrating the predictable safety profile of tapinarof cream 1% QD.

Dermatology

Silverberg JI, Guttman-Yassky E, Simpson EL, Papp KA, Blauvelt A, Chu CY, Hong HCH, **Gold LFS**, Bieber T, Kabashima K, Rosmarin D, Gamelli A, Calimlim B, Vigna N, Hu XF, Yang Y, Wu XQ, Huang XH, Suravaram S, Teixeira HD, Raymundo E, and Irvine AD. Efficacy and safety of upadacitinib through 140 weeks in adolescents and adults with moderate-to-severe atopic dermatitis: phase 3 randomized clinical trial results. *Br J Dermatol* 2024; 190:II8-II8. Full Text

Introduction & Objectives: Upadacitinib (UPA) is an oral Janus kinase 1 (JAK1) inhibitor approved in multiple countries for the treatment of adolescents and adults with moderate-to-severe atopic dermatitis (AD). Here, we present the efficacy and safety of UPA administered over 140 weeks in an ongoing randomized, double-blinded, multicenter phase 3 study (Measure Up 1, NCT03569293). Materials & Methods: Patients (12–75 years) with moderate-to-severe AD were randomized 1:1:1 to receive UPA 15 mg (UPA15), UPA 30 mg (UPA30), or placebo (PBO) once daily at baseline. At week 16, PBO-treated patients were re-randomized 1:1 to receive UPA15 (PBO/UPA15) or UPA30 (PBO/UPA30) once daily. Co-primary endpoints were the proportion of patients achieving ≥75% reduction in EASI (EASI 75) from baseline and vIGA-AD of clear (0) or almost clear (1) with ≥2 grades of reduction from baseline (vIGA-AD 0/1) at week 16. A meaningful improvement in itch, defined as a ≥4-point reduction in Worst Pruritus Numeric Rating Scale (ΔWP-NRS≥4), was assessed among patients with baseline WP-NRS≥4. All efficacy endpoints were summarized using the Observed Cases (OC) approach, and no missing data

imputation was applied. Safety was assessed by monitoring of serious adverse events (SAEs), treatment-emergent adverse events (TEAEs), and treatment-emergent adverse events of special interest (AESI), which were analysed as exposure-adjusted rates per 100 patient-years (PY). Results: Efficacy results were sustained up to week 140 since week 16. Proportions of patients in the UPA15 (205), UPA30 (206), PBO/UPA15 (91), and PBO/UPA30 (94) groups achieving EASI 75 at week 140 were 88.8% (182), 90.3% (186), 83.5% (76), and 89.4% (84), respectively, and for vIGA-AD 0/1 was 63.4% (130), 65.5% (135), 60.4% (55), and 75.5% (71), respectively. Proportions of patients achieving an improvement (reduction) in WP-NRS≥4 from baseline at week 140 were 68.0% (136), 70.5% (146), 71.3% (62), and 81.3% (74) respectively. Overall, the rates of AESIs were similar across treatment groups, which aligned with prior reports at earlier time points. Both UPA15 and UPA30 were well-tolerated in all patients, and no new safety signals were observed compared to the known safety profile of UPA. Data from two additional pivotal studies will be available at the time of presentation. Conclusion: In this interim analysis, sustained skin clearance and itch and a consistent safety profile were observed with UPA 15 mg and UPA 30 mg across 140 weeks in adolescent and adult patients with moderate-to-severe AD.

Dermatology

Simpson E, Silverberg J, Bissonnette R, **Gold LS**, Armstrong A, Hebert AA, Serrao RT, Jakus JR, Brown PM, Rubenstein DS, Piscitelli SC, Tallman AM, and Eichenfield LF. Rapid and early onset of itch relief with tapinarof cream 1% once daily in two pivotal phase 3 trials in adults and children down to two years of age with atopic dermatitis. *Br J Dermatol* 2024; 190:II18-II19. Full Text

Introduction: Itch is the most bothersome symptom for patients with atopic dermatitis (AD), with a significant negative impact on health-related quality of life. Rapid onset of pruritus relief with sustained efficacy is a key outcome for AD therapies. In a phase 2 trial in adults and adolescents with moderate to severe AD, tapinarof cream 1% once daily (QD) demonstrated efficacy versus vehicle and was well tolerated. Objective: Here, we evaluate time to onset of itch relief in the pivotal phase 3 trials with tapinarof cream 1% QD in the treatment of adults and children down to 2 years of age with AD. Materials and Methods: In ADORING 1 and 2, two identical, double-blind, vehicle-controlled trials, patients were randomized 2:1 to tapinarof cream 1% or vehicle QD for 8 weeks. Patients with a Validated Investigator Global Assessment for Atopic DermatitisTM score of ≥3, an Eczema Area and Severity Index score of ≥6, and body surface area involvement of 5–35% were included. Efficacy endpoints that evaluated itch relief were mean changes in Peak Pruritus-Numerical Rating Scale (PP-NRS) score (daily and by visit [Weeks 1, 2, 4, and 8]) from baseline through Week 8. The PP-NRS considers a person's worst itch over the past 24 hours, assessed on an 11-point scale (0 indicates "no itch" and 10 is "worst imaginable itch"). Daily PP-NRS scores were recorded in diaries. Patients aged ≥12 years self-completed the PP-NRS, while caregivers completed it for children aged <12 years. Results: 407 and 406 patients were randomized in ADORING 1 and 2. At baseline, mean (standard deviation [SD]) PP-NRS scores were 6.7 (2.4) and 6.8 (2.3) in both trials, respectively. For daily evaluations of itch from baseline, greater reductions in PP-NRS scores (mean [SD]) for tapinarof versus vehicle were observed as early as Day 1, 24 hours after initial application, in ADORING 1 (–1.2 [2.2] vs –0.9 [2.0]) and Day 2 in ADORING 2 (–1.6 [2.4] vs –1.4 [2.1]). Improvements in daily PP-NRS scores (mean [SD]) with tapinarof versus vehicle continued through the first 2 weeks (Day 14; –3.0 [2.8] vs –2.0 [2.4] and –2.9 [2.7] vs –1.8 [2.6]), and through Week 8 of both trials. There were statistically significant and clinically meaningful reductions in mean weekly PP-NRS scores as early as Week 1, the first assessment, for patients treated with tapinarof compared with vehicle (–2.0 vs –1.2 [P<0.0001]) and (–2.0 vs –1.3 [P=0.0010]), in ADORING 1 and 2, respectively. Significantly greater reductions in mean PP-NRS scores with tapinarof versus vehicle were seen for all visits through Week 8 (–4.1 vs –2.6 and –4.1 vs –2.4 [both P<0.0001]), for both trials. Conclusions: Tapinarof cream 1% QD demonstrated rapid, clinically meaningful, and significant onset of pruritus relief as early as 24 hours after initial application compared with vehicle. Improvements in itch with tapinarof cream increased through Week 8 in both trials in adults and children down to 2 years with AD.

Dermatology

Zirwas M, Chovatiya R, **Gold LS**, Shumel B, Praestgaard A, Chen Z, Gonzalez T, Gherardi G, and Lawless E. Conjunctivitis adverse events in dupilumab clinical trials. *Br J Dermatol* 2024; 190:II58-II59. Full Text

Introduction: Dupilumab inhibits signaling of IL-4 and IL-13, key drivers of Type 2 inflammatory diseases such as atopic dermatitis (AD), asthma, chronic rhinosinusitis with nasal polyposis (CRSwNP), eosinophilic esophagitis (EoE), prurigo nodularis (PN), and Chronic Spontaneous Urticaria (CSU). Adults with AD have a significant and disease severity-dependent increased risk of developing ocular surface diseases, including conjunctivitis and keratitis, compared with the general population.3 In randomized placebo-controlled trials of dupilumab in patients with moderate-to-severe AD, more conjunctivitis events were reported in patients who received dupilumab treatment than in placebo-treated patients. Objective: This analysis reviewed the incidence, severity, and resolution of conjunctivitis adverse events (AEs) in patients from clinical trials evaluating dupilumab in AD, asthma, CRSwNP, EoE, PN, and CSU. Methods: "Conjunctivitis" refers to the group of MedDRA Preferred Terms (PTs) that include the term 'conjunctivitis', namely conjunctivitis, allergic conjunctivitis, bacterial conjunctivitis, viral conjunctivitis, adenoviral conjunctivitis, and atopic keratoconjunctivitis. All cases of conjunctivitis were included regardless of etiology (including blepharoconjunctivitis, which was coded as the MedDRA PT conjunctivitis, and excluding blepharitis in the absence of conjunctivitis. This analysis excludes events of keratitis. Randomized, double-blinded, placebo-controlled trials included in this analysis were: Liberty AD Solo 1, Liberty AD Solo 2, Liberty AD Chronos, LIBERTY AD ADOL, LIBERTY AD PEDS, LIBERTY AD PRESCHOOL Part B (AD); Liberty Asthma Quest, Liberty Asthma Venture (asthma); Liberty NP Sinus-24, Liberty NP Sinus-52 (CRSwNP); Liberty EoE Treet (EoE); Liberty PN Prime, Liberty-PN Prime2 (PN); and Liberty-CSU Cupid Part A (CSU). Results: Overall conjunctivitis incidence was higher in patients receiving dupilumab vs placebo in all randomized AD trials, with 7.9% to 19.4% of adult dupilumab-treated patients and 4.8% to 14.8% of dupilumab-treated patients aged 6 months to <18 years experiencing conjunctivitis events. In contrast, conjunctivitis rates were <5% and similar between dupilumab and placebo in the asthma, CRSwNP, EoE, PN, and CSU trials. Most conjunctivitis cases observed in adult patients with AD receiving dupilumab treatment were mild to moderate in severity, with severe conjunctivitis being reported at rates of ≤0.6%. A majority of all conjunctivitis cases in dupilumab-treated adults with AD were resolved during the treatment period. Conclusions: Overall conjunctivitis events were more frequent in dupilumab-treated vs placebo-receiving patients in AD trials across ages, whereas rates were low and similar between dupilumab and placebo groups in the asthma, CRSwNP, EoE, PN, and CSU trials. Most conjunctivitis cases observed in adult patients with AD receiving dupilumab treatment were mild to moderate in severity and resolved by the end of the study period. Current evidence suggests that conjunctivitis associated with dupilumab occurs predominantly in patients with AD. It is possible that pre-existing ocular disorders and a dupilumab–AD disease-specific interaction may be responsible for this increased incidence in dupilumab-treated patients with AD.

Diagnostic Radiology

George M, **Clark J**, **Gartrelle K**, **Nassif G**, **Hartway K**, **Long D**, **Salas-Escabillas D**, **Wombwell A**, **Wen HJ**, **Benitz S**, **Zwernick S**, **Shah R**, **Park H**, **Philip P**, **Khan G**, **Crawford H**, **Theisen B**, **Kwon D**, and **Steele N**. TIGIT expression increases with advancing clinical stages of resected pancreatic cancer. *Ann Surg Oncol* 2024; 31(1):S176-S176. Full Text

Emergency Medicine

Andrews TQ, **Bunch C**, **Basir MB**, and **Miller J**. PYOPNEUMOPERICARDITIS SECONDARY TO ENTERO-PERICARDIAL FISTULA: A RARE ETIOLOGY OF DYSPNEA. *J Am Coll Cardiol* 2024; 83(13):4399. Full Text

Background Entero-pericardial fistulae are rare pathophysiologic communications between the gastrointestinal tract and the pericardium, most often a delayed complication of gastroesophageal surgeries. Despite aggressive multidisciplinary action, mortality rate remains >50%. Case An elderly female with remote history of Roux-en-Y gastric bypass and rheumatoid arthritis requiring chronic steroids presented with acute onset dyspnea. CT chest & esophagram demonstrated pneumopericardium (Figure 1). Esophagogastroduodenoscopy confirmed jejunal-pericardial fistula at the site of an ulcer distal to the gastro-jejunal anastomosis. Decision-making A pericardial drain was urgently placed, and subsequent cultures grew methicillin resistant Staphylococcus aureus (MRSA), Streptococcus parasanguinis, and Actinomyces odontolyticus. The patient underwent fistula take-down and was treated with a three-week course of vancomycin for MRSA and S. parasanguinis pericarditis and discharged with a 6-month course of amoxicillinclavulanate for Actinomyces pericarditis. A 3-month course of aspirin and colchicine was

chosen for empiric coverage of pericarditis. Conclusion Entero-pericardial fistulas are often complicated by pneumopericardium, tamponade, and pericarditis that require prompt source control, broad spectrum antimicrobial coverage, and cardiovascular support. Despite multidisciplinary action and aggressive surgical and medical management, mortality remains high. [Formula presented]

Emergency Medicine
Fadel R, **Miller J**, **Cook B**, **Nguyen F**, **Alqarqaz M**, **Fuller B**, **Basir MB**, **Frisoli TM**, **Villablanca PA**, **Jabri A**, **Alaswad K**, **Khandelwal AK**, **Lingam N**, **O'Neill BP**, **Kim HE**, **Pielsticker EJ**, **Koenig GC**, Mills NL, and Mahler SA. THE INCIDENCE OF UNSTABLE ANGINA IN PATIENTS WITH LOW HIGH-SENSITIVITY TROPONIN I VALUES: A SUBGROUP ANALYSIS OF THE RACE-IT TRIAL. *J Am Coll Cardiol* 2024; 83(13):1268. Full Text

Background We sought to identify the incidence of unstable angina in patients with low high-sensitivity cardiac troponin I (hs-cTnI) in Emergency Departments (EDs). Methods This was a preplanned secondary analysis of the Rapid Acute Coronary Syndrome Exclusion using high-sensitivity I cardiac Troponin (RACE-IT) stepped-wedge randomized trial, which compared two rule-out protocols (0/1-hour and 0/3-hour) for myocardial infarction (MI) in 9 EDs from 7/2020-3/2021. A hs-cTnI assay from Beckman Coulter was used (99th percentile 18 ng/L). In the accelerated protocol (AP), MI was excluded if hs-cTnI was <4 ng/L at presentation, or =4 ng/L at presentation with a 1-hour value <8 ng/L. Those that did not rule-out within 1 hour required a 3-hour hs-cTnI ≤18 ng/L to rule-out. In the standard care (SC), MI was excluded if hs-cTnI values were ≤18 ng/L at 0 and 3 hours. Patients were excluded if hs-cTnI was >18 ng/L within 3 hours of presentation. Unstable angina was adjudicated based on the ISCHEMIA trial definition, which required electrocardiographic changes or findings at coronary angiography (ruptured/ulcerated plaque or thrombus). Adjudication was performed by interventional cardiologists for patients undergoing coronary angiography, and by cardiology fellows in patients with hs-cTnI >18 ng/L >3 hours after presentation. Results Of the 32,608 patients in the trial, 58 patients (0.18%) met the definition of unstable angina (35 in the AP and 23 in the SC protocol). In the AP 12/35 (34.3%) patients with unstable angina had a presenting hs-cTnI <4 ng/L. In the AP, among patients who ruledout for MI within 1 hour, 13/10444 (0.12%) had unstable angina vs. 22/8659 (0.25%) among those who did not meet early rule-out criteria (adjusted odds ratio 0.73, 95% CI 0.33 - 1.60, p=0.43). Within 30 days there were 113 (0.35%) patients in the entire cohort who had a revascularization procedure and in the unstable angina group there were 38 (65.5%). Conclusion Unstable angina is rare in patients with a low hs-cTnI values at presentation to the ED and few receive revascularization procedures. However, of those ultimately diagnosed with unstable angina in the AP, a substantial portion had an extremely low hs-cTnI at presentation.

Emergency Medicine
Smith N, **Ezell G**, **Condon M**, **Joyce K**, **Joseph J**, and **Pitts DS**. 844 Timeliness of diagnosis and treatment of postpartum hypertensive disorders in the Emergency Department. *Am J Obstet Gynecol* 2024; 230(1):S448. Full Text

Objective: This study aims to assess the time to diagnosis and treatment of hypertensive disorders during the postpartum period in the Emergency Department, particularly focusing on potential disparities in care and identify areas for quality improvement. Study Design: The study was conducted at a multi-centered large medical institution in the metro-Detroit area, analyzing postpartum ED visits from November 2015 to December 2022. The primary analysis focused on the time elapsed between severe range blood pressure readings and the administration of antihypertensives. Secondary analyses included the presence of essential laboratory work up such as complete blood count, complete metabolic panel, urine protein and creatinine. Results: Among the 430 women who presented to the ED during the postpartum period with hypertension, 72.6% had preeclampsia with severe features, and 13% had chronic hypertension with superimposed severe preeclampsia. Of the patients with severe hypertension, only 72% received a complete blood count, 66% underwent evaluation of creatinine and liver profile, and 4% had a urine protein ordered. The average time from severe range blood pressure to antihypertensive administration was 189 minutes for Black patients and 370 minutes for White patients. There were no statistically significant differences in the time of first blood pressure reading, laboratory evaluation, or treatment of severe range blood pressure between racial groups. Conclusion: This study identified the most significant area for improvement in the timely administration of antihypertensive medication following severe range

blood pressure readings. Additional areas for improvement were observed in ordering essential laboratory tests to assess the severity of preeclampsia. Surprisingly, our institution demonstrated equal expeditious care for both white and black patients, contrary to existing literature indicating potential disparities. Based on these findings, a targeted quality improvement plan will be implemented to enhance the identified areas of concern.

Hematology-Oncology
Alhushki SK, Al-Bzour AN, Al-Bzour NN, Abushukair HM, and **Rous FA**. A comprehensive analysis of the molecular landscape of HER3 expression in adenocarcinoma of the lung. *ESMO Open* 2024; 9. Full Text

Background: HER3, a member of the epidermal growth factor family, is aberrantly expressed in lung cancer. It is a promising target for treatment with many antibody-drug conjugates (ADCs) developed, including Patritumab deruxtecan. In our study we aim to evaluate the difference between HER3 high and low groups based on a comprehensive multiomics analyses. Methods: We utilized The Cancer Genomic Atlas lung adenocarcinoma (LUAD) project data. Clinical, histopathological, genomic, and proteomic data for 599 LUAD patients was retrieved through the cBioPortal database. Patients with the highest and lowest 25% HER3 mRNA expression were grouped into the high- and low-HER3 groups, respectively. Differential gene expression analysis was conducted using the DESeq2 R package and enrichment analysis for upregulated genes was done using the gene ontology (GO) and KEGG pathways libraries. Results: LUAD patients with mRNA expression data (n=510) were grouped into high-HER3 (Z-score: 3.11-7.25, n=128) and low-HER3 (Z-score: -20.47-0.23, n=127). High-HER3 patients had a trend for higher age (68.0 vs. 63.0, p=0.052) compared to the low-HER3 group. Overall survival and progression-free survival were not significantly different between the two groups. Mutational analysis showed that KRAS, STK11, and CDKN2B were more commonly mutated in the high-HER3 group, whereas mutations in TP53, PCDHB8, CDK12, and CD274 (PD-L1) were more common in the low-HER3 group. In terms of mRNA expression, immune checkpoint genes such as PDCD1, CD274, CTLA4, and LAG3 were more expressed in low-HER3 group. Moreover, immune infiltration analysis using CIBERSORT algorithm showed significantly higher levels of CD4+ activated memory T cells and M1 macrophages in the low-HER3 group. The enriched pathways in the low-HER3 group were related to ‘CXCR chemokine receptor binding’, ‘TNF signaling’, and ‘IL-17 signaling’ pathways. Conclusions: Low-HER3 patients might experience improved responses to immunotherapy due to higher expression of immune checkpoint genes and higher infiltration of immune cells. High-HER3 patients had more KRAS mutations which could be a target for combination therapy in addition to HER3 ADCs. Legal entity responsible for the study: The authors. Funding: Has not received any funding. Disclosure: All authors have declared no conflicts of interest.

Hematology-Oncology
George M, **Clark J**, **Gartrelle K**, **Nassif G**, **Hartway K**, **Long D**, **Salas-Escabillas D**, **Wombwell A**, **Wen HJ**, **Benitz S**, **Zwernick S**, **Shah R**, **Park H**, **Philip P**, **Khan G**, **Crawford H**, **Theisen B**, **Kwon D**, and **Steele N**. TIGIT expression increases with advancing clinical stages of resected pancreatic cancer. *Ann Surg Oncol* 2024; 31(1):S176-S176. Full Text

Hematology-Oncology
Hummel HD, Champiat S, Garcia MEO, Boyer M, He K, Steeghs N, Izumi H, Johnson ML, Yoshida T, Bouchaab H, Dowlati A, Borghaei H, Felip E, Jost PJ, **Gadgeel S**, Chen X, Yu Y, Martinez P, Parkes A, and Paz-Ares L. 195MO Tarlatamab in previously treated small cell lung cancer (SCLC): DeLLphi-300 phase I study long-term outcomes and intracranial activity. *ESMO Open* 2024; 9. Full Text

Background: Tarlatamab, a bispecific T cell engager (BiTE®) immunotherapy targeting delta-like ligand 3 (DLL3), showed durable antitumor activity and manageable safety in previously treated SCLC. Here we report long-term outcomes and intracranial activity from the DeLLphi-300 phase I study. Methods: Tarlatamab was evaluated in patients (pts) with previously treated SCLC. Pts with treated, stable brain metastases were eligible. Primary endpoint was safety. Secondary endpoints included objective response rate (ORR) per mRECIST 1.1 by investigator, duration of response (DOR), progression-free survival (PFS), and overall survival (OS). In retrospective exploratory analyses, CNS tumor sum of diameters (SOD) was assessed per mRANO-BM by BICR in pts with ≥ 1 brain lesion at baseline. This report, with

data cutoff (DCO) 14.5 months (mos) beyond Paz-Ares, J Clin Oncol 2023, includes fully enrolled cohorts of pts treated with clinically relevant doses (≥ 10 mg) of tarlatamab. Results: 152 pts were treated with tarlatamab ≥ 10 mg (follow-up range 0.2–34.3 mos; median 12.1 mos). Across cohorts, ORR was 25.0% with mDOR of 11.2 mos (table). 25 pts had treatment duration ≥ 52 weeks (range 52–150), including 8 pts treated ≥ 104 weeks. mPFS and mOS were 3.5 mos and 17.5 mos, respectively, with PFS and OS estimates at 12 mos of 16.7% and 57.9%. Of 16 pts with a baseline CNS lesion ≥ 10 mm, CNS tumor SOD decreased ≥ 30% in 10 pts (62.5%). Of 8 pts who completed brain radiotherapy (RT) ≥ 50 days before tarlatamab initiation, 3 pts (37.5%) had ≥ 30% decrease in CNS tumor SOD. No new safety signals were identified. [Formula presented] Conclusions: In longer follow-up of DeLLphi-300, tarlatamab demonstrated durable responses and unprecedented survival outcomes in previously treated SCLC. While limited to analyses of treated, stable brain metastases, CNS tumor shrinkage following tarlatamab therapy and long after RT supports further study of intracranial efficacy of tarlatamab. Clinical trial identification: NCT03319940.

Hematology-Oncology
Kulkarni R, **Gonzalez LF**, **Lin CH**, **Rose C**, **Emole J**, **Alavi A**, **Peres E**, **Abidi MH**, and **Farhan S**. Standard Risk Assessment Tools Fall Short to Assess Risk in Transplant Patients. *Transplantation and Cellular Therapy* 2024; 30(2):S125. Full Text

L.F. Gonzalez, Hematology-Oncology, Henry Ford Hospital, Detroit, MI, United States

Introduction: The HCT-CI (Hematopoietic Cell Transplantation-specific Comorbidity Index) and the Disease Risk Index (DRI) Assessment Tool are models used for pre-transplant risk assessment. HCT-CI ≥3 is associated with higher non-relapse mortality (NRM) and lower overall survival (OS). The DRI was developed to predict overall survival per disease status. Objectives: This retrospective study was done to understand reasons for increased mortality in transplant patients at our center in 2021 compared to 2020 by comparing HCT-CI and DRI of transplant patients between the two years. Methods: This was an IRB-approved study. Relevant patient comorbidities, disease characteristics, and transplant-related data were collected. Patients were risk stratified using the online DRI Assessment Tool. Data was analysed using R version 4.3.1, and a p-value less than 0.05 was considered statistically significant. Results: A total of 165 transplants were reviewed. Patient characteristics are elucidated in Table 1. Mean age at HCT in 2020 was 59.8 and 59.3 in 2021. Allogeneic HCT was done in 38.4% of HCT in 2020 and 37% in 2021. HCT-CI was ≥3 in 68.5% in 2020 and 70.7% in 2021. DRI was high or very high in 20.5% patients in 2020 and 20.6% in 2021. The 2-year OS of Allo HCT was worse in 2021 compared to 2020 although not statistically significant (50.6% vs. 57.7% respectively, p=0.52, figure 1 A). The cumulative incidence of relapse in Allo HCT at year 1 and 2 were significantly less in 2021 compared to 2020 (Table 2). However, there was a numerically higher incidence of non-relapse mortality (Table 2 and Figure 1 B). The hazard for NRM for patients who underwent Allo HCT was 2.89 compared to Auto (p=0.046). The hazard for relapse for patients with high DRI was 4.24 (p<0.001) times relative to patients with low DRI, controlling for year, HCT type, HCT-CI, and demographics. The hazard for NRM for patients with high DRI was 2.60 (p=0.070), however 16 patients (12 in 2021 and 4 in 2020) were excluded from this analysis as they underwent transplants for diseases that are currently not included in the DRI assessment tool. These included aplastic anemia (AA), inherited bone marrow failure syndromes (BMF), solid tumors, primary CNS lymphomas, mycosis fungoides and hemophagocytic lymphohistiocytosis (HLH). Of these 8 patients, 7 died due to causes other than disease relapse. Conclusion: In this small single-center retrospective analysis, 2021 has statistically significant less relapse by second year with a trend towards higher NRM and worse OS in 2021 (though not statistically significant, possibly limited by sample size). The DRI or another tool however could not be used in those patients. Most predictive models are mainly applied to hematological malignancies, but are not specific for inherited or acquired BMF disorders, HLH or solid tumor malignancies. We sent a proposal to CIBMTR for further consideration to help with this unmet need.

Hematology-Oncology
Wobig R, **Bensenhaver JM**, **Thaker H**, **Joliat C**, **Schwartz TL**, **Lehrberg AV**, **Dalla Vecchia LK**, **Nathanson SD**, **Susick LL**, **Springer K**, **Petersen LF**, and **Ali H**. Upstaging from cT1 to pT2 in Triple Negative and Her2 Positive Breast Cancer: an Opportunity to Identify cT1 Breast Cancer Patients for

whom Neoadjuvant Chemotherapy Should be Considered. *Ann Surg Oncol* 2024; 31(1):S109-S109. Full Text

Hematology-Oncology
Wu M, Khan A, **Peres E**, **Emole J**, **Alavi A**, **Abidi MH**, **Reddy M**, and **Farhan S**. Engraftment Day Electrolytes and Hydration and the Risk of Atrial Fibrillation Early after Hematopoietic Stem Cell Transplant. *Transplantation and Cellular Therapy* 2024; 30(2):S133. Full Text

M. Wu, Wayne State University, DETROIT, MI, United States

Background: Atrial fibrillation (AF) in hematopoietic stem cell transplant (HSCT) recipients is associated with significant morbidity. We have previously reported that obstructive sleep apnea (OSA), older age and presence of dilated left atrium (LA) are significant predictors of AF early post HSCT. In the current study, we sought to evaluate if TSH pre HSCT and serum electrolytes and eGFR at engraftment in patients undergoing HSCT are associated with increased risk of AF. Methods: This is a single center retrospective study, involving 748 consecutive patients undergoing autologous and allogenic HSCT from 2012 to 2022. Patients' charts were reviewed to acquire clinical information (age, gender, HTN, body mass index [BMI], Obstructive sleep apnea [OSA], TSH, and LA volume index that was obtained from pre-HSCT echocardiogram, in addition to potassium [K], magnesium [Mg], and GFR at time of engraftment [ENG]). Results: For the 748 patients, the median age at HSCT was 61. Majority of patients were male (57%). Most common diagnoses were Myeloma (42.5%), acute leukemia (19.5%), lymphoma (19.5%), myelodysplastic syndromes and myeloproliferative neoplasms (11%). A total of 116 (15.5%) patients developed AF early post-HSCT. AF patients' mean LA measurement was 37.3ml/m2, whereas non-AF patients' mean measure was 30.6ml/m2 (P-value: 0.002). For age at HSCT, AF patients' mean was 62.4 years old and non-AF patients' mean was 57.4 years old (P-value: <0.001). OSA diagnosis, 39 (29.5%) of AF patients had OSA and 67 (11.3%) of non-AF patients had OSA (P-value: <0.001). At time of ENG, AF patients had higher mean K of 4.1 (P-value: 0.001) and lower mean GFR of 81.1 (P-value<0.001) versus non-AF patients with mean K of 3.7 and GFR of 94.3. In the multivariable regression analysis, larger LA size (P-value: 0.016), older age at HSCT (P-value: 0.001), diagnosis of OSA (P-value: <0.001), and higher K (P-value: 0.010) and lower GFR (P-value: 0.007) at ENG were significant predictors of AF. Male gender, HTN, BMI, use of ATG or Melphalan based chemotherapies, pre-HSCT TSH, and Mg at ENG were not predictive of AF post-HSCT (table 1). Conclusion: In our single center retrospective study, we found that compared to patients who did not develop AF early post-HSCT, the AF patients, in addition to having dilated LA, being older and more OSA, surprisingly they had higher K and lower GFR at day of ENG. A limitation of our study is the diagnosis of OSA, which sometimes was not supported with a sleep study or diagnosis came from an external practitioner. Another limitation of our study would be the fluctuations in electrolytes around time of engraftment and overhydration due to IV fluids during the inpatient stay. Further research is needed to develop a risk calculator to identify high risk patients and study the effects of prophylactic therapies on the incidence of post-HSCT AF.

Internal Medicine
Almajed MR, **Almajed A**, **El-khatib L**, **Modi K**, **Zweig B**, and **Rao A**. LOEFFLER ENDOCARDITIS PRESENTING AS RECURRENT CARDIOEMBOLIC STROKES. *J Am Coll Cardiol* 2024; 83(13):2990. Full Text

Background Loeffler endocarditis (LE) describes endomyocardial disease due to eosinophilic infiltration in hypereosinophilic syndrome (HES). Rarely, valvular disease occurs, in some cases acting as a nidus for thromboembolism. Case A 77-year-old woman presented with acute right-sided visual loss. History was notable for asthma, rhinosinusitis, and a cryptogenic stroke four months earlier. Laboratory workup showed eosinophilic leukocytosis and elevated inflammatory markers. Infectious workup was unremarkable. Head imaging demonstrated multiple strokes of variable age and distributions, concerning for cardioembolic stroke. Transesophageal echocardiography revealed mitral valve disease consistent with HES causing LE. [Formula presented] Decision-making Our patient met diagnostic criteria for idiopathic HES with persistent eosinophilia and organ involvement. She was managed with steroids and anticoagulation with warfarin to reduce the risk of recurrent stroke. Definitive management in LE with mitral valve disease is surgical valve replacement, biological valves are preferred due to less valve

thrombosis. Our patient was deemed not a surgical candidate, she was planned for future reconsideration if recurrent strokes occur. Six months later, she had no further strokes and echocardiography showed stable mitral valve disease. Conclusion LE is managed with eosinophilia suppression, therapeutic anticoagulation for thromboembolism management, and surgical valve replacement for valvular disease.

Internal Medicine

Almajed MR, **Almajed A**, **Khan N**, **Major J**, and **Ananthasubramaniam K**. INHERITED PREDILECTION TO SPONTANEOUS CORONARY ARTERY DISSECTION: A CASE ASSOCIATED WITH ALPK3 MUTATION. *J Am Coll Cardiol* 2024; 83(13):3387. Full Text

Background Spontaneous coronary artery dissection (SCAD) is a rare cause of ACS that involves spontaneous separation of the coronary artery walls that is not traumatic or iatrogenic. SCAD results in an intramural hematoma that obstructs the arterial lumen causing myocardial ischemia and infarction. Etiology is multifactorial involving an arteriopathy that is compromised by a pathophysiologic stressor. Young women are more commonly affected. Associations have been drawn with fibromuscular dysplasia, connective tissue disorders, and genetic mutations such as ALPK3. Case A 51-year-old woman with hypertension presented with typical angina. She had no history of CAD, and a Coronary CTA reported a coronary calcium score of zero. HsTnI was 897 ng/L and BNP was 37 pg/mL. Electrocardiogram showed lateral lead ST-segment elevation. Emergent invasive coronary angiography for STEMI demonstrated spontaneous coronary artery dissection of the right posterior descending artery with distal embolization. The coronary arteries were notably tortuous and without atherosclerosis. Echocardiogram revealed an LV EF of 65% with mid-distal apical wall hypokinesis. Decision-making Our was diagnosed with STEMI secondary to SCAD. Coronary artery intervention was not performed. She was medically managed with aspirin, statin, beta-blocker, and angiotensin-converting-enzyme inhibitor therapy with symptom resolution. Further SCAD evaluation was performed with CTA to evaluate for fibromuscular dysplasia which was negative for an arteriopathy. A genetic analysis revealed a significant mutation in the ALPK3 gene which in recent studies has been associated with SCAD. Conclusion We describe a case of SCAD associated with an ALPK3 genetic mutation in the absence of other associations. This highlights the importance of including genetic analysis in the evaluation of patients presenting with SCAD for patients with SCAD to further our understanding of this condition and identify patients who could benefit from monitoring and medical management. Further studies are necessary to assess whether routine genetic screening and vascular imaging of first-degree relatives in gene positive patients is beneficial.

Internal Medicine

Almajed MR, **Almajed A**, **Viacava RAC**, **Antishin S**, **Saleem A**, **Wexler B**, and **Hudson MP**. COLLISION CARDIOMYOPATHY: BLUNT CARDIAC INJURY IN THE SETTING OF A MOTOR VEHICLE ACCIDENT. *J Am Coll Cardiol* 2024; 83(13):3233. Full Text

Background Blunt cardiac injury (BCI) encompasses a spectrum of myocardial disease secondary to blunt thoracic trauma (BTT). Patients develop arrhythmias, valvular injury, chamber rupture, and myocardial infarction. BCI can be asymptomatic or present as chest pain, dyspnea, or sudden death. Electrocardiogram is the most sensitive initial testing modality for BCI. Abnormal findings include ectopic beats, conduction defects, atrial fibrillation, and ventricular fibrillation. Further testing including cardiac biomarkers and echocardiography are recommended in patients with an abnormal initial workup. Case A 62-year-old man with hypertension presented after being struck by a vehicle while riding his bicycle. Prior to this, he performed a labor-intensive job and had no symptoms. During the accident, he was ejected off his bicycle causing him to land on the ground with impact to his anterior chest. Trauma evaluation for injuries was notable for lumbar midline and paraspinal back tenderness without other overt signs of trauma. Imaging revealed an acute lumbar spine fracture that did not require surgical intervention. EKG showed a NSR with frequent ectopic ventricular beats; telemetry monitoring revealed a high ectopic burden. Cardiac biomarkers were abnormal with a hsTnI peak of 28 ng/L and high BNP of 178 pg/mL. Echocardiogram was significant for an LV EF of 40%. Decision-making Our patient was found to have cardiac dysfunction in the setting of BTT without overt signs or symptoms of heart failure. His constellation of ventricular ectopy and a reduced LV EF were concerning for BCI. Ischemic evaluation with a Coronary CTA showed minimal non-obstructive CAD, thereby ruling out ischemia. Medical management for HFrEF with GDMT including a beta-blocker resulted in a significant decrease in

ventricular ectopy. He was discharged with plans for ambulatory cardiac monitoring and Cardiac MRI for further cardiomyopathy evaluation. Conclusion BCI is a clinical diagnosis made in patients with newly identified cardiac dysfunction in the setting of BTT. Since no diagnostic criteria exists, high clinical suspicion and extensive workup is necessary in this population to exclude alternative etiologies.

Internal Medicine
Almajed MR, **Chao S**, **Rothstein-Costris A**, **Patton J**, and **Rao A**. INVADING THE VENTRICLE: MASSIVE RIGHT VENTRICULAR METASTASIS FROM RENAL CELL CARCINOMA. *J Am Coll Cardiol* 2024; 83(13):3512. Full Text

Background Cardiac tumors are rare, the majority of which are secondary metastatic tumors rather than primary cardiac tumors. Cardiac metastases confer a poor prognosis through mass-effect on vital cardiac structures and chambers. Case A 63-year-old woman with clear-cell renal cell carcinoma (RCC) treated with immunotherapy underwent cardiac risk stratification prior to a spinal debulking surgery. She had extensive tumor involvement of the renal vein and inferior vena cava with metastases to the lungs and spine. EKG showed a new RBBB. Echocardiogram was subsequently obtained and revealed significant right ventricular dysfunction with a homogenous hyperechoic echodensity in the mid-apical RV. Chest CT showed a 7 x 3 x 5 cm mass in the RV extending from the tricuspid valve to the apex. Cardiac MRI defined this mass as characteristic of cardiac metastasis with foci of tumor thrombi. [Formula presented] Decision-making Our patient's large metastatic tumor to the RV resulting in cardiac dysfunction necessitated urgent treatment. Evaluation by cardiac surgery deemed the tumor unresectable and she was deemed to have prohibitive risk to undergo surgery for her spinal metastases. Despite several lines of immunotherapy, no curative treatments available and she was recommended a palliative approach which she opted for. Conclusion Cardiac metastases confer a poor prognosis. Curative treatment is typically dependent on systemic therapy with chemotherapy and immunotherapy as surgical resection is often not possible.

Internal Medicine
Almajed MR, **Khan N**, **Heil H**, **Wexler B**, **Antishin S**, **Saleem A**, **Mohammed M**, and **Hudson MP**. TICKING TIME BOMB: CORONARY ARTERY ANEURYSM THROMBOSIS IN A PATIENT WITH MARFAN SYNDROME. *J Am Coll Cardiol* 2024; 83(13):2720. Full Text

Background Coronary artery aneurysm (CAA) in adults is associated with Marfan syndrome (MFS), connective tissue disorders, and vasculitides. CAA are at risk for thrombosis which obstructs coronary flow resulting in myocardial infarction. Case A 56-year-old man with MFS and prior aortic-root replacement presented with several hours of typical angina. Workup revealed a hsTnI elevation to 16211 ng/L and inferior lead T-wave inversions. He was medically managed for ACS. Invasive coronary angiography showed diffuse severe aneurysmal disease involving all coronary arteries; the distal-RCA was poorly visualized with contrast pooling in the aneurysmal mid-RCA, suggestive of aneurysm thrombosis causing coronary occlusion. No intervention was performed. Decision-making Our patient's extensive CAA predisposed him to RCA aneurymsla thrombosis, resulting in coronary occlusion. Coronary CTA confirmed CAA up to 2.3 cm in the distal RCA with a thrombosed fusiform aneurysm. Literature on revascularization in such cases is limited. Since our patient's symptoms resolved without intervention, he was managed for NSTEMI and maintained on therapeutic anticoagulation with a Vitamin K Antagonist to reduce the risk of coronary artery thrombosis. [Formula presented] Conclusion CAA is a lesser-known complication of MFS. It confers high morbidity and mortality due to the risk of aneurysm thrombosis. Dedicated imaging to screen for and monitor CAA in this patient population could be useful to prevent disease progression.

Internal Medicine
Almajed MR, **Mittal A**, **Ama S**, **Muhammad N**, and **Michaels AT**. SPECTRUM OF SYNTHETASE SHORTAGE: FAMILIAL CARDIOMYOPATHY DUE TO TMEM70 ATP SYNTHASE DEFICIENCY. *J Am Coll Cardiol* 2024; 83(13):3205. Full Text

Background Mitochondrial encephalocardiomyopathy involves mitochondrial degeneration due to genetic mutations in the TMEM70 gene, resulting in ATP synthase deficiency. Initial reports described neonatal

presentations with a poor prognosis and short lifespan. However, recent studies describe a spectrum of disease as some patients survive to adulthood with cognitive impairment, hypotonia, and cardiomyopathy. Case A 25-year-old man presented with new-onset decompensated heart failure. Family history was significant for cardiomyopathy with end-stage heart failure in early life. His paternal grandfather died at the age of 40; he had ten children, eight died from heart failure between the ages of 25 to 40. Echocardiogram demonstrated a left ventricular ejection fraction of 15% with diastolic dysfunction and severe aortic insufficiency. Right-heart catheterization revealed elevated filling pressures. Invasive coronary angiography revealed normal coronary arteries. Cardiac magnetic resonance imaging showed severe biventricular dilation and a bicuspid aortic valve, there was no evidence of inflammatory or infiltrative cardiomyopathy. Decision-making Our patient was medically managed for heart failure. Despite this, he developed cardiogenic shock refractory to inotropic therapy and underwent mechanical circulatory support (MCS) with extra-corporeal membrane oxygenation. A heart team determined him to be a candidate for durable MCS implantation with a destination therapy left-ventricular assist device (LVAD). He underwent surgical LVAD implantation and aortic valve replacement (AVR). Genetic testing identified a pathogenic variant in TMEM70 that is associated with autosomal recessive ATP synthase deficiency, a cause of mitochondrial encephalocardiomyopathy. Conclusion We report a case of a 25-year-old man with end-stage heart failure who was managed with LVAD and AVR. Genetic testing identified a mutation in the TMEM70 gene to be the likely cause of his familial cardiomyopathy. This case demonstrates the role of advanced therapies in the treatment of genetic cardiomyopathy and the importance of identifying the etiology to assist with counseling.

Internal Medicine

Almajed MR, **Saleem A**, **Wexler B**, **Patton J**, **Villablanca PA**, and **Rabbani B**. RECIPE FOR DISASTER: PROSTHETIC AORTIC VALVE FAILURE, BETA-BLOCKERS, AND CALCIUMCHANNEL BLOCKERS. *J Am Coll Cardiol* 2024; 83(13):2996. Full Text

Background Beta-blocker (BB) therapy is discouraged in patients with AR as negative chronotropy prolongs diastole thereby increasing regurgitant volume. Coadministration of BB and nondihydropyridine calcium channel blocker (CCB) results in profound negative chronotropy causing symptomatic bradycardia and heart block. Treatment of BB and CCB toxicity includes intravenous fluids, atropine, glucagon, vasopressors, and inotropes. Case A 75-year-old man presented with syncope. His history was notable for CAD for which he underwent LCx stenting two weeks prior and IE for which he underwent SAVR. He had inadvertently taken higher doses of both BB and nondihydropyridine CCB an hour before symptom onset. He was found to be hypothermic, bradycardic, and in undifferentiated shock that did not respond to initial resuscitation. Due to concern for medication overdose, he was treated with atropine, glucagon, and calcium with minimal response; initiation of continuous epinephrine resolved his shock state. Upon reevaluation, he reported exertional dyspnea and was noted to have an early diastolic murmur. Echocardiogram revealed severe insufficiency of the prosthetic aortic valve (AV) with a flail left coronary cusp leaflet and pressure half time of 132 ms. Invasive coronary angiography revealed a patent LCx stent and non-obstructive CAD. Decision-making Our patient's presentation in shock was initially concerning for toxicity associated with the accidental use of both a BB and nondihydropyridine CCB. Further workup revealed that the patient's underlying prosthetic AV failure with severe AI predisposed him to this decompensation. A heart team deemed him high-risk for SAVR, therefore, our patient underwent valve-in-valve TAVR. Conclusion Overdose of BB and nondihydropyridine CCB represents a fatal adverse event involving commonly prescribed medications. Patients with cardiac dysfunction, such as our patient with severe AI, are at increased risk of intolerance of these medications. In our patient with severe symptomatic AI of a prosthetic valve, definitive treatment is aortic valve replacement.

Internal Medicine

Andrews TQ, **Bunch C**, **Basir MB**, and **Miller J**. PYOPNEUMOPERICARDITIS SECONDARY TO ENTERO-PERICARDIAL FISTULA: A RARE ETIOLOGY OF DYSPNEA. *J Am Coll Cardiol* 2024; 83(13):4399. Full Text

Background Entero-pericardial fistulae are rare pathophysiologic communications between the gastrointestinal tract and the pericardium, most often a delayed complication of gastroesophageal surgeries. Despite aggressive multidisciplinary action, mortality rate remains >50%. Case An elderly

female with remote history of Roux-en-Y gastric bypass and rheumatoid arthritis requiring chronic steroids presented with acute onset dyspnea. CT chest & esophagram demonstrated pneumopericardium (Figure 1). Esophagogastroduodenoscopy confirmed jejunal-pericardial fistula at the site of an ulcer distal to the gastro-jejunal anastomosis. Decision-making A pericardial drain was urgently placed, and subsequent cultures grew methicillin resistant Staphylococcus aureus (MRSA), Streptococcus parasanguinis, and Actinomyces odontolyticus. The patient underwent fistula take-down and was treated with a three-week course of vancomycin for MRSA and S. parasanguinis pericarditis and discharged with a 6-month course of amoxicillinclavulanate for Actinomyces pericarditis. A 3-month course of aspirin and colchicine was chosen for empiric coverage of pericarditis. Conclusion Entero-pericardial fistulas are often complicated by pneumopericardium, tamponade, and pericarditis that require prompt source control, broad spectrum antimicrobial coverage, and cardiovascular support. Despite multidisciplinary action and aggressive surgical and medical management, mortality remains high. [Formula presented]

Internal Medicine

Andrews TQ, **Hana A**, **Lee JC**, and **Frisoli TM**. TRANSCATHETER MITRAL VALVE-IN-VALVE IN RING WITH VENTRICULAR SEPTAL DEFECT OCCLUDER ASSIST FOR PERIVALVULAR LEAK. *J Am Coll Cardiol* 2024; 83(13):4233. Full Text

Background Mitral ring annuloplasty failure is uncommon, however, ring dehiscence accounts for 42% of occurrences and allows for detrimental mitral regurgitation (MR). Transcatheter mitral valve replacement (TMVR) has been described as an effective treatment for ring annuloplasty failure with trans-ring and para-ring MR. Case An 86-year-old male with medical history of severe MR post incomplete ring annuloplasty presented with three months of progressive dyspnea. Transesophageal echocardiogram (TEE) demonstrated severe eccentric MR at P2 and originating focally at the site of ring dehiscence from the native mitral annulus. Decision-making Given comorbid conditions and re-do sternotomy status, minimally invasive management was pursued. A transcatheter edge-to-edge repair was aborted due to mitral anatomical limitations. Following, a 29 mm valve was deployed without significant resolution of perivalvular leak (PVL). An additional 29 mm valve was placed with persistent PVL in the posterolateral annulus of the dehisced annuloplasty ring. Ultimately, three ventricular septal defect occluders were placed (8mm and two 10mm) within the dehisced area to completely abolish the PVL. Conclusion TMVR has been described as an effective, minimally invasive option for mitral ring annuloplasty failure. However, incomplete annular apposition in TMVR remains a procedural complication. Small caliber ventricular septal occluder devices may serve as a sufficient adjuvant implant for persistent PVL. [Formula presented]

Internal Medicine

Ayyad A, **Halboni A**, **Al-suraimi A**, and **Peterson K**. TROJAN HEARTBEATS: ACUTE MYELOID LEUKEMIA DISGUISED AS ACUTE CORONARY SYNDROME. *J Am Coll Cardiol* 2024; 83(13):4371. Full Text

Background Leukostasis, a manifestation that affects 15% of acute myeloid leukemia (AML) patients, with rare cardiac involvement including myocardial ischemia, arrhythmias, and pericarditis. We discuss an AML case resembling acute coronary syndrome (ACS) due to leukostasis-induced myocardial ischemia. Case A 52-year-old female, presents to the ED with acute chest pain. EKG indicated t-wave inversions in leads II, V5, V6 and 1 mm ST elevations in leads 1, aVL. Troponins surged to 371 ng/L. Laboratory findings highlighted WBC at 211,000 cell/uL, constituting 83% blasts. Peripheral smear revealed a diagnosis of acute myeloid leukemia (AML) accompanied by pronounced leukocytosis. Decision-making An echocardiogram was performed and revealed a normal left ventricular function without wall motion abnormalities. Furthermore, a coronary angiography showed no evidence of obstructive pathologies or stenotic lesions. In light of the newly established diagnosis of AML, in conjunction with a pristine echocardiogram and a normal coronary angiography, leukostasis was identified as the trigger for the ACS. Immediate leukapheresis and Hydroxyurea administration led to a WBC count reduction to 30,000 cells/μL, subsequently alleviating the angina and EKG changes. [Formula presented] Conclusion ACS can be a rare presentation of AML. Prompt leukapheresis can effectively clear microvascular blockages. Our experience with this patient highlights the importance of recognition of an uncommon presentation of acute leukemia.

Internal Medicine
Ellauzi R, Hamza I, Ismayl M, Ellauzi H, and Kumar A. RACIAL DISPARITIES IN THE USE AND OUTCOMES OF EXTRA-CORPOREAL MEMBRANE OXYGENATION FOR HIGH-RISK PULMONARY EMBOLISM. *J Am Coll Cardiol* 2024; 83(13):505. Full Text

Background In high-risk pulmonary embolism (PE) patients experiencing cardiogenic shock, temporary mechanical circulatory support (MCS) devices have emerged as pivotal interventions. The existence and extent of racial disparities in outcomes related to these interventions have not been well-studied. Methods We analyzed data from the 2016-2020 National Inpatient Sample database to identify hospitalizations that included ECMO support for high-risk PE patients in the United States and to compare outcomes across different racial and ethnic groups. The primary outcome was in-hospital mortality. Secondary outcomes included complications such as acute kidney injury, stroke, and hospital length of stay (LOS). Results The total cohort consisted of 510 patients hospitalized for high-risk PE requiring ECMO support, of whom 71% were of White race, 22% of Black race, and 4% of Hispanic ethnicity. After adjustment, Black patients had lower odds of in-hospital mortality (adjusted odds ratio [aOR] 0.04, 95% confidence interval [CI] 0.004-0.38) and Hispanic patients had similar odds of in-hospital mortality (aOR 0.74, 95% CI 0.05-10.89) compared to White patients. Black patients had similar odds of acute kidney injury (aOR 2.07, CI 0.49-8.70) and stroke (aOR 0.38, 95% CI 0.05-2.99) and a longer LOS (mean difference 23.53 days, 95% CI 1.80-45.25, p<0.03) compared to White patients. Hispanic patients had similar odds of acute kidney injury (aOR 3.41, CI 0.49- 23.81) and a similar LOS (mean difference -10.35 days, 95% CI -22.62 to 1.91, p=0.09) compared to White patients Conclusion In patients with high-risk PE requiring ECMO support, Black patients had lower in-hospital mortality and Hispanic patients had similar in-hospital mortality compared to White patients. Further comparative studies are needed to better understand these racial disparities and their implications on treatment strategies.

Internal Medicine
Ellauzi R, Kumar A, Ismayl M, Hamza I, Hamza T, and Anavekar N. 800.22 Transcatheter vs. Surgical Valve Replacement in Severe Aortic Stenosis with Small Annulus: A Meta-Analytical Review of Two-Year Outcomes. *JACC Cardiovasc Interv* 2024; 17(4):S72. Full Text

Background: The optimal approach for severe aortic stenosis (AS) patients with small aortic annulus (SAA) remains uncertain when comparing transcatheter (TAVR) and surgical aortic valve replacement (SAVR). Methods: We conducted a pooled analysis of data from observational studies and randomized controlled trials that compared TAVR and SAVR in patients with severe aortic stenosis and small aortic annulus. The key endpoints evaluated were all-cause mortality, stroke, and myocardial infarction over a 2-year follow-up period. We used inverse variance method with Paule-Mandel estimator for tauˆ2 and Hartung-Knapp adjustment for random effects model accounting for small study effect and heterogeneity in the current analysis. All analysis was carried out using R version 4.0.3. Results: The meta-analysis incorporated data from three studies, evaluating a total of 279 TAVR and 231 SAVR patients with severe aortic stenosis and small aortic annulus. The analysis demonstrated no significant difference in all-cause mortality at 2 years follow-up, with a pooled risk ratio of 0.82 (95% CI [0.56; 1.21]), and no heterogeneity (I2 = 0%) [Figure, PANEL A]. The risk of stroke was comparable between TAVR and SAVR, with a risk ratio of 1.34 (95% CI [0.06; 28.44]) and moderate heterogeneity (I2 = 59%) [Figure, PANEL B]. Myocardial infarction was also comparable between TAVR and SAVR, yielding a risk ratio of 0.66 (95% CI [0.10; 4.15]) with no detected heterogeneity (I2 = 0%) [Figure, PANEL C]. Conclusion: In patients with severe aortic stenosis and small aortic annulus, TAVR and SAVR reported comparable results in all-cause mortality, stroke, and myocardial infarction at 2 years. Selection of valve replacement therapy should be individualized, considering these findings. [Formula presented]

Internal Medicine
Ellauzi R, Kumar A, Ismayl M, Hamza I, Kalra A, and Anavekar NS. SODIUM RESTRICTION IN HEART FAILURE: A META-ANALYSIS OF CLINICAL OUTCOMES FROM RCTS TARGETING <2G INTAKE. *J Am Coll Cardiol* 2024; 83(13):797. Full Text

Background Sodium restriction is recommended as part of heart failure (HF) management, yet its clinical efficacy remain controversial. Methods We sourced studies from multiple databases to included RCTs that examined the effects of <2 g sodium interventions compared with no restriction on clinical outcomes in patients with HF. Key outcomes assessed were all-cause mortality, all-cause hospitalization, cardiovascular hospitalization, and HF hospitalization. Inverse variance method with Paule-Mandel estimator for tau^2 and Hartung-Knapp adjustment for random effects model was used to pool outcomes. Results Eight RCTs were included. For all-cause mortality, sodium restriction exhibited a risk ratio (RR) of 1.10 (95% CI: 0.67-1.80) compared with no restriction, without significant heterogeneity (I^2 = 0%) [PANEL A]. For all-cause hospitalization, the RR for sodium restriction compared with no restriction was 0.93 (95% CI: 0.63-1.37) with no evident heterogeneity (I^2 = 0%) [PANEL B]. Regarding cardiovascular hospitalization, the RR for sodium restriction compared with no restriction was marked at 0.92 (95% CI: 0.03-26.45), presenting a modest heterogeneity (I^2 = 22%) [PANEL C]. Concerning HF hospitalization, sodium restriction compared with no restriction yielded an RR of 0.82 (95% CI: 0.16-4.34), accompanied by moderate heterogeneity (I^2 = 45%) [PANEL D]. Conclusion Our analysis underscores that < 2 g of sodium restriction in patients with HF yields nuanced outcomes. [Formula presented]

Internal Medicine
Gregerson S, **Fang JX**, **O'Neill B**, **Giustino G**, **Wang D**, **Lee J**, **Frisoli T**, **Gonzalez PE**, **O'Neill W**, and **Villablanca P**. 800.67 Feasibility And Periprocedural Outcomes of Transcatheter Mass Extraction in Left Heart and Aortic Arch. *JACC Cardiovasc Interv* 2024; 17(4):S79. Full Text

Background: Transcatheter vacuum-assisted mass extraction (TVME) is an alternative to surgical thrombectomy in high-risk patients especially for right-sided heart chambers. TVME in the left heart is less frequently performed owing to the need for transeptal puncture or alternative access, and the potential need for embolic protection, and the higher risk of blood loss. We report a case series of left-sided TVME at a high-volume center in USA. Methods: We performed left sided TVME in 24 consecutive patients from January 2019 to July 2023 at Henry Ford Hospital, MI, USA. The AngioVAC (Angiodynamics Inc, USA) was used. The preferred placement location for the blood return cannula was into the arterial system. Large bore access and closure were performed with standard techniques. TVME was performed for mass in the left atrium in 3 patients, left atrial appendage in 9 patients, left ventricle in 7 patients, aortic arch in 5 patients. Transeptal puncture was performed in all cases of left atrial and left ventricular masses. Transcaval access was performed in 4 out of 5 cases of aortic arch masses in order to gain enough catheter reach. Embolic protection device was used in 20 out of 24 patients. Concurrent left-atrial appendage occlusion was done in 5 patients with left-atrial appendage thrombus and concurrent balloon mitral valvuloplasty in two patients. Procedural success was defined as debulking of the total mass volume by 70% or more on echocardiogram. Results: The mean age of the patients was 59. Half were male. Mean left ventricular ejection fraction was 45%. The mean diameter of the mass was 3.2 cm. The procedure was completed in 96% (23 out of 24) of cases and aborted in 1 case. Successful debulking was achieved in 79% of cases. The median procedure time was 186 minutes. The mean procedural blood loss was 161 ml. The return cannula was placed on the arterial side in 66.6% (16 out of 24) of cases and on the venous side in 33.3% (8 out of 24) of cases. Periprocedural complications were uncommon. One patient developed stroke. One patient developed retroperitoneal bleeding. One patient developed a right femoral pseudoaneurysm. 2 patients required blood transfusion periprocedurally. The median length of hospitalization was 10 days. All patients were discharged alive from the hospital. Conclusions: TVME is technically feasible and safe for left-sided and aortic arch lesions.

Internal Medicine
Heil H, **Almajed MR**, **Almajed A**, **Khan N**, **Mohammed M**, and **Entz A**. SEVERE HYPOKALEMIA AND PARALYSIS IN A 19-YEAR-OLD PATIENT. *J Am Coll Cardiol* 2024; 83(13):3699. Full Text

Background Familial hypokalemic periodic paralysis (FHPP) is a rare, autosomal-dominant neuromuscular disorder characterized by episodes of hypokalemia that cause muscle weakness and paralysis. FHPP is more common in men and symptomatic episodes are often triggered by a high carbohydrate diet, exercise, and emotional stress. Primary prevention of episodes involves potassium replacement, avoidance of hypokalemia triggers, and carbonic anhydrase inhibitors. Case A 19-year-old healthy male presented to the hospital with acute, asymmetric muscle weakness and paralysis. His vitals

were normal, and he had no other symptoms. For four years, he has had monthly episodes of similar muscle weakness provoked by exercise, high carbohydrate foods, and travel. Serum studies showed hypokalemia at 1.9 mEq/L. ECG showed sinus bradycardia with U-waves and normal QTc. TSH was normal at 2.96. Renin and aldosterone were both normal. He was admitted to the hospital with cardiac monitoring while undergoing further investigations. Subsequent outpatient genetic testing revealed a pathogenic variant of the CACNA1S gene, consistent with FHPP. Decision-making Initial treatment for the patient focused on normalizing his potassium. His ECG corrected to normal sinus rhythm with normalization of his potassium. Prior to confirmation with genetic testing, other etiologies of his hypokalemia and muscle weakness were considered and included hyperaldosteronism, familial and thyrotoxic hypokalemic periodic paralysis, and Andersen-Tawil syndrome. Given his normal QTc, lack of dysmorphic features, and normal TSH, thyrotoxic hypokalemic periodic paralysis and Andersen-Tawil syndrome were less favored for his diagnosis. He was started on potassium replacement, a carbonic anhydrase inhibitor, and instructed to avoid episode triggers. Close follow-up with genetic testing and neurology were provided. Conclusion Familial hypokalemic periodic paralysis is a life-threatening neuromuscular disorder and requires prompt diagnosis to prevent severe hypokalemia, cardiac arrhythmias, and death. Ruling-out other etiologies of hypokalemic periodic paralysis is important to guide appropriate treatment.

Internal Medicine

Maraj D, and **Othman H**. INFERIOR MYOCARDIAL INFARCTION, COMPLICATED BY BILATERAL PAPILLARY MUSCLE RUPTURE, LEADING TO CARDIOGENIC SHOCK. *J Am Coll Cardiol* 2024; 83(13):3345. Full Text

Background Papillary muscle rupture (PMR) is a rare life-threatening complication following myocardial infarction (MI) and most commonly involves the posteromedial muscle. Here, we report a bilateral papillary muscle rupture following a late presenting inferior MI. Case We present a case of a 63-year-old male with a past medical history of hypertension, who presented with chest pain. Upon arrival, the patient was hypotensive, and his electrocardiogram findings were significant for ST elevations in the inferior leads, with reciprocal changes in the lateral leads. The patient was emergently taken to the cardiac catheterization lab. Angiogram showed total thrombotic occlusion of the obtuse marginal (OM) branch and concurrent severe left anterior descending (LAD) and right coronary artery disease (RCA). He underwent angioplasty with stent placement to OM. Despite successful revascularization of the culprit lesion, he remained hemodynamically unstable. A left ventriculogram showed severe mitral regurgitation and a bedside echocardiogram confirmed acute rupture of posteromedial papillary muscle. He was taken emergently for surgical repair of the mitral valve, where intraoperatively he was noted to have bilateral papillary muscle rupture. He underwent mitral valve replacement with double bypass to his LAD and RCA. His postoperative course was remarkable for an initial good recovery, however, later in his course he developed hemorrhagic shock and expired. Decision-making When patients remain hemodynamically unstable after cardiac catheterization, it's important look for alternate causes that require emergent surgical intervention, such as a papillary muscle rupture, to reduce mortality. Conclusion PMR is a rare, well-known complication following late presenting MI, with an incidence of 1-5%. Bilateral PMR is extremely rare and to our knowledge this is the first reported case of bilateral PMR. Diagnosis of PMR is suspected in a late-presenting patient with persistent hypotension and pulmonary edema despite revascularization. It is suggested by a ventriculogram and confirmed by echocardiogram. Once diagnosed, emergent surgical repair is indicated with a high mortality rate.

Internal Medicine

McBride P, **Gupta K**, **Lemor A**, **Alkhatib A**, **Cowger JA**, **Grafton G**, **Alaswad K**, **O'Neill WW**, **Villablanca PA**, and **Basir MB**. USE OF PERCUTANEOUS MECHANICAL CIRCULATORY SUPPORT FOR RIGHT VENTRICULAR FAILURE. *J Am Coll Cardiol* 2024; 83(13):456. Full Text

Background RV dysfunction is a significant cause of in-hospital morbidity/mortality due to under recognition and lack of experience with right ventricular mechanical circulatory support (RV-MCS). The purpose of this project was to identify if intervention, in addition to timing, impacted outcomes. Methods Single center retrospective cohort study of patients treated with RV-MCS for any indication between 2015-2022. Baseline comorbidities, hemodynamic, and laboratory data were collected. Primary outcome

was in-hospital mortality analyzed as a logistic outcome in a multivariable model. Results Among 58 patients, median age was 66 years. 31% of patients were female. 50% of patients were hospitalized for acute on chronic heart failure. 64% were SCAI SHOCK Stage D. Median time from index hospitalization to placement of RV-MCS was 2 days. 50% were treated with Impella RP and 50% received Protek Duo. Left ventricular mechanical circulatory support (LV-MCS) was used concomitantly with 45% of people. RV-MCS resulted in lower MAP (79.5 vs 67.6, p<0.001), and CVP (20 vs 15 mmHg, p<.002). Additionally, increased CO (3.8 vs 5.8, p <.001), CI (1.9 vs 2.7, p<.001), and RV SWI (8.9 vs 12.7 g*m/m2, p<.006) were observed at 24 hours. Lactate levels were significantly lower at 24 hours (3.5 vs 1.8, p<.05). In-hospital mortality of individuals treated with RV-MCS was 48.3%. In these individuals, median CVP and CVP/PCWP trended towards being increased (24 vs 19, p =.052 and 1.2 vs 1.0, p=.086, respectively). Median serum lactate was also significantly higher (4.1 vs 2.2, p<.007). In the multivariable logistic model, age (OR 1.11 [1.01, 1.22], p<.033), diabetes mellitus (OR 7.7 [1.0, 59.0], p<.048), CVP (OR 1.18 [1.03, 1.35], p<.017) and serum lactate (OR 1.32 [1.06, 1.65], p<.013) prior to placement of RV-MCS were associated with mortality. Conclusion Patients treated with RV-MCS had an in-hospital mortality of 48%. Use of RV-MCS was associated with reduced MAP, and improved CVP, systolic PA pressure, CO, CI, RVSWI, and lactate clearance. Diabetes mellitus, elevated CVP, and elevated lactate at presentation were independently associated with increased mortality.

Internal Medicine

Muhammad N, **Fadel R**, **Ama S**, and **Ananthasubramaniam K**. UTILITY OF PET CT IN DIAGNOSING CARDIAC SARCOIDOSIS, ESPECIALLY AS A COMPLEMENTARY MODALITY TO CARDIAC MRI. *J Am Coll Cardiol* 2024; 83(13):3506. Full Text

Background Cardiac sarcoidosis (CS) is an infiltrative cardiomyopathy resulting from granulomatous inflammation. Advanced imaging with positron emission tomography (PET) and magnetic resonance imaging (MRI) has the added benefit of detecting active inflammation and fibrosis due to CS, and can guide management. Case A 59-year-old male presented with presyncope for 2 weeks. Electrocardiogram demonstrated complete heart block. Transthoracic echocardiogram demonstrated mildly reduced left ventricular ejection fraction of 50-55%. Cardiac MRI demonstrated late gadolinium enhancement involving the mid myocardial basal septum and subepicardial mid inferior wall of the left ventricle suggestive of CS (figure1). A follow-up FDG-PET demonstrated similar distribution of active myocardial inflammation. The patient was treated with prednisone. Decision-making Utility of advanced imaging is key in the setting of suspected CS. MRI brings high spatial resolution and fibrosis detection, while PET provides myocardial inflammatory information. Both modalities identify different histopathologic features of CS, hence the complimentary use of both tests in defining the need for treatment and assisting in risk stratification. Conclusion In patients with high suspicion of CS, combination of MRI and PET can help establish the diagnosis as well as identify distribution of active inflammation, and guide treatment options/prognosis. [Formula presented]

Internal Medicine

Obeidat L, **Maki M**, **Jebbawi LA**, **El-khatib L**, **Fram G**, and **Michaels AT**. ISOLATED RIGHT VENTRICULAR FAILURE REQUIRING MECHANICAL CIRCULATORY SUPPORT AS A PRESENTING MANIFESTATION OF RECURRENT VIRAL MYOCARDITIS. *J Am Coll Cardiol* 2024; 83(13):3993. Full Text

Background Myocarditis can manifests in various forms, ranging from asymptomatic to cardiogenic shock (CGS). It is often triggered by viral infections, such as adenovirus. The Human Coxsackievirus and Adenovirus receptor (hCAR), which is localized to the intercalated discs, plays a significant role in the pathogenesis of recurrent viral myocarditis. Case A 20 year old female with a history of Coxsackie B myocarditis presented with CGS following several days of fever and sore throat. She was tachycardic, and hypotensive, requiring vasopressors. Laboratory results indicated lactic acidosis, elevated BNP and high sensitivity troponin, AKI, shock liver, and a respiratory panel positive for adenovirus. An EKG with ST depression in the precordial leads. An echocardiogram revealed a preserved EF of 55-60%, normal left ventricular function, an enlarged severely hypokinetic right ventricle (RV), and a flattened interventricular septum, consistent with acute RV failure. Despite initial resuscitation and inotropic support, she remained in refractory CGS, necessitating the placement of a RV assist device (RVAD). Her symptoms were

attributed to a disseminated adenovirus infection, and was started on Cidofovir therapy. She later rapidly improved, and RVAD support was subsequently weaned. Endomyocardial biopsy (EMB) and cardiac MRI (cMRI) performed later during her stay were negative, indicating a positive response to therapy. Decision-making Our patient's case was likely related to the expression of hCAR, explaining her susceptibility to these viruses and the subsequent development of recurrent myocarditis and RV failure. EMB is the gold standard for diagnosis; however, its value can be limited due to presence of areas spared from pathology. cMRI is an alternative diagnostic tool; however, findings can be nonspecific. Conclusion We emphasize the significance of identifying isolated RV failure as a rare yet possible manifestation of myocarditis, particularly in cases of recurrent viral infections. Furthermore, it's crucial to consider an underlying heritable cardiomyopathy, like arrhythmogenic cardiomyopathy in such cases, and discuss the potential need for genetic testing.

Internal Medicine
Stephan J, **Viacava RAC**, **McClafferty A**, and **Frisoli TM**. A DIAGNOSIS WITHOUT EXCLUSION: REVERSE TAKOTSUBO IN A 26-YEAR-OLD FEMALE. *J Am Coll Cardiol* 2024; 83(13):3582. Full Text

Background Takotsubo cardiomyopathy is a diagnosis of exclusion that typically requires a left heart catheterization. Reverse takotsubo has a prevalence of approximately 2% of all takotsubo cardiomyopathies. Case A 26-year-old female with no past medical history presented for elective bilateral salpingectomy. Intra-operatively, the patient became bradycardic and suffered a cardiac arrest. She was resuscitated but was found to be in shock. CT angiogram of the chest was negative for pulmonary embolism and showed diffuse pulmonary edema. Echocardiogram showed an ejection fraction (EF) of 15-20% with akinesis of the basal-mid anterior, inferior, anteroseptal, inferoseptal and lateral wall (figure 1). The patient improved with inotropic support and diuresis. Repeat echocardiogram, four days later, showed improvement of EF to 45%. She was placed on guideline-directed medical therapy and EF recovered 1 month after presentation. [Formula presented] Decision-making The multiple regions of akinesis with preserved apical contraction seen on echocardiogram do not fit a coronary territory, and thus these findings are incompatible with a coronary pathology. The diagnosis of reverse takotsubo was made without the use of a left heart catheterization given the patient's clinical presentation, characteristic imaging findings, and rapid normalization of wall motion abnormalities. Conclusion We present a case of reverse takotsubo in a 26-year-old female where the diagnosis was made conclusively by echocardiogram.

Internal Medicine
Viacava RAC, **Naimi A**, **Almajed MR**, **Al-Suraimi A**, **Thomas M**, and **Kim HE**. USE OF TANDEM HEART FOR CARDIOGENIC SHOCK AND SEVERE AORTIC INSUFFICIENCY IN BARTONELLA HENSELAE INFECTIVE ENDOCARDITIS. *J Am Coll Cardiol* 2024; 83(13):3177. Full Text

ackground Bartonella species infection, especially Bartonella henselae, is an increasingly common cause of culture-negative Infective Endocarditis (IE), which carries an exceedingly high morbidity and mortality. The necessity of valvular intervention for these cases has been found to be higher than on culture positive IE. Case A 53-year-old Hispanic man with no past medical history presented to the with palpitations, exertional dyspnea, orthopnea, and a non-intentional thirty-pound weight loss. His social history was significant for cohabitating with 20 domestic cats. Initial workup revealed leukocytosis, azotemia and transaminitis. Microbiologic studies showed negative blood cultures. Chest radiograph showed signs of bilateral pulmonary edema. Transthoracic echocardiogram showed preserved ejection fraction, no diastolic dysfunction and signs of bicuspid aortic valve with severe aortic insufficiency (AI). Transesophageal echocardiogram confirmed the previous findings and revealed vegetations on the aortic valve. Blood gases revealed severely low cardiac indices. Due to his rapid clinical deterioration, he was admitted to the Cardiac Intensive Care Unit and started on vasopressors and inotropic agents. Infectious Diseases and Cardiac Surgery were consulted. Decision-making Upon further workup for culture-negative IE, Bartonella antibody titers were found positive. Cardiac Surgery recommended no surgical intervention due to the patient being to hemodynamically unstable and high risk. Despite maximizing inotropic agents and preload management, his course was complicated by SCAI Stage D cardiogenic shock and multiorgan system failure. Due to the severe AI, intraaortic balloon pump was contraindicated; and due to risk of septic embolism, devices such an Impella were contraindicated. Ultimately, a percutaneous

Tandem Heart left ventricular assist device was placed and helped to successfully stabilize the patient. Conclusion IE can have several complications such as severe valvular disease leading to refractory cardiogenic shock. The usefulness of MCS in these patients is extremely high as a transient step until a definite valvular intervention.

Internal Medicine

Viacava RAC, **Naimi A**, **Almajed MR**, and **Swanson B**. INTERROGATING THE QUESTION: PACEMAKER-INDUCED CARDIOMYOPATHY SECONDARY TO TRANSCATHETER AORTIC VALVE REPLACEMENT-INDUCED HIGH-DEGREE HEART BLOCK. *J Am Coll Cardiol* 2024; 83(13):3176. Full Text

Background Pacemaker-induced cardiomyopathy (PICM) is defined as a drop in the left ventricular ejection fraction (LVEF) in the setting of long-standing high burden right ventricular pacing. The rise in use of implantable cardiac pacemakers has increased patient's quality of life, however complications such as infections, lead malfunction, and cardiomyopathy may arise. Case A 90-year-old white gentleman, with a past medical history of hypertension, coronary artery disease (CAD), sick sinus syndrome (SSS) requiring a dual-chamber permanent pacemaker implantation, severe aortic stenosis requiring a transcatheter aortic valve replacement (TAVR), presented for three weeks of exertional dyspnea, orthopnea, and bilateral leg swelling. He was hemodynamically stable, but hypoxic requiring oxygen supplementation. Initial workup revealed elevated BNP and elevated troponins. Electrocardiogram showed an AV-paced rhythm and no signs of ischemia. Chest radiograph showed bilateral pulmonary edema. Transthoracic echocardiogram showed a new decreased LVEF of 38% (previously 56%), no regional wall motion abnormalities, and a 26 mm Edwards Sapien 3 transcatheter aortic valve prosthesis with mild perivalvular regurgitation and TAPSE of 2.02 cm. Decision-making Device interrogation found an AV-paced rhythm with a right ventricular pacing of 99%. The last one, six months prior to this admission (four months before TAVR) showed a right ventricular pacing of 1%. Upon our discussion, patient was diagnosed with PICM. Electrophysiology was consulted, and upon stabilization of the patient's congestive heart failure, performed a device upgrade to a Cardiac Resynchronization Therapy (CRT), without any complications. Patient's condition improved significantly with this procedure and the use of intravenous loop diuretics. Ultimately, patient was discharged without oxygen supplementation requirements. Conclusion Conduction abnormalities are well-known complications of TAVR that often require pacemaker implantation. Patients with pacemakers require a careful device interrogation and right ventricular pacing assessment to diagnose PICM, for which CRT is a treatment of choice.

Internal Medicine

Walji M, **Khassawneh AR**, and **Arnautovic J**. A VASCULAR ODYSSEY: RECURRENT GRANULOMATOSIS WITH POLYANGIITIS PRESENTING AS CORONARY NECROTIZING VASCULITIS. *J Am Coll Cardiol* 2024; 83(13):3262. Full Text

Background Granulomatosis with polyangiitis (GPA) is a small vessel necrotizing vasculitis classically involving the kidneys and respiratory tracts. The incidence of GPA is estimated to be around 10-20 cases per million worldwide. A small subset of those have cardiac involvement, around 3-10%. Pericarditis, coronary artery disease (CAD), conduction abnormalities, and myocarditis are the most common of these presentations; dilated cardiomyopathy with acute congestive heart failure, however, is exceedingly rare with only a few cases ever documented. Case A 34-year-old gentleman arrived to the ED after gaining 32 lbs. over four weeks with lower extremity edema and dyspnea. He had a past medical history of biopsy confirmed GPA treated and in remission 5 years ago. One month prior to presentation, the patient was diagnosed with heart failure with an ejection fraction (EF) of 35%. Serological testing at this time was positive for c-ANCA and anti-PR3. He was discharged on oral steroids and maximally tolerated guideline-directed medical therapy but had been non-compliant with follow-up since then. Decision-making Cardiac catheterization was preformed which was negative for CAD but did reveal an unusual anatomy of the mid left anterior descending (LAD) artery tapering into a small dual LAD system. Encouragingly, echocardiogram demonstrated an EF of 45%, indicating a positive response to treatment. Given the patient's history of GPA, a renal biopsy was performed which showed diffuse global and segmental sclerosis compatible with remote ANCA-related renal injury. Due to the improved EF and negative findings for infiltrative disease on cardiac MRI and full-body CT, the patient was diagnosed with new

onset dilated non-ischemic cardiomyopathy secondary to coronary necrotizing vasculitis. A FDG PET scan was recommended to further evaluate the small vessels. Conclusion This case highlights the natural progression of GPA which can rapidly lead to multi-organ failure. With a 5-year relapse rate of 40-50%, this case emphasizes the need for vigilant follow-up and intricate interplay between GPA and cardiac manifestations, necessitating a comprehensive and multidisciplinary approach to management.

Obstetrics, Gynecology and Women's Health Services
Pezzillo M, **Luck A**, and **Miller M**. Repair of a rectovaginal cloacal defect. *Am J Obstet Gynecol* 2024; 230(4):S1299-S1300. Full Text

Obstetrics, Gynecology and Women's Health Services
Smith N, **Ezell G**, **Condon M**, **Joyce K**, **Joseph J**, and **Pitts DS**. 844 Timeliness of diagnosis and treatment of postpartum hypertensive disorders in the Emergency Department. *Am J Obstet Gynecol* 2024; 230(1):S448. Full Text

Objective: This study aims to assess the time to diagnosis and treatment of hypertensive disorders during the postpartum period in the Emergency Department, particularly focusing on potential disparities in care and identify areas for quality improvement. Study Design: The study was conducted at a multi-centered large medical institution in the metro-Detroit area, analyzing postpartum ED visits from November 2015 to December 2022. The primary analysis focused on the time elapsed between severe range blood pressure readings and the administration of antihypertensives. Secondary analyses included the presence of essential laboratory work up such as complete blood count, complete metabolic panel, urine protein and creatinine. Results: Among the 430 women who presented to the ED during the postpartum period with hypertension, 72.6% had preeclampsia with severe features, and 13% had chronic hypertension with superimposed severe preeclampsia. Of the patients with severe hypertension, only 72% received a complete blood count, 66% underwent evaluation of creatinine and liver profile, and 4% had a urine protein ordered. The average time from severe range blood pressure to antihypertensive administration was 189 minutes for Black patients and 370 minutes for White patients. There were no statistically significant differences in the time of first blood pressure reading, laboratory evaluation, or treatment of severe range blood pressure between racial groups. Conclusion: This study identified the most significant area for improvement in the timely administration of antihypertensive medication following severe range blood pressure readings. Additional areas for improvement were observed in ordering essential laboratory tests to assess the severity of preeclampsia. Surprisingly, our institution demonstrated equal expeditious care for both white and black patients, contrary to existing literature indicating potential disparities. Based on these findings, a targeted quality improvement plan will be implemented to enhance the identified areas of concern.

Otolaryngology – Head and Neck Surgery
Hughes RT, **Chang S**, Truong MT, and Yom SS. A Review of the Evolution of Quality of Life Measures in Head and Neck Cancer Clinical Trials. *International Journal of Radiation Oncology Biology Physics* 2024; 118(5):e61. Full Text

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Purpose/Objective(s): To best study the complex toxicity profiles experienced by patients treated with radiotherapy (RT) for head and neck (HN) cancer, a greater focus on quantifiable, reproducible quality of life (QOL) measures is needed. Both clinician-rated outcomes (CRO) and patient-reported outcome (PRO) measures of toxicity and QOL have been collected in HN clinical trials for over two decades. A clear understanding of existing PRO practices in these studies may inform future study design and spark innovative QOL-focused hypothesis-generating research. Materials/Methods: The protocol documents for HN-specific clinical trials activated within the National Cancer Institute (NCI) National Clinical Trials Network cooperative groups since 2002 were reviewed. Both active and closed trials were included, regardless of publication status. Phase I trials and those that were terminated without enrolling patients were excluded. All protocol specified QOL measures (CRO, PRO, and/or functional assessments [FA]) and the time points of these measurements were abstracted from the protocols, as were basic trial

details. Data collection was performed between May 26 and October 12, 2023. Descriptive statistics were performed. Results: A total of 30 trials including 76 QOL (66 PRO, 10 CRO) and 10 FA were included. These trials were activated between 2002-2023; 13 were phase II, 9 phase II/III, and 8 phase III. The most common disease process studied was squamous cell carcinoma of the HN (n=12), oropharynx (n=6), and nasopharynx (n=5). Most studies enrolled patients treated with curative intent (n=20), while 10 enrolled patients with recurrent/metastatic disease. The most frequent study interventions were systemic (n=14) and RT (n=13). Across all studies, 27 distinct PRO measures were utilized, and the most frequent measures were EuroQol-5D (12 trials), FACT-HN (8), PRO-CTCAE (6), MDADI (6), and EORTC-QLQ-C30 (4). The most frequent CRO measure was PSS-HN (7); the most common functional assessment was audiogram (7) followed by modified barium swallow (n=2) and objective salivary flow (n=1). The median number of PRO measures per trial was 2 (range, 0-8) and the median number of data points was 11 (range, 0-35). In trials activated prior to 2012, 17 of 24 (71%) QOL measures (not including FA) were PROs compared to 49 of 52 (94%) measures in trials activated on or after 2012 (p=0.009). Conclusion: Over time, the use of patient-reported measures of QOL in HN cancer cooperative group clinical trials has increased. This reflects patients' increasing prioritization of QOL as well as requirements by the NCI for increased standardization and quantitation of these impacts on patients in clinical trials. This dataset may inform future study of QOL in patients with HN cancer through a better understanding of specific PRO data that has been or will be collected within current and future NCI-supported clinical trials.

Pathology and Laboratory Medicine

Fadel R, **Miller J**, **Cook B**, **Nguyen F**, **Alqarqaz M**, **Fuller B**, **Basir MB**, **Frisoli TM**, **Villablanca PA**, **Jabri A**, **Alaswad K**, **Khandelwal AK**, **Lingam N**, **O'Neill BP**, **Kim HE**, **Pielsticker EJ**, **Koenig GC**, Mills NL, and Mahler SA. THE INCIDENCE OF UNSTABLE ANGINA IN PATIENTS WITH LOW HIGH-SENSITIVITY TROPONIN I VALUES: A SUBGROUP ANALYSIS OF THE RACE-IT TRIAL. *J Am Coll Cardiol* 2024; 83(13):1268. Full Text

Background We sought to identify the incidence of unstable angina in patients with low high-sensitivity cardiac troponin I (hs-cTnI) in Emergency Departments (EDs). Methods This was a preplanned secondary analysis of the Rapid Acute Coronary Syndrome Exclusion using high-sensitivity I cardiac Troponin (RACE-IT) stepped-wedge randomized trial, which compared two rule-out protocols (0/1-hour and 0/3-hour) for myocardial infarction (MI) in 9 EDs from 7/2020-3/2021. A hs-cTnI assay from Beckman Coulter was used (99th percentile 18 ng/L). In the accelerated protocol (AP), MI was excluded if hs-cTnI was <4 ng/L at presentation, or =4 ng/L at presentation with a 1-hour value <8 ng/L. Those that did not rule-out within 1 hour required a 3-hour hs-cTnI ≤18 ng/L to rule-out. In the standard care (SC), MI was excluded if hs-cTnI values were ≤18 ng/L at 0 and 3 hours. Patients were excluded if hs-cTnI was >18 ng/L within 3 hours of presentation. Unstable angina was adjudicated based on the ISCHEMIA trial definition, which required electrocardiographic changes or findings at coronary angiography (ruptured/ulcerated plaque or thrombus). Adjudication was performed by interventional cardiologists for patients undergoing coronary angiography, and by cardiology fellows in patients with hs-cTnI >18 ng/L >3 hours after presentation. Results Of the 32,608 patients in the trial, 58 patients (0.18%) met the definition of unstable angina (35 in the AP and 23 in the SC protocol). In the AP 12/35 (34.3%) patients with unstable angina had a presenting hs-cTnI <4 ng/L. In the AP, among patients who ruledout for MI within 1 hour, 13/10444 (0.12%) had unstable angina vs. 22/8659 (0.25%) among those who did not meet early rule-out criteria (adjusted odds ratio 0.73, 95% CI 0.33 - 1.60, p=0.43). Within 30 days there were 113 (0.35%) patients in the entire cohort who had a revascularization procedure and in the unstable angina group there were 38 (65.5%). Conclusion Unstable angina is rare in patients with a low hs-cTnI values at presentation to the ED and few receive revascularization procedures. However, of those ultimately diagnosed with unstable angina in the AP, a substantial portion had an extremely low hs-cTnI at presentation.

Pathology and Laboratory Medicine

George M, **Clark J**, **Gartrelle K**, **Nassif G**, **Hartway K**, **Long D**, **Salas-Escabillas D**, **Wombwell A**, **Wen HJ**, **Benitz S**, **Zwernick S**, **Shah R**, **Park H**, **Philip P**, **Khan G**, **Crawford H**, **Theisen B**, **Kwon D**, and **Steele N**. TIGIT expression increases with advancing clinical stages of resected pancreatic cancer. *Ann Surg Oncol* 2024; 31(1):S176-S176. Full Text

Public Health Sciences

Kulkarni R, **Gonzalez LF**, **Lin CH**, **Rose C**, **Emole J**, **Alavi A**, **Peres E**, **Abidi MH**, and **Farhan S**. Standard Risk Assessment Tools Fall Short to Assess Risk in Transplant Patients. *Transplantation and Cellular Therapy* 2024; 30(2):S125. Full Text

L.F. Gonzalez, Hematology-Oncology, Henry Ford Hospital, Detroit, MI, United States

Introduction: The HCT-CI (Hematopoietic Cell Transplantation-specific Comorbidity Index) and the Disease Risk Index (DRI) Assessment Tool are models used for pre-transplant risk assessment. HCT-CI ≥3 is associated with higher non-relapse mortality (NRM) and lower overall survival (OS). The DRI was developed to predict overall survival per disease status. Objectives: This retrospective study was done to understand reasons for increased mortality in transplant patients at our center in 2021 compared to 2020 by comparing HCT-CI and DRI of transplant patients between the two years. Methods: This was an IRB-approved study. Relevant patient comorbidities, disease characteristics, and transplant-related data were collected. Patients were risk stratified using the online DRI Assessment Tool. Data was analysed using R version 4.3.1, and a p-value less than 0.05 was considered statistically significant. Results: A total of 165 transplants were reviewed. Patient characteristics are elucidated in Table 1. Mean age at HCT in 2020 was 59.8 and 59.3 in 2021. Allogeneic HCT was done in 38.4% of HCT in 2020 and 37% in 2021. HCT-CI was ≥3 in 68.5% in 2020 and 70.7% in 2021. DRI was high or very high in 20.5% patients in 2020 and 20.6% in 2021. The 2-year OS of Allo HCT was worse in 2021 compared to 2020 although not statistically significant (50.6% vs. 57.7% respectively, p=0.52, figure 1 A). The cumulative incidence of relapse in Allo HCT at year 1 and 2 were significantly less in 2021 compared to 2020 (Table 2). However, there was a numerically higher incidence of non-relapse mortality (Table 2 and Figure 1 B). The hazard for NRM for patients who underwent Allo HCT was 2.89 compared to Auto (p=0.046). The hazard for relapse for patients with high DRI was 4.24 (p<0.001) times relative to patients with low DRI, controlling for year, HCT type, HCT-CI, and demographics. The hazard for NRM for patients with high DRI was 2.60 (p=0.070), however 16 patients (12 in 2021 and 4 in 2020) were excluded from this analysis as they underwent transplants for diseases that are currently not included in the DRI assessment tool. These included aplastic anemia (AA), inherited bone marrow failure syndromes (BMF), solid tumors, primary CNS lymphomas, mycosis fungoides and hemophagocytic lymphohistiocytosis (HLH). Of these 8 patients, 7 died due to causes other than disease relapse. Conclusion: In this small single-center retrospective analysis, 2021 has statistically significant less relapse by second year with a trend towards higher NRM and worse OS in 2021 (though not statistically significant, possibly limited by sample size). The DRI or another tool however could not be used in those patients. Most predictive models are mainly applied to hematological malignancies, but are not specific for inherited or acquired BMF disorders, HLH or solid tumor malignancies. We sent a proposal to CIBMTR for further consideration to help with this unmet need.

Public Health Sciences

Wobig R, **Bensenhaver JM**, **Thaker H**, **Joliat C**, **Schwartz TL**, **Lehrberg AV**, **Dalla Vecchia LK**, **Nathanson SD**, **Susick LL**, **Springer K**, **Petersen LF**, and **Ali H**. Upstaging from cT1 to pT2 in Triple Negative and Her2 Positive Breast Cancer: an Opportunity to Identify cT1 Breast Cancer Patients for whom Neoadjuvant Chemotherapy Should be Considered. *Ann Surg Oncol* 2024; 31(1):S109-S109. Full Text

Radiation Oncology

Ferris RL, Torres-Saavedra P, Uppaluri R, Yao M, Chen J, Jordan R, Geiger JL, Jujjavarapu S, Chakravati A, Phan M, **Siddiqui F**, Kulkarni A, Upadhyay P, Tu F, Vujanovic L, Isett B, Sica GL, Harris J, Le QT, and Bauman J. NRG-HN003: Phase I and Expansion Cohort Study of Adjuvant Pembrolizumab, Cisplatin and Radiation Therapy in Pathologically High-Risk Head and Neck Cancer with Exploratory Biomarker Correlatives. *International Journal of Radiation Oncology Biology Physics* 2024; 118(5):e10-e11. Full Text

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Purpose/Objective(s): Patients with locoregional, pathologically high-risk HNSCC recur frequently despite adjuvant cisplatin-radiation therapy (CRT). Targeting PD1 may reverse immunosuppression induced by HNSCC and CRT. Materials/Methods: We conducted a phase I trial (n=34) adding pembrolizumab (200mg q3 weeks) to adjuvant CRT, with correlative studies to identify biomarkers of clinical benefit. Eligible patients had resected HPV-negative, AJCC 7 stage III-IV oral cavity, pharynx, or larynx HNSCC, with extracapsular nodal extension or positive margin. We assessed PD-L1 expression using the 22c3 Ab in a CLIA laboratory test and correlated with disease-free survival (DFS) and overall survival (OS) using a combined positive score (CPS) threshold of ≥20/ or <20. The CPS threshold of 1+/< 1 could not be evaluated due to insufficient patients in the <1 group. DFS and OS rates were estimated by Kaplan-Meier method, and groups were compared by 2-sided log-rank tests. Hazard ratios (HR; CPS ≥20/ or <20) were estimated by Cox models. To determine mechanisms and biomarkers of clinical benefit, additional exploratory analyses to assess the relationship between clinical outcomes and serum (Luminex, soluble checkpoints, cytokines, and chemokines), tumor/tissue (single-plex IHC, 7-color multispectral tumor staining, whole-exome sequencing, CD8 T cell infiltration, CD8/Treg ratio, and mutational status), and PBMC (spectral flow cytometry and T cell frequencies and activation states) biomarkers are being performed. Results: Adding pembrolizumab to adjuvant CRT was well tolerated. Nine (26.5%) and 25 (73.5%) patients had CPS <20 or ≥20. At a median follow-up of 3.1 years (0.04-3.3), 15 (10) DFS (OS) events were reported, 3 (2) in the CPS <20 group and 12 (8) in the CPS 20+ group. Biomarker effect HR was 1.94 (95% confidence interval [CI] 0.54-6.89; p=0.30) for DFS and 1.70 (95% CI 0.36-8.00; p=0.50) for OS. Two-year DFS estimates were 77.8% (95% CI 50.6-100) for CPS <20 and 52.3% (95% CI 31.9-72.7) for CPS 20+. Two-year OS estimates were 77.8% (95% CI 50.6-100) for CPS <20 and 69.6% (95% CI 50.8-88.4) for CPS 20+. Conclusion: In this small patient sample, no significant association of PD-L1 expression with clinical outcomes was identified. Circulating inflammatory cytokine and immune checkpoint biomarkers have been performed and are being correlated with clinical outcomes.

Radiation Oncology

Zhu S, **Gilbert M**, Liu P, and **Siddiqui F**. Imaging-based Prognostic Artificial Intelligence Model for Oropharyngeal Carcinoma after Radiation Therapy. *International Journal of Radiation Oncology Biology Physics* 2024; 118(5):e64. Full Text

S. Zhu, Department of Radiation Oncology, James Cancer Hospital, The Ohio State University, Columbus, OH, United States

Purpose/Objective(s): Predicting treatment prognosis for oropharyngeal carcinoma (OPC) remains a significant challenge. This study hypothesizes that pre-treatment CT imaging holds important prognostic information. We developed an artificial intelligence (AI) model to predict locoregional recurrence (LRR) post-radiation therapy (RT) for OPC. Materials/Methods: In an IRB-approved study, we collected imaging and outcome data from 1095 patients newly diagnosed with oropharyngeal carcinoma. They were treated with RT with curative intent, with or without chemotherapy, and none underwent surgery. Data originated from multiple institutions: 124 from ours and 971 from The Cancer Imaging Archive, contributed by four institutions in the US, Canada, and Europe. We excluded patients with a follow-up duration of less than 2 years unless they experienced LRR within this period. Each patient's pre-treatment CT images, along with segmentations for the gross tumor volume of the primary tumor and lymph nodes (if present), served as model input. We clipped the Hounsfield values of CT images within the range [-200, 200]. A 3D convolutional neural network, adapted from the ConvNeXt architecture, was employed as the deep learning model. The primary endpoint was the risk of 2-year LRR. The training used a weighted binary cross-entropy loss function, and we developed the model through five-fold cross-validation on 730 cases. For inference, the ensemble model provided a risk score between 0 and 1, indicating the probability of 2-year LRR on the 365 patients in the test cohort. Results: On the independent test set, the model attained a Harrel's concordance index of 0.72 for predicting 2-year LRR. Using 0.5 as a threshold to classify the test cohort into low- and high-risk groups, the log-rank test highlighted a significant difference in LRR risk between the two groups ($p=3.6 \times 10^{-7}$). Conclusion: Our study demonstrates the potential of an imaging-based AI model for predicting OPC prognosis. However, further research is required to validate this model and integrate more clinical parameters as inputs.

Sleep Medicine

Dauvilliers Y, **Roth T**, Thorpy MJ, Morse AM, Kushida CA, Harsh J, Ortiz LE, Dubow J, and Gudeman J. Comparison of demographics and baseline narcolepsy symptoms between participants with NT1 and NT2 from the Phase 3 REST-ON clinical trial. *Sleep Med* 2024; 115:210. Full Text

Introduction: Narcolepsy is classified into 2 subtypes: narcolepsy type 1 (NT1; with cataplexy and orexin deficiency) and narcolepsy type 2 (NT2; without cataplexy or orexin deficiency). Limited data are available regarding subtype differences in clinical characteristics and disease severity. The efficacy and safety of a once-nightly formulation of sodium oxybate (ON-SXB; FT218; LUMRYZTM) was investigated in patients with NT1 and NT2. ON-SXB demonstrated significant improvements for the 3 coprimary endpoints of change from baseline in mean sleep latency on the Maintenance of Wakefulness test (MWT), Clinical Global Impression of Improvement rating, and weekly cataplexy attacks (all P<0.001) and was well tolerated. The objective of this post hoc analysis from the REST-ON trial was to compare baseline clinical characteristics between participants with NT1 and NT2. Materials and Methods: REST-ON was a multicenter, phase 3, randomized, double-blind, placebo-controlled clinical trial (NCT02720744). Participants were ≥16 years of age with NT1 or NT2 and had excessive daytime sleepiness (sleep latency <11 min on the MWT and Epworth Sleepiness Scale [ESS] score >10) and cataplexy (average of 8 episodes per week; NT1 only). Stable concurrent alerting agent use was permitted. Randomization (1:1 to ON-SXB or placebo) was stratified by narcolepsy type; the study population was oversampled for NT1. Baseline characteristics were compared between narcolepsy types. Results: The safety analysis set included 212 participants (NT1, n=162; NT2, n=50). At baseline, characteristics of participants with NT1 vs NT2 were as follows: mean (SD) age, 32.1 (11.1) vs 28.3 (10.0) years, respectively; sex, 72.8% vs 52.0% female; race, 76.5% vs 72.0% white and 17.9% vs 14.0% Black; body mass index, 28.9 (7.5) vs 25.7 (5.6) kg/m2; and use of concurrent alerting agents, 59.2% vs 68.0%. The modified intent-to-treat population included 190 participants (NT1, n=145; NT2, n=45). Mean (SD; 95% CI) baseline clinical characteristics in patients with NT1 vs NT2 were as follows: sleep latency (MWT), 4.9 (2.9; 4.4–5.3) vs 4.9 (2.9; 4.1–5.8) minutes; Clinical Global Impression scores (CGI-Severity), 5.2 (1.1; 5.0–5.4) vs 4.7 (1.1; 4.4–5.0); ESS scores, 17.6 (4.0; 16.9–18.2) vs 15.4 (3.2; 14.4–16.3); number of sleep stage shifts to lighter stage of sleep or wake measured by polysomnography (PSG), 61.5 (22.2; 57.9–65.2) vs 55.8 (23.5; 48.8–62.9); number of nocturnal arousals by PSG, 81.5 (42.4; 74.6–88.5) vs 73.2 (35.9; 62.4–84.0); sleep quality (visual analog scale [VAS; 1 = did not sleep and 100 = slept very well]), 54.5 (22.0; 50.9–58.2) vs 55.8 (20.8; 49.5–62.1); and refreshing nature of sleep (VAS; 1 = not refreshed and 100 = refreshed), 49.9 (22.6; 46.2–53.6) vs 42.6 (21.6; 36.1–49.1). Conclusions: When comparing baseline characteristics between patients with NT1 and NT2, numerical differences were observed with respect to the proportion of female participants and concomitant use of alerting agents. At baseline, 95% CIs of mean values did not overlap for subjective measures, but did overlap for objective measures of EDS, suggesting that those with NT2 perceived themselves as more sleepy than those with NT1. Acknowledgements: Funded by Avadel Pharmaceuticals.

Sleep Medicine

Kushida CA, Thorpy MJ, Morse AM, Harsh J, Ortiz LE, **Roth T**, Dauvilliers Y, Dubow J, and Gudeman J. Magnitude of improvement in excessive daytime sleepiness with the once-at-bedtime oxybate for narcolepsy. *Sleep Med* 2024; 115:221. Full Text

Introduction: The safety and efficacy of once-nightly sodium oxybate (ON-SXB; FT218; LUMRYZ™) was investigated in the phase 3 REST-ON trial. Study results demonstrated statistically significant improvements for the coprimary endpoints of change from baseline in mean sleep latency on the Maintenance of Wakefulness test, Clinical Global Impression-Improvement (CGI-I) rating, and weekly cataplexy attacks for ON-SXB 6 g (week 3), 7.5 g (week 8), and 9 g (week 13) vs placebo (all P<0.001). Participants also had statistically significant improvements in excessive daytime sleepiness (EDS) measured using the Epworth Sleepiness Scale (ESS; secondary endpoint) at all doses beginning at week 2 (post hoc analysis, ON-SXB 6 g vs placebo at week 2). The objective of this analysis was to assess the magnitude of improvement in the patient-reported outcome of EDS following treatment with ON-SXB. Materials and Methods: In this multicenter, double-blind, placebo-controlled REST-ON clinical trial (NCT02720744), participants aged ≥16 years with narcolepsy type 1 (NT1) or 2 (NT2) were randomly assigned 1:1 to ON-SXB or placebo. Doses were 4.5 g week 1; 6 g weeks 2−3; 7.5 g weeks 4−8; and 9 g

weeks 9−13. This post hoc analysis examined median (Q1-Q3; interquartile range [IQR]) ESS scores to assess magnitude of improvement in EDS at the end of each dosing period. Results: The mean age of participants was 31.2 years, 68% were female, 75.5% were white, and 76.4% had NT1. The modified intent-to-treat population included 190 participants (ON-SXB, n=97; placebo, n=93). Baseline median (IQR) ESS scores were 17 (14−19) for ON-SXB and 18 (15−21) for placebo. After 1 week of treatment, median (IQR) ESS scores were 16 (12−18) for ON-SXB 4.5 g vs 17 (13−20) for placebo. At week 3 (ON-SXB 6 g), median (IQR) ESS scores were 14 (10−18) vs 17 (14−20) for placebo. With the 7.5-g dose of ON-SXB at week 8, median (IQR) ESS scores were 12 (8−16) vs 15.5 (12−20) for placebo. At the end of the study (week 13), median (IQR) ESS scores for ON-SXB 9.0 g were 9.5 (6.0−15.0) vs 15 (11−19) for placebo. ON-SXB was well tolerated; the most common adverse drug reactions were dizziness, nausea, vomiting, headache, and enuresis (consistent with the known safety profile of sodium oxybate). Conclusions: Treatment with ON-SXB resulted in statistically significant and clinically meaningful improvement in EDS with doses >6 g in that at the end of the study, median ESS scores were within the range considered normal (≤10). ON-SXB should be considered an effective intervention in treatment of EDS for patients with NT1 or NT2 with a once-at-bedtime dose. Acknowledgements: This study was funded by Avadel Pharmaceuticals.

Sleep Medicine
Reffi A, **Kalmbach D**, **Seymour G**, **Solway M**, **Moore D**, **Mahr G**, and **Drake C**. Early identification of patients most vulnerable to acute insomnia after trauma. *Sleep Med* 2024; 115:169. Full Text

Introduction: Acute sleep disturbances are a common, modifiable consequence of trauma that, if left untreated, increase risk of PTSD by nearly two-fold. This suggests acute sleep disturbances after trauma are an important contributor to the etiology of PTSD that could be targeted early to prevent the disorder. Yet, effective strategies to prevent PTSD cannot currently be implemented because we cannot identify who is most at risk of acute sleep disturbances after trauma, thus obstructing the ability to identify high-risk groups in need of early intervention. This study will test sleep reactivity – a trait predisposition to experience sleep disturbances after stress – as a predictor of posttraumatic sleep disturbances within one month following trauma exposure. Materials and Methods: We recruited patients (N = 88, Mage = 39.53 ± 14.31) admitted to Henry Ford Hospital's intensive care unit in Detroit, Michigan for traumatic injury (e.g., gunshot wound). While in the hospital, patients reported their pre-trauma sleep reactivity (Ford Insomnia Response to Stress Test; FIRST) and insomnia symptoms from the past two weeks (Insomnia Severity Index; ISI). Patients then completed the ISI again one month later (n = 48). We tested high sleep reactivity (FIRST ≥ 21) as a prospective predictor of clinically significant posttraumatic sleep disturbances (ISI ≥ 10). Results: Patients were mostly black men (67%), and nearly half reported an annual income ≤ $20,000 (47.7%). Motor vehicle collisions were the most common trauma that precipitated patients' hospital admission (42%), followed by assaults with a weapon (30.7%). While adjusting for age and pre-trauma sleep disturbance, high sleep reactivity predicted increased odds of sleep disturbances one month after trauma (b = 2.08, SE =.98, p =.033, OR = 8.01, CI = 1.19 – 54.15). Conclusions: Individuals with high sleep reactivity are at increased susceptibility of clinically significant sleep disturbances after trauma. The 9-item FIRST is a brief and clinically useful indicator that offers providers the ability to predict the onset of acute sleep disturbances after trauma, which are novel targets for early intervention. This might enable the early identification of potentially vulnerable individuals who might develop PTSD, toward whom sleep-focused preventive efforts can be targeted. Acknowledgements: We are grateful to Henry Ford Hospital's Dept. of Surgery, Division of Acute Care Surgery for supporting our research, and of course, we thank the patients who enrolled in our study during such a stressful time.

Sleep Medicine
Thorpy MJ, **Roth T**, Kushida CA, Morse AM, Harsh J, Ortiz LE, Dubow J, Gudeman J, and Dauvilliers Y. Consistent efficacy of once-nightly sodium oxybate regardless of patient demographic and baseline disease characteristics. *Sleep Med* 2024; 115:211. Full Text

Introduction: Once-nightly formulation of sodium oxybate (ON-SXB; LUMRYZ™) was investigated in patients with narcolepsy in the phase 3 REST-ON trial; treatment with 6, 7.5, and 9 g resulted in significant improvements (all P<0.001) for the coprimary endpoints of change from baseline in mean sleep latency on the Maintenance of Wakefulness Test (MWT), Clinical Global Impression-Improvement

(CGI-I) rating, and weekly number of cataplexy attacks (NCA), and the secondary endpoint, Epworth Sleepiness Scale (ESS) score. ON-SXB was well tolerated; the most common adverse events were nausea, dizziness, headache, enuresis, and vomiting. As narcolepsy is a chronic disease with different phenotypes, this post hoc analysis assessed ON-SXB efficacy in various subgroups. Materials and methods: Participants in the REST-ON clinical trial (NCT02720744) were aged ≥16 years with narcolepsy type 1 (NT1) or 2 (NT2) and were randomized to ON-SXB (4.5 g for 1 week, 6 g for 2 weeks, 7.5 g for 5 weeks, and 9 g for 5 weeks) or matching placebo for 13 weeks. Differences in least squares mean (LSM) changes from baseline for ON-SXB vs placebo were compared for mean sleep latency on MWT, NCA (NT1 only), and ESS and odds ratios for “much”/“very much” improved on CGI-I among subgroups of baseline demographics (age [<35 y/≥35 y], sex, race [white/other], body mass index [BMI] category [underweight/normal; overweight/obese]) and narcolepsy disease characteristics (NT1/NT2; concomitant alerting agent use). Results: The modified intent-to-treat population included 190 participants (ON-SXB, n=97; placebo, n=93). LSM differences for ON-SXB 9 g vs placebo in change from baseline on the MWT in minutes at week 13 revealed significant improvements (P<0.05) for subgroups based on age (<35 years: 7.3; ≥35: 4.2), sex (female: 6.8; male: 5.3), race (white: 7.0; non-white: 4.8), BMI (low: 10.0; high: 4.0), narcolepsy type (NT1: 6.0; NT2: 6.3), and alerting agent/no alerting agent use (6.0 and 6.3, respectively). Odds ratios were significant in favor of ON-SXB 9 g vs placebo for “much” or “very much” improved on CGI-I at week 13 (P<0.05) for both low/high age, female sex, white/non-white, high BMI, NT1, and alerting agent/no alerting agent use, and ranged from 3.3 (no alerting agent) to 7.1 (age <35); 3 subgroups (male, low BMI, and NT2) could not be calculated. LSM differences were significant in favor of ON-SXB 9 g vs placebo for change from baseline in NCA (P<0.05) in all subgroups, except non-white and male. Among the subgroups that were significant, reductions ranged from –5.5 to –7.6; for the non-white and male subgroups, reductions were –3.8 and –5.1, respectively. For the ESS, all subgroups exhibited significant improvements with ON-SXB 9 g vs placebo except NT2 (LSM difference [95% CI]: –2.72 [–6.09, 0.65]); the largest reduction was in low BMI (LSM difference [95% CI]: –6.25 [–8.83, –3.68]). Similar, albeit smaller, differences were found with lower doses. Conclusions: Post-hoc subgroup analyses demonstrate the robust efficacy of ON-SXB and provide further insight into its effectiveness in different demographic and clinical subgroups. Acknowledgements: This study was funded by Avadel Pharmaceuticals.

Surgery
Ahmed O, Doyle MBM, **Abouljoud M**, Alonso D, Batra R, Brockmeier D, Cannon R, Chavin K, Delman A, Dubay D, Finn J, Fridell J, Friedman B, Fritz D, Merani S, Halff G, Shah S, Kumer S, Locke J, Meier R, Mejia A, Goldberg D, Karp S, Shafer T, and Orloff S. A National Multicenter Analysis on Liver Transplant Activity Post Allocation Policy Changes: Where do we Stand and at What Cost. *Am J Transplant* 2024; 24(1):S35-S35. Full Text

Surgery
George M, **Clark J**, **Gartrelle K**, **Nassif G**, **Hartway K**, **Long D**, **Salas-Escabillas D**, **Wombwell A**, **Wen HJ**, **Benitz S**, **Zwernick S**, **Shah R**, **Park H**, **Philip P**, **Khan G**, **Crawford H**, **Theisen B**, **Kwon D**, and **Steele N**. TIGIT expression increases with advancing clinical stages of resected pancreatic cancer. *Ann Surg Oncol* 2024; 31(1):S176-S176. Full Text

Surgery
Kadiyala D, **Dobesh K**, **Pairawan S**, **Shepard A**, **Natour AK**, **Nypaver T**, and **Kabbani LS**. Quality of Life and Ambulation Outcomes in Acute Limb Ischemia Patients. *Ann Vasc Surg* 2024; 100:272. Full Text

Introduction and Objectives: Quality of life (QoL) assessment is critical for shared decision making in patients with critical limb ischemia but has been poorly studied in acute limb ischemia (ALI). We sought to assess patient-centered outcomes in ALI using the European QoL 5D-5L and the VascuQoL-6 surveys. Methods: A prospective database was created of patients presenting with ALI between May 2016 to July 2023. Variables collected included patient demographics, history, inpatient variables, outcomes, and ambulatory function at last follow-up. EQ-5D and VascuQoL-6 surveys were administered. Results: Among 236 eligible patients, 47 (20%) completed the surveys with an average age of 58.3; the majority were black males. Limb salvage rates for respondents were 93.6% at thirty days and 85% at one year. Functional status at last follow-up included: 26 (55%) patients with unhindered ambulation; 13 (28%) with

limited ambulation; 5 (11%) who were ambulatory with a prosthetic; 2 (4%) non-ambulatory after amputation and with 1 (2%) non-ambulatory without amputation.VascuQoL-6 scores significantly correlated with age (p=0.002), and ambulatory status (p=0.03) but not limb salvage (p=0.36 at 30 days and p=0.89 at 1 year). Similar findings were observed with the EQ-5D survey (p=0.02 for both age and ambulatory status). (Table 1) No association was found between QoL and Rutherford classification, causative factors, procedure type, or length of stay. [Formula presented] Conclusion: This data suggests that younger patients have worse QoL on follow-up. Reduced ambulatory function was also associated with poorer QoL scores; however, this was not necessarily associated with limb salvage. Regaining ambulatory function without pain or neurologic deficits, even if this required amputation with prosthetic rehabilitation, had a greater positive impact on well-being than actual limb salvage.

Surgery
Malinzak L, **Gartrelle K**, **Sragi Z**, **Segal A**, **Prashar R**, and **Jesse M**. Minimal Access to Robotic Assisted Kidney Transplant for Recipients: A Systematic Review and Call for Reporting Standards. *Am J Transplant* 2024; 24(1):S29-S29. Full Text

Surgery
Nassif G, **Gartrelle K**, **Kwon H**, **Shah R**, **Cools K**, **Steffes C**, and **Kwon D**. Routine Intensive Care Unit Admission After Pancreaticoduodenectomy: Is it Worth it? *Pancreas* 2024; 53(1):e116. Full Text

G. Nassif, Henry Ford Health, Detroit, MI, United States

Background: Routine intensive care unit admission (rICUa) is still being utilized after pancreaticoduodenectomy (PD) given the high rates of post-operative morbidity. However, the impact of rICUa on post-operative outcomes is unclear. We hypothesized that rICUa after PD might increase costs of care without significantly improving post-operative outcomes. Methods: Retrospective analysis of our prospectively maintained pancreatic cancer database was conducted. Patients who underwent PD between 2018 and 2022 were stratified by post-operative rICUa and regular ward admission (RWa). Post-operative complications, intensive care unit readmission, lengths of stay, reoperation, and 30- and 90-day outcomes were compared between the two groups. Results: 175 patients underwent PD between 2018 and 2022 at our institution. 62.9 % (N = 110) had a rICUa post-operatively, while 37.1% (N = 65) had a RWa. Demographics, comorbidities, disease pathologies, and intra-operative variables were similar between the two groups. There were no significant differences in major post-operative complications, pancreas-specific complications, and intensive care unit readmissions between the two groups. Patients with rICUa had significantly longer lengths of stay than those with RWa (Wilcoxon Rank Sum Test p = 0.024). RWa patients had significantly more 30-day emergency department visits (15.4% versus 4.5%, p = 0.013). Otherwise, rates of 30- and 90-day emergency department presentation, hospital readmission, reoperation, and mortality were similar between the two groups. Conclusions: Patients with rICUa and RWa had similar rates of morbidity and mortality post PD. Our data suggests that rICUa after PD might increase healthcare resource utilization and costs without improving post-operative outcomes. ICU admission should be considered on a case-by-case basis and tailored to patients' demographics, comorbidities, and intra-operative events.

Surgery
Wobig R, **Bensenhaver JM**, **Thaker H**, **Joliat C**, **Schwartz TL**, **Lehrberg AV**, **Dalla Vecchia LK**, **Nathanson SD**, **Susick LL**, **Springer K**, **Petersen LF**, and **Ali H**. Upstaging from cT1 to pT2 in Triple Negative and Her2 Positive Breast Cancer: an Opportunity to Identify cT1 Breast Cancer Patients for whom Neoadjuvant Chemotherapy Should be Considered. *Ann Surg Oncol* 2024; 31(1):S109-S109. Full Text

Urology
Bhanvadia RR, Holland L, Popokh B, Taylor J, Margulis V, Sundaram CP, Derweesh IH, **Abdollah F**, Ferro M, Djaladat H, Autorino R, Simone G, Mehrazin R, Gonzalgo ML, Wu Z, Porpiglia F, and Eun DD. ASSOCIATION BETWEEN SMOKING BURDERN AND ONCOLOGIC OUTCOMES OF UPPER TRACT UROTHELIAL CARCINOMA: ANALYSIS OF THE ROBUUST COLLABORATION. *Urologic Oncology: Seminars and Original Investigations* 2024; 42:S25-S26. Full Text

Introduction: Most studies in urothelial cancer have examined smoking status (current, former, never), but often fail to quantify smoking burden/exposure, which has been shown to be prognostic in other malignancies. The impact of smoking burden on oncologic outcomes for upper tract urothelial carcinoma (UTUC) remains understudied with current literature providing mixed results.;Limitations of the;existing literature;include the lack;of patients who received neoadjuvant chemotherapy (NAC) and only a low proportion of patients receiving adjuvant therapy (AC). The relationship between smoking burden and pathologic downstaging after NAC in UTUC is largely unknown, and survival data has been mixed. We therefore performed a contemporary analysis of smoking burden;on oncologic outcomes in patients with UTUC undergoing radical nephroureterectomy (RNUx) utilizing a larrge;multicentered, multinational cohort (ROBUUST 2.0). Methods: We performed a retrospective analysis from a large multicentered cohort of 1,730 patients with UTUC across 17 institutions from 2005-2022. We excluded patients with incomplete smoking history, pathologic data, non-urothelial histology, and prior or concurrent cystectomy. All patients underwent RNUx. Smoking history included current smoking status, cigarettes per day (CPD), total pack-years (TPY), and cumulative smoking exposure. Based on prior studies, cumulative smoking exposure was stratified as light (≤19 CPD & ≤19 years smoking), or heavy (>20 CPD & >20 years smoking), with all other cases being moderate exposure. For analysis, light and moderate smoking exposure groups were combined.;Survival outcomes of cancer specific (CSS) and overall survival (OS) were assessed using the Kaplan-Meier method and multivariable competing risk regression to adjust for competing risk of non-cancer mortality from smoking exposure. A multivariable regression analysis was performed to examine odds of achieving pathologic down-staging;(<ypT2) after cisplatin NAC. Results: 1,041;patients met criteria for analysis. Median follow up (IQR) was 24(10-48) months.;5 year CSS was 97% in non-smokers,;89% in light to moderate smokers, and;75% in heavy smokers (p<0.001, Figure 1). 5 year OS was 91% in non-smokers, 68% in light to moderate smokers and 60% in heavy smokers (p<0.001). On multivariable competing risk regression, both light to moderate smoking burden (HR: 2.98,;p=0.02) and heavy smoking burden (HR:;3.24,;p=0.02) were associated with greater cancer mortality compared to non-smokers (Table 1). Further, both light to moderate smoking burden (HR: 3.58,;p<0.001) and heavy smoking burden (HR: 2.69,;p<0.001) were associated with greater overall mortality compared to non-smokers. Models adjusted for active;smoking status, NAC, pathologic T & N stage, grade, necrosis, lymphovascular invasion, and AC usage. Smoking burden was not associated with pathologic down staging after NAC on multivariable regression. Conclusions:;In this contemporary multicentered UTUC cohort, increasing smoking burden was associated with worse cancer specific and overall survival, even among former smokers.;This contemporary analysis;supports;existing literature that increasing smoking burden;is associated with worse survival outcomes and underscoring continued need for more aggressive smoking cessation and prevention programs. Smoking burden was not associated with lower odds of achieving pathologic down staging after NAC, suggesting that NAC and AC should be continued to be emphasized in this patient population at high risk of cancer specific mortality.;Future and on-going UTUC trials should assess the influence of smoking burden on response to NAC and oncologic outcomes.

Urology

Corsi N, **Cirulli GO**, **Chiarelli G**, **Finati M**, **Davis M**, **Rogers C**, **Abdollah F**, **Rakic I**, **Morrsion C**, **Stephens A**, Sood A, Lughezzani G, Salonia A, Buffi N, Briganti A, Montorsi F, and Carrieri G. EVALUATING THE IMPACT OF LYMPOVASCULAR INVASION ON SURVIVAL OF SURGICALLY TREATED PATIENTS WITH UPPER TRACT UROTHELIAL CARCINOMA: A NATIONWIDE ANALYSIS. *Urol Oncol* 2024; 42:S106. Full Text

Introduction: Lymphovascular invasion (LVI) is recognized as an adverse prognostic factor in many cancers. However, its utility in upper tract urothelial carcinoma (UTUC) has not been well-defined. Our aim was to assess the prognostic ability of LVI in UTUC as a predictor of overall survival (OS) using a large North American cohort. Methods: Our cohort included 5,940 cM0 UTUC patients who underwent a radical nephroureterectomy (RNU), between 2004 and 2016, within the National Cancer Database (NCDB). The main variable of interest was LVI status, and its interaction with pathological nodal (pN) status. Kaplan-Meier curves were used to depict the OS also stratifying patients on LVI status. Cox regression analysis tested the impact of LVI status on OS after accounting for the available covariates. Results: Median (IQR) for age at diagnosis was 71 (63 – 78) and most patients had pT1 stage disease

(48.6%). Nodal status was pN0, pN1 and pNx in 45.8%, 6.3% and 47.9%, respectively. Overall, 22.1% had LVI. The median (IQR) follow-up time was 32.6 (16 – 53.3) months. At 5-years postoperative follow-up, the estimated OS rate was 28% in patients with LVI vs. 66% in those without LVI (p<0.001). When patients were stratified based on nodal status those rates were 32% vs 68% in pN0 patients (p<0.001; Figure 1), 23% vs 30% in pN1 patients (p = 0.8), and 28% vs 65% in pNx patients (p<0.001). On multivariable analysis, the presence of LVI was associated with less favorable OS (HR 1.79, 95% CI: 1.60-1.99, p<0.001). Conclusions: Our study assessed the impact of LVI on OS in UTUC patients in a large North American nationwide cohort. Our series, as the largest to-date, indicate that LVI is associated with less favorable survival outcomes in UTUC patients after RNU, and this variable could be used as a risk-stratification tool for future adjuvant therapy trials.

Urology
Corsi N, Taylor J, Margulis V, **Stephens A**, **Finati M**, **Abdollah F**, **Morrison C**, **Davis M**, Sundaram C, Derweesh IH, Ferro M, Djaladat H, Simone G, Mehrazin R, Gonzalgo ML, Wu Z, and Autorino R. NEOADJUVANT CHEMOTHERAPY AND RADICAL NEPHROURETERECTOMY (RNU) VS. RNU ALONE FOR UPPER TRACT UROTHELIAL CARCINOMA: A MULTI-INSTITUTIONAL COHORT ANALYSIS (ROBUUST COLLABORATIVE). *Urol Oncol* 2024; 42:S24-S25. Full Text

Introduction: Neoadjuvant chemotherapy (NAC) has grown in popularity in the management of upper tract urothelial carcinoma (UTUC). Retrospective data on NAC has shown promise in pathological downstaging rates, a surrogate endpoint of improved cancer-specific survival. However, most NAC series are limited to single centers and no randomized trials have been published. The aim of our study is to provide a multinational matched comparison of pathological complete response (pCR) and nodal downstaging (NDS) rates between patients who receive NAC + RNU vs. RNU alone. Methods: Patients were abstracted from an international cohort of 13 high-volume centers across the United States, Europe, and Asia (Robotic surgery for Upper Tract Urothelial Cancer Study, ROBUUST 2.0) undergoing treatment for UTUC from 2011-2022. We then focused on cM0, histologically confirmed UTUC. Clinical and pathologic data was collected. Endpoints consisted of PCR (defined as ≤pT0N0) and NDS (cN > pN). Subgroup analyses for >cN0 was completed for NDS.;;Inverse probability of treatment weighting (IPTW) adjusted Cox regression analyses were used to assess odds of pCR and NDS. To minimize baseline differences among groups, IPTW weighted by age, sex, multifocality, tumor site, presence of hydroureteronephrosis, and clinical tumor stage (cT). Patients with missing data on age, tumor site, pT, pN, etc. were excluded. Results: 72 (6.5%) and 1,035 (93.5%) patients were treated with NAC + RNU vs. RNU alone, respectively. Follow-up length was 26.0 (22.7) and 31 (25.9) months for the NAC+RNU and RNU alone. The most common NAC regimen consisted of Gemcitabine/Cisplatin (61%), followed by ddMVAC (24%) (Figure 1), with a median (IQR) number of cycles of 4 (3-4). IPTW-adjusted Cox regression analysis demonstrated pCR to be significantly higher in the NAC+RNU group with an OR of 2.49 (95% CI: 1.75 – 3.54, P<0.001). Additionally, those who received NAC were significantly more likely to experience NDS, OR: 9.56 (95% CI: 4.11-22.26, P<0.001). Standardized differences between the two treatment groups were < 0.1 for all variables, indicating strong matching. Conclusions: Real world data from high volume centers suggests that neoadjuvant chemotherapy confers patients 2.49 times greater odds of experiencing a pathological complete response, compared to a matched UTUC cohort on multivariable analysis. This is one of the largest multinational experiences of neoadjuvant chemotherapy in UTUC to date. Ultimately, these results should be interpreted within the framework of a retrospective design, and randomized trials evaluating the efficacy of NAC are necessary.

Urology
Qian ZJ, Chen X, Cole AP, Iyer HS, Kibel AS, Trinh QD, and **Abdollah F**. CHANGES IN PROSTATE SPECIFIC ANTIGEN SCREENING FOLLOWING THE 2018 UNITED STATES PREVENTIVE SERVICES TASK FORCE GUIDELINES AND THROUGH THE COVID-19 PANDEMIC. *Urol Oncol* 2024; 42:S90. Full Text

Introduction: Prostate cancer, the second leading cause of male cancer death, raises debates on optimal screening strategies due to overtreatment risks. The USPSTF revised their recommendation in 2018, promoting shared decision-making for PSA screening among men aged 55-69. However, the COVID-19 outbreak could have decreased cancer screening utilization. Our study investigates the effects of these

key events on PSA screening in the recommended age group. Methods: We analyzed NHIS database from selected years (2013, 2015, 2018, 2019, 2021) to track changes in PSA screening pre- and post-2018 guidelines and COVID-19. We studied men aged 55-69 and those over 69 (reference group). Those who reported PSA testing within the last year were considered screened. Adjusted odds ratios between PSA screening prevalence and demographic characteristics were estimated. We applied a Difference-in-Difference (DID) design for comparing changes between age groups, accounting for unmeasured time-invariant characteristics. Results: A total of 24,308 men were included. PSA screening prevalence was 35.4% (95%CI: 33.7%, 37.1%), 32.1% (95%CI: 30.3%, 33.9%), 33.3% (95%CI: 31.6%, 34.9%), 37.2% (95%CI: 35.7%, 38.8%), and 34.9% (95%CI: 33.3%, 36.5%) respectively for included years (Figrue 1). From 2015 to 2019, PSA screening increased 4.6% among men aged 55-69 (95%CI: 1.7, 7.5%) and increased 6.5% among men >70 (95%CI: 2.7, 10.4%). From 2019 to 2021, PSA screening decreased 3.1% among men aged 55-69 (95%CI: 0.58%, 5.8%); PSA screening also decreased 0.8% among older men but did not reach significance (95%CI: -2.6%, 4.2%). DID analysis did not show difference in changes between men aged 55-69 in reference to men >70 from both 2015 to 2019 (DID=-1.9%, 95%CI, -6.7%, 2.9%) and 2019 to 2021 (DID=-2.3%, 95%CI, -6.5%, 1.9%). Conclusions: Our analysis, based on a large national survey, suggested that the 2018 USPSTF recommendations increased PSA screening among men aged 55-69 and those >69. Yet, COVID-19 reversed this trend. Future research should explore the long-term impacts of the 2018 USPSTF guidelines and the pandemic on prostate cancer screening and clinical outcomes.

Urology

Saitta C, Afari JA, Hakimi K, Nguyen MV, Meagher MF, Wang L, Derweesh IH, Autorino R, Pandolfo S, **Chiarelli G**, **Abdollah F**, **Davis M**, **Stephens A**, Bell SH, Simone G, Lughezzani G, Buffi NM, Tuderti G, Ferro M, Yong C, Sundaram CP, Tozzi M, Taylor J, Margulis V, Checcucci E, Porpiglia F, Wood E, Ghoreifi A, Djaladat H, Wang L, Eilender BM, Mehrazin R, Gonzalgo ML, Mendiola DF, Wu Z, and Eun DD. DEVELOPMENT AND VALIDATION OF A NOVEL NOMOGRAM TO PREDICT LYMPH NODE INVASION IN UPPER TRACT UROTHELIAL CARCINOMA. *Urol Oncol* 2024; 42:S103. Full Text

Introduction: The role of lymphadenectomy in upper tract urothelial carcinoma (UTUC) remains controversial. We sought to develop a preoperative nomogram to predict nodal tropism (NT) defined as nodes invasion at the histological report (NI) or presence of nodes metastasis (NM) at follow up. Methods: We conducted a retrospective analysis of the ROBUUST database of UTUC patients who underwent robotic nephroureterectomy. NI was defined as presence of positive nodes at final histological report, while NM was defined as the emergence of newly detected retroperitoneal lymphadenopathy (>10 mm) during the follow-up period. Patients who underwent neoadjuvant or adjuvant chemotherapy were excluded from analysis. Primary objective was to develop a predictive model for NT. The model was developed through a stepwise multivariable logistic regression (MLR).;;Secondary outcomes pertain to internal validation though cross validation analysis. Accuracy of the model was tested with receiver operator characteristic/area under the curve (AUC), and calibration plot. Results: 1,117 were analyzed [755(64.1%) male and 422(35.8%) female]. On MVR cN+[Odds ratio(OR) 8.19, p<0.001];;cT4 vs cTa (OR 10.38, p=0.012);;history of bladder cancer (OR 6.66, p<0.001) high-grade cytology (OR 2.90, p<0.001), platelets lymphocyte ratio≥130 (OR 1.77, p=0.021), diabetes mellitus (OR 1.90, p=0.023), and symptoms at diagnosis (OR 2.16, p=0.008) were independent predictors for NT. A nomogram was developed based on the MVL (Figure 1). AUC of the model was 0.83 (Figure 2). AUC after internal validation was 0.81 (95% confidence interval 0.76-0.87;;Figure 2). A 7% threshold probability demonstrated 80.2% sensitivity, 75.4% specificity and 97.5% negative predictive value. Conclusions: By integrating patient characteristics and serum biomarkers, we've engineered a predictive model for node tropism. This model has the potential to improve clinical choices, with respect to the performance of lymphadenectomy at the time of surgery, post-surgery monitoring, and may spur considerations;for supplementary treatment.;Further investigation is requisite.

Books and Book Chapters

Surgery
Battistelli L. Bariatric Procedures. In: Width M, and Reinhard T, eds. *The Essential Pocket Guide for Clinical Nutrition*. Jones & Bartlett Learning; 2024**:** 127-128. PMID: Not assigned. Request Book

Surgery
Pietrowsky T. Intestinal Transplantation. In: Width M, and Reinhard T, eds. *The Essential Pocket Guide for Clinical Nutrition*. Jones & Bartlett Learning; 2024**:** 235-237. PMID: Not assigned. Request Book