

Henry Ford Health Publication List – April 2023

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, and Web of Science during the month, and then imported into EndNote for formatting. There are 128 unique citations listed this month, including 111 articles and 17 conference abstracts.

Articles are listed first, followed by [conference abstracts](#). Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health authors.

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Articles

Administration

Weinstock JS, Gopakumar J, **Williams LK**, **Xiao S**, **Yang M**, et al. Aberrant activation of TCL1A promotes stem cell expansion in clonal haematopoiesis. *Nature* 2023; 616(7958):755-763. PMID: 37046083. [Full Text](#)

Mutations in a diverse set of driver genes increase the fitness of haematopoietic stem cells (HSCs), leading to clonal haematopoiesis(1). These lesions are precursors for blood cancers(2-6), but the basis of their fitness advantage remains largely unknown, partly owing to a paucity of large cohorts in which the clonal expansion rate has been assessed by longitudinal sampling. Here, to circumvent this limitation, we developed a method to infer the expansion rate from data from a single time point. We applied this method to 5,071 people with clonal haematopoiesis. A genome-wide association study revealed that a common inherited polymorphism in the TCL1A promoter was associated with a slower expansion rate in clonal haematopoiesis overall, but the effect varied by driver gene. Those carrying this protective allele exhibited markedly reduced growth rates or prevalence of clones with driver mutations in TET2, ASXL1, SF3B1 and SRSF2, but this effect was not seen in clones with driver mutations in DNMT3A. TCL1A was not expressed in normal or DNMT3A-mutated HSCs, but the introduction of mutations in TET2 or ASXL1 led to the expression of TCL1A protein and the expansion of HSCs in vitro. The protective allele restricted TCL1A expression and expansion of mutant HSCs, as did experimental knockdown of TCL1A expression. Forced expression of TCL1A promoted the expansion of human HSCs in vitro and mouse HSCs in vivo. Our results indicate that the fitness advantage of several commonly mutated driver genes in clonal haematopoiesis may be mediated by TCL1A activation.

Administration

Weinstock JS, Laurie CA, **Gui H**, **Xiao S**, **Williams LK**, et al. The genetic determinants of recurrent somatic mutations in 43,693 blood genomes. *Sci Adv* 2023; 9(17):eabm4945. PMID: 37126548. [Full Text](#)

Nononcogenic somatic mutations are thought to be uncommon and inconsequential. To test this, we analyzed 43,693 National Heart, Lung and Blood Institute Trans-Omics for Precision Medicine blood whole genomes from 37 cohorts and identified 7131 non-missense somatic mutations that are recurrently mutated in at least 50 individuals. These recurrent non-missense somatic mutations (RNMSMs) are not clearly explained by other clonal phenomena such as clonal hematopoiesis. RNMSM prevalence increased with age, with an average 50-year-old having 27 RNMSMs. Inherited germline variation associated with RNMSM acquisition. These variants were found in genes involved in adaptive immune function, proinflammatory cytokine production, and lymphoid lineage commitment. In addition, the presence of eight specific RNMSMs associated with blood cell traits at effect sizes comparable to Mendelian genetic mutations. Overall, we found that somatic mutations in blood are an unexpectedly common phenomenon with ancestry-specific determinants and human health consequences.

Anesthesiology

Alfirevic A, Marciniak D, Duncan AE, Kelava M, Yalcin EK, **Hamadnalla H**, Pu X, Sessler DI, Bauer A, Hargrave J, Bustamante S, Gillinov M, Wierup P, Burns DJP, Lam L, and Turan A. Serratus anterior and pectoralis plane blocks for robotically assisted mitral valve repair: a randomised clinical trial. *Br J Anaesth* 2023; Epub ahead of print. PMID: 37055276. [Full Text](#)

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BACKGROUND: Minimally invasive cardiac surgery provokes substantial pain and therefore analgesic consumption. The effect of fascial plane blocks on analgesic efficacy and overall patient satisfaction remains unclear. We therefore tested the primary hypothesis that fascial plane blocks improve overall benefit analgesia score (OBAS) during the initial 3 days after robotically assisted mitral valve repair. Secondly, we tested the hypotheses that blocks reduce opioid consumption and improve respiratory mechanics. **METHODS:** Adults scheduled for robotically assisted mitral valve repairs were randomised to combined pectoralis II and serratus anterior plane blocks or to routine analgesia. The blocks were ultrasound-guided and used a mixture of plain and liposomal bupivacaine. OBAS was measured daily on postoperative Days 1-3 and were analysed with linear mixed effects modelling. Opioid consumption was assessed with a simple linear regression model and respiratory mechanics with a linear mixed model. **RESULTS:** As planned, we enrolled 194 patients, with 98 assigned to blocks and 96 to routine analgesic management. There was neither time-by-treatment interaction ($P=0.67$) nor treatment effect on total OBAS over postoperative Days 1-3 with a median difference of 0.08 (95% confidence interval [CI]: -0.50 to 0.67; $P=0.69$) and an estimated ratio of geometric means of 0.98 (95% CI: 0.85-1.13; $P=0.75$). There was no evidence of a treatment effect on cumulative opioid consumption or respiratory mechanics. Average pain scores on each postoperative day were similarly low in both groups. **CONCLUSIONS:** Serratus anterior and pectoralis plane blocks did not improve postoperative analgesia, cumulative opioid consumption, or respiratory mechanics during the initial 3 days after robotically assisted mitral valve repair. **CLINICAL TRIAL REGISTRATION:** NCT03743194.

Anesthesiology

Ayoub CH, Abou Chawareb E, Kasti A, **Alhalabi E**, El-Asmar JM, Abou Mrad A, and El Hajj A. The 5-item frailty index predicts 30-day morbidity and mortality in radical nephrectomy patients: A propensity matched analysis. *Urol Oncol* 2023; Epub ahead of print. PMID: 37120371. [Full Text](#)

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PURPOSE: To assess the ability of the 5-item frailty index (5-IFi) score to predict 30-day morbidity and mortality post-radical nephrectomy (RN). **METHODS:** ACS-NSQIP database was used to select patients who underwent RN from 2011 to 2020. 5-IFi score was calculated by assigning a point for each of the following comorbidities: chronic obstructive pulmonary disease or pneumonia, congestive heart failure, dependent functional status, hypertension, and diabetes. Patients were divided into 3 frailty groups 0, 1, and ≥ 2 . Patient demographics, medical comorbidities, prolonged length of stay, and prolonged operative time were compared between different groups; mortality and morbidity using the Clavien-Dindo classification (CVD). Multivariable logistic regression models and propensity score matching were performed as a sensitivity analysis to control for possible confounders. **RESULTS:** Cohort consisted of 36,682 patients whereby 5-IFi class 0, 1, and ≥ 2 included 11,564 (31.5%), 16,571 (45.2%), and 8,547 (25.3%) patients respectively. A multivariable analysis and propensity score matching revealed that patients with 5-IFi classes 1 and ≥ 2 were more likely to have a prolonged length of stay (OR = 1.11, 1.3, respectively) and to mortality (OR = 1.85 for frailty class ≥ 2); in addition to CVD class 1 & 2 (OR = 1.51, OR = 1.13, respectively), and CVD ≥ 4 (OR = 1.41, 1.86, respectively) as compared to 5-IFi class 0 ($P < 0.001$). **CONCLUSION:** The 5-IFi score was found to be an independent predictor of prolonged length of stay, morbidity, and mortality after RN. This tool can play a major role in preoperative risk assessment and patient counseling based on individualized risks.

Anesthesiology

Nanchal R, Subramanian R, Alhazzani W, Dionne JC, Peppard WJ, Singbartl K, Truwit J, Al-Khafaji AH, Killian AJ, Alquraini M, Alshammari K, Alshamsi F, Belley-Cote E, Cartin-Ceba R, Hollenberg SM, **Galusca DM**, Huang DT, Hyzy RC, Junek M, Kandiah P, Kumar G, Morgan RL, Morris PE, Olson JC, Sieracki R, Steadman R, Taylor B, and Karvellas CJ. Executive Summary: Guidelines for the Management of Adult Acute and Acute-on-Chronic Liver Failure in the ICU: Neurology, Peri-Transplant Medicine, Infectious Disease, and Gastroenterology Considerations. *Crit Care Med* 2023; 51(5):653-656. PMID: 37052435. [Full Text](#)

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Anesthesiology

Nanchal R, Subramanian R, Alhazzani W, Dionne JC, Peppard WJ, Singbartl K, Truwit J, Al-Khafaji AH, Killian AJ, Alquraini M, Alshammari K, Alshamsi F, Belley-Cote E, Cartin-Ceba R, Hollenberg SM, **Galusca DM**, Huang DT, Hyzy RC, Junek M, Kandiah P, Kumar G, Morgan RL, Morris PE, Olson JC, Sieracki R, Steadman R, Taylor B, and Karvellas CJ. Guidelines for the Management of Adult Acute and Acute-on-Chronic Liver Failure in the ICU: Neurology, Peri-Transplant Medicine, Infectious Disease, and Gastroenterology Considerations. *Crit Care Med* 2023; 51(5):657-676. PMID: 37052436. [Full Text](#)

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OBJECTIVES: To develop evidence-based recommendations for clinicians caring for adults with acute liver failure (ALF) or acute on chronic liver failure (ACLF) in the ICU. **DESIGN:** The guideline panel comprised 27 members with expertise in aspects of care of the critically ill patient with liver failure or methodology. We adhered to the Society of Critical Care Medicine standard operating procedures manual and conflict-of-interest policy. Teleconferences and electronic-based discussion among the panel, as well as within subgroups, served as an integral part of the guideline development. **INTERVENTIONS:** In part 2 of this guideline, the panel was divided into four subgroups: neurology, peri-transplant, infectious diseases, and gastrointestinal groups. We developed and selected Population, Intervention, Comparison, and Outcomes (PICO) questions according to importance to patients and practicing clinicians. For each PICO question, we conducted a systematic review and meta-analysis where applicable. The quality of evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation approach. We used the evidence to decision framework to facilitate recommendations formulation as strong or conditional. We followed strict criteria to formulate best practice statements. **MEASUREMENTS AND MAIN RESULTS:** We report 28 recommendations (from 31 PICO questions) on the management ALF and ACLF in the ICU. Overall, five were strong recommendations, 21 were conditional recommendations, two were best-practice statements, and we were unable to issue a recommendation for five questions due to insufficient evidence. **CONCLUSIONS:** Multidisciplinary, international experts formulated evidence-based recommendations for the management ALF and ACLF patients in the ICU, acknowledging that most recommendations were based on low quality and indirect evidence.

Behavioral Health Services/Psychiatry/Neuropsychology

Kleinman MB, Anvari MS, Seitz-Brown CJ, Bradley VD, Tralka H, **Felton JW**, Belcher AM, Greenblatt AD, and Magidson JF. Psychosocial challenges affecting patient-defined medication for opioid use disorder treatment outcomes in a low-income, underserved population: Application of the social-ecological framework. *J Subst Use Addict Treat* 2023; 149:209046. PMID: 37061189. [Full Text](#)

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INTRODUCTION: Successful engagement with medication treatment for opioid use disorder is an important focus in reducing mortality associated with the opioid crisis. Mortality remains at unacceptably high levels, pointing to a need for improved understanding of factors that affect medication for opioid use disorder outcomes. This study aims to understand how barriers co-occur and interact to interfere with outcomes in methadone treatment for a low-income, underserved patient population with opioid use disorder. **METHODS:** This study was conducted at a community-based drug treatment center that serves a predominately low-income, racially diverse population. Guided by the social-ecological framework, we analyzed semi-structured interviews and focus groups with patients and providers working in opioid use disorder care and recovery across Baltimore City (N = 32) to assess factors that influence methadone treatment outcomes, and how barriers co-occur and interact to worsen treatment outcomes. The study used patient-centered definitions to describe successful treatment outcomes. **RESULTS:** Barriers described by both patients and providers fit into several broad levels: individual, interpersonal, institutional, community, and stigma. Participants described co-occurrence of many barriers. Further, the study identified potential interactive effects, such that interrelated barriers were seen as fueling one another and having a deleterious effect on treatment outcomes. Specifically, interrelationships between barriers were described for 1) unstable housing with social influences and mental health factors; 2) transportation with poor physical health and other competing responsibilities; 3) treatment program

policies and schedule with competing responsibilities; and 4) stigma with poor physical and mental health. CONCLUSIONS: Understanding barriers to successful medication for opioid use disorder outcomes and considering their co-occurrence may help to identify and promote interventions to mitigate their impact. This work is intended to guide future research to adapt conceptual frameworks for understanding psychosocial and structural barriers affecting opioid use disorder treatment and ultimately intervention efforts to improve treatment outcomes.

Behavioral Health Services/Psychiatry/Neuropsychology

Rana GS, Nordsletten A, **Sivananthan M**, and Hong V. A 6-year retrospective review of psychiatric emergency service utilization by school-age children. *Clin Child Psychol Psychiatry* 2023; 28(1):367-381. PMID: 35594032. [Full Text](#)

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To explore utilization patterns and associated clinical factors of school-age children who present to a psychiatric emergency department. This was a 6-year retrospective chart review study of children 5-12 years of age who presented to a psychiatric emergency service from July 2012 to June 2018 (n = 1654 patients). Demographic variables, clinical diagnoses, lifetime adverse events (physical abuse, sexual abuse, and bullying), and history of self-harm were documented for each visit. We performed a chi square analysis to identify association between demographic and clinical features with key outcomes. Increased service utilization as defined by inpatient psychiatric admission, recurrent visits, or increased length of stay were found in patients who were adopted, presented with suicidal ideation or self-harm behaviors, had a history of abuse, and had a diagnosis of depression or autism. Trends over the course of the study indicated a significantly increased percentage of patients presenting with suicidal ideation, bullying, and self-harm behaviors. The data add to the limited literature regarding school-age children with a psychiatric emergency. Increased emergency service utilization for certain subgroups of children and trends over the course of the study underscore the need for enhanced treatment options for individuals with certain demographic or clinical features, and increased outpatient, intermediate, and inpatient treatment options, as well as preventative care.

Behavioral Health Services/Psychiatry/Neuropsychology

Zhang L, Yuan Y, Peng W, Tang B, Li MJ, **Gui H**, Wang Q, and Li M. GBC: a parallel toolkit based on highly addressable byte-encoding blocks for extremely large-scale genotypes of species. *Genome Biol* 2023; 24(1):76. PMID: 37069653. [Full Text](#)

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Whole -genome sequencing projects of millions of subjects contain enormous genotypes, entailing a huge memory burden and time for computation. Here, we present GBC, a toolkit for rapidly compressing large-scale genotypes into highly addressable byte-encoding blocks under an optimized parallel framework. We demonstrate that GBC is up to 1000 times faster than state-of-the-art methods to access and manage compressed large-scale genotypes while maintaining a competitive compression ratio. We also showed that conventional analysis would be substantially sped up if built on GBC to access genotypes of a large population. GBC's data structure and algorithms are valuable for accelerating large-scale genomic research.

Cardiology/Cardiovascular Research

Almajed MR, Mahmood S, Obri M, Nona P, Gonzalez PE, Chiang M, Wang DD, Frisoli T, Lee J, Basir M, O'Neill B, O'Neill W, and Villablanca P. Application of Impella mechanical circulatory support devices in transcatheter aortic valve replacement and balloon aortic valvuloplasty: A single center experience. *Cardiovasc Revasc Med* 2023; Epub ahead of print. PMID: 37012106. [Full Text](#)

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BACKGROUND/PURPOSE: Percutaneous valve interventions for aortic stenosis (AS) include transcatheter aortic valve replacement (TAVR) and balloon aortic valvuloplasty (BAV). Intraprocedural mechanical circulatory support (MCS) with Impella devices (Abiomed, Danvers, MA) is used in select high-risk patients, although data regarding its efficacy is limited. This study sought to evaluate the clinical outcomes of Impella use in patients with AS who underwent TAVR and BAV at a quaternary-care center. **METHODS/MATERIALS:** All patients with severe AS who underwent TAVR and BAV with Impella between 2013 and 2020 were included. Patient demographics, outcomes, complications, and 30-day mortality data was analyzed. **RESULTS:** Over the study period 2680 procedures were performed, 1965 TAVR and 715 BAV. 120 utilized Impella support, 26 TAVR and 94 BAV. Among TAVR Impella cases, justifications for MCS included cardiogenic shock (53.9 %), cardiac arrest (19.2 %), and coronary occlusion (15.4 %). Among BAV Impella cases, justifications for MCS included cardiogenic shock (55.3 %) and protected percutaneous coronary intervention (43.6 %). The 30-day mortality rate in TAVR Impella was 34.6 % and in BAV Impella was 28 %. BAV Impella cases involving cardiogenic shock had a higher rate of 45 %. Impella remained in-use past 24 h from the procedure in 32.2 % cases. Vascular access-related complications occurred in 4.8 % cases and bleeding complications occurred in 1.5 % cases. Conversion to open-heart surgery occurred in 0.7 % cases. **CONCLUSIONS:** MCS is an option for high-risk patients with severe AS who require TAVR and BAV. Despite hemodynamic support, the 30-day mortality rate remained high especially in cases where support was employed for cardiogenic shock.

Cardiology/Cardiovascular Research

Humes HD, Aaronson KD, Buffington DA, **Sabbah HN**, Westover AJ, Yessayan LT, Szamosfalvi B, and Paganì FD. Translation of immunomodulatory therapy to treat chronic heart failure: Preclinical studies to first in human. *PLoS One* 2023; 18(4):e0273138. PMID: 37023139. [Full Text](#)

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BACKGROUND: Inflammation has been associated with progression and complications of chronic heart failure (HF) but no effective therapy has yet been identified to treat this dysregulated immunologic state.

The selective cytopheretic device (SCD) provides extracorporeal autologous cell processing to lessen the burden of inflammatory activity of circulating leukocytes of the innate immunologic system. AIM: The objective of this study was to evaluate the effects of the SCD as an extracorporeal immunomodulatory device on the immune dysregulated state of HF. HF. METHODS AND RESULTS: SCD treatment in a canine model of systolic HF or HF with reduced ejection fraction (HFrEF) diminished leukocyte inflammatory activity and enhanced cardiac performance as measured by left ventricular (LV) ejection fraction and stroke volume (SV) up to 4 weeks after treatment initiation. Translation of these observations in first in human, proof of concept clinical study was evaluated in a patient with severe HFrEF/HFrEF ineligible for cardiac transplantation or LV LV assist device (LVAD) due to renal insufficiency and right ventricular dysfunction. Six hour SCD treatments over 6 consecutive days resulted in selective removal of inflammatory neutrophils and monocytes and reduction in key plasma cytokines, including tumor necrosis factor-alpha (TNF- α), interleukin (IL)-6, IL-8, and monocyte chemoattractant protein (MCP)-1. These immunologic changes were associated with significant improvements in cardiac power output, right ventricular stroke work index, cardiac index and LVSV index.... Stabilization of renal function with progressive volume removal permitted successful LVAD implantation. CONCLUSION: This translational research study demonstrates a promising immunomodulatory approach to improve cardiac performance in HFrEF/HFrEF and supports the important role of inflammation in the progression of HFHF.

Cardiology/Cardiovascular Research

Madan N, Hur DJ, Gannon MP, Gupta S, Weir-McCall JR, Johns C, Kumar A, Nagpal P, Fentanes E, **Lee J**, Choi AD, Ferencik M, Maroules CD, Villines TC, and Nicol ED. Contemporary cardiovascular computed tomography (CCT) training: Serial surveys of the international CCT community by the Fellow and Resident Leaders of the Society of Cardiovascular Computed Tomography (SCCT) Committee (FIRST) and SCCT Future Leaders Program (FLP). *J Cardiovasc Comput Tomogr* 2023; Epub ahead of print. PMID: 37015851. [Full Text](#)

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BACKGROUND: As cardiovascular computed tomography (CCT) practice evolves, the demand for specialists continues to increase. However, CCT training remains variable globally with limited contemporaneous data to understand this heterogeneity. We sought to understand the role of CCT globally and the training available to underpin its use. METHODS: We performed two consecutive surveys of cardiology and radiology physicians, two years apart, utilizing the Society of Cardiovascular Computed Tomography (SCCT) website, weblinks, social media platforms, and meeting handouts to maximize our response rate. We compared United States (US)-based vs. international responses to understand global similarities and differences in practice and training in the surveys. RESULTS: 235 respondents (37% trainees and 63% educators/non-trainees) initiated the first survey with 174 (74%) completing the core survey, with 205 providing their work location (114 US and 91 international). Eighty-

four percent (92/110) of educator respondents stated a need for increased training opportunities to meet growing demand. Dedicated training fellowships are heterogeneous, with limited access to structural heart imaging training, despite structural scanning being performed within institutions. The lack of a standardized curriculum was identified as the main obstacle to effective CCT learning, particularly in the US, with web-based learning platforms being the most popular option for improving access to CCT training. 148 trainees initiated the second survey with 107 (72%) completing the core components (51% North America, 49% international). Only 68% said they would be able to meet their required CCT education needs via their training program. Obstacles in obtaining CCT training again included a lack of a developed curriculum (51%), a lack of dedicated training time (35%), and a lack of local faculty expertise (31%). There was regional variability in access to CCT training, and, in contrast to the first survey, most (89%) felt 1:1 live review of cases with trained/expert reader was most useful for improving CCT training alongside formal curriculum/live lectures (72%). CONCLUSIONS: There is a need to expand dedicated CCT training globally to meet the demand for complex CCT practice. Access to CCT education (didactic and 1:1 case-based teaching from expert faculty), implementation of recently published global training curricula, and increased teaching resources (web-based) as an adjunct to existing experiential learning opportunities, are all deemed necessary to address current educational shortfalls.

Cardiology/Cardiovascular Research

Nassif M, Birmingham MC, **Lanfear DE**, Golbus JR, Gupta B, Fawcett C, Harrison MC, and Spertus JA. Recruitment Strategies of a Decentralized Randomized Placebo Controlled Clinical Trial: The Canagliflozin Impact on Health Status, Quality of Life and Functional Status in Heart Failure (CHIEF-HF) Trial. *J Card Fail* 2023; Epub ahead of print. PMID: 37040839. [Full Text](#)

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BACKGROUND: There has been growing interest in patient-centered clinical trials using mobile technologies to reduce the need for in-person visits. The CHIEF-HF trial was designed as a double-blind, randomized, fully decentralized clinical trial (DCT) that identified, consented, treated, and followed participants without any in-person visits. Patient-reported questionnaires were the primary outcome, which were collected by a mobile application. To inform future DCTs, we sought to describe the strategies used in successful trial recruitment. **METHODS:** This paper describes the operational structure and novel strategies employed in a completely DCT by summarizing the recruitment, enrollment, engagement, retention, and follow-up processes used in the execution of the trial at 18 centers. **RESULTS:** A total of 18 sites contacted 130,832 potential participants, of which 2,572 (2.0%) opened a hyperlink to the study website, completed a brief survey, and agreed to be contacted for potential inclusion. Of these, 1,333 were eligible and 658 consented with 182 screen-failures, primarily due to baseline Kansas City Cardiomyopathy Questionnaire scores not meeting inclusion criteria, resulting in 476 participants being enrolled (18.5%). There was significant site-level variation in the number of patients invited (median = 2,976; range 73-46,920) and in those agreeing to be contacted (median = 2.4%; range 0.05% - 16.4%). At the highest enrolling site, patients contacted by electronic medical record portal messaging were more likely to successfully opt-into the study than those contacted by email alone (7.8% vs 4.4%). **CONCLUSIONS:** CHIEF-HF used a novel design and operational structure to test the efficacy of a therapeutic treatment but marked variability across sites and strategies in recruiting participants was observed. While this approach may be advantageous for clinical research across a broader range of therapeutic areas, further optimizing recruitment efforts is warranted. **REGISTRATION:** NCT04252287: <https://clinicaltrials.gov/ct2/show/NCT04252287>.

Cardiology/Cardiovascular Research

Nelson RK, **Solomon R**, Hosmer E, and Zuhl M. Cardiac rehabilitation utilization, barriers, and outcomes among patients with heart failure. *Heart Fail Rev* 2023; Epub ahead of print. PMID: 37039955. [Full Text](#)

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Exercise-based cardiac rehabilitation (CR) is effective for improving both primary (i.e., mortality and hospitalizations) and secondary (i.e., functional capacity and quality of life among) clinical outcomes among patients with heart failure (HF). The mechanisms that explain these benefits are complex and are linked to exercise adaptations such as central and peripheral hemodynamics combined with improved overall medical management. Despite the benefits of CR, utilization rates are low among CR eligible patients. Clinician-, patient-, and health system-related barriers have been identified as primary factors contributing to the lack of CR utilization among HF patients. These include patient referrals (clinician-related), psychosocial factors (patient-related), and patient access to CR services (health system-related). The aims of this review are to detail the components of each barrier as well as identify evidence-based strategies to improve CR utilization and adherence among HF. The improvements in primary and secondary outcomes along with the mechanisms that are linked to these changes will also be examined.

Cardiology/Cardiovascular Research

Obeidat L, Albusoul L, Maki M, Ibrahim H, and Parikh S. Infliximab-Induced Lupus in a Patient With Psoriatic Arthritis Who Presented With Cardiac Tamponade: A Case Report. *Cureus* 2023; 15(3):e36424. PMID: 37090269. [Full Text](#)

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Psoriatic arthritis (PsA) is a chronic, immune-mediated inflammatory condition, and the proinflammatory cytokine tumor necrosis factor- α (TNF- α) plays a major pathogenic role in the development and progression of PsA. Anti-TNF- α therapies, such as the monoclonal antibody infliximab, are used to treat patients whose PsA has not responded favorably to conventional anti-rheumatic drugs. However, exposure to anti-TNF- α therapeutics can lead to drug-induced lupus erythematosus (DILE), which may rarely be accompanied by cardiac manifestations. Here, we describe a rare case of drug-induced lupus erythematosus secondary to infliximab therapy for PsA and psoriasis in a patient who presented with life-threatening acute pericarditis and cardiac tamponade. Newly developed skin rashes, newly elevated autoimmune indicators, and punch biopsy results indicating subacute cutaneous lupus collectively supported a DILE diagnosis within the context of infliximab use. Pericardiocentesis, colchicine, and corticosteroids alleviated symptoms, and infliximab was replaced with alternate therapy. This case highlights the importance of early recognition of the possible serious and uncommon adverse reactions from infliximab therapy. Prompt initiation of appropriate treatment and discontinuation of the offending agent are critical in cases of drug-induced lupus erythematosus, particularly when rare cardiac complications occur.

Center for Health Policy and Health Services Research

Harry ML, Sanchez K, **Ahmedani BK**, Beck AL, Coleman KJ, Coley RY, Daida YG, Lynch FL, Rossom RC, Waring SC, and Simon GE. Assessing the differential item functioning of PHQ-9 items for diverse racial and ethnic adults with mental health and/or substance use disorder diagnoses: A retrospective cohort study. *J Affect Disord* 2023; Epub ahead of print. PMID: 37127116. [Full Text](#)

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BACKGROUND: Improving health equity in depression care and suicide screening requires that measures like the Patient Health Questionnaire 9 (PHQ-9) function similarly for diverse racial and ethnic groups. We evaluated PHQ-9 differential item functioning (DIF) between racial/ethnic groups in a retrospective cohort study of secondary electronic health record (EHR) data from eight healthcare systems. **METHODS:** The population (n = 755,156) included patients aged 18-64 with mental health and/or substance use disorder (SUD) diagnoses who had a PHQ-9 with no missing item data in the EHR for primary care or mental health visits between 1/1/2009-9/30/2017. We drew two random samples of 1000 from the following racial/ethnic groups originally recorded in EHRs (n = 14,000): Hispanic, and non-Hispanic White, Black, Asian, American Indian/Alaska Native, Native Hawaiian/Other Pacific Islander, multiracial. We assessed DIF using iterative hybrid ordinal logistic regression and item response theory with $p < 0.01$ and 1000 Monte Carlo simulations, where change in model $R^2 > 0.01$ represented non-negligible (e.g., clinically meaningful) DIF. **RESULTS:** All PHQ-9 items displayed statistically significant, but negligible (e.g., clinically unmeaningful) DIF between compared groups. The negligible DIF varied between random samples, although six items showed negligible DIF between the same comparison groups in both random samples. **LIMITATIONS:** Our findings may not generalize to disaggregated racial/ethnic groups or persons without mental health and/or SUD diagnoses. **CONCLUSIONS:** We found the PHQ-9 had clinically unmeaningful cross-cultural DIF for adult patients with mental health and/or SUD diagnoses. Future research could disaggregate race/ethnicity to discern if within-group identification impacts PHQ-9 DIF.

Center for Health Policy and Health Services Research

Hecht LM, Adams R, Dutkiewicz D, Radloff D, Wales MN, Whitmer J, Murphy D, and Santarossa S. "Healing Can Be a Very Jagged Line": Reflections on Life as a COVID-19 Long Hauler. *J Patient Cent Res Rev* 2023; 10(2):77-81. PMID: 37091113. [Full Text](#)

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"Long COVID" - a term referring to COVID-19-associated symptoms and conditions (ie, sequelae) that remain or emerge after resolution of a SARS-CoV-2 infection - is a multifaceted condition about which little is known. As part of formalized patient-engaged research at a large Midwestern health system, patient stakeholders with long COVID (N=5) wrote stories based on their lived experience, as this was their preferred format for detailing their experience with the condition. These patient stakeholders reviewed one another's stories, identified relevant quotes, and provided opportunities for elaboration. Independently, a trained researcher extracted quotes from the stories, identified themes, and wove the quotes together to share the independent, yet similar, stories. Emergent themes were that of uncertainty about the symptomatology of long COVID and its effects on patients' mental health, physical functioning, family unit, self-identity, and future outlook. Further patient-engaged research on understanding the lived experience of long COVID may serve to advance knowledge and treatment. Health care providers caring for those with long COVID can benefit from listening and validating the stories of individuals suffering from this condition.

Center for Individualized and Genomic Medicine Research

Weinstock JS, Gopakumar J, **Williams LK, Xiao S, Yang M**, et al. Aberrant activation of TCL1A promotes stem cell expansion in clonal haematopoiesis. *Nature* 2023; 616(7958):755-763. PMID: 37046083. [Full Text](#)

Mutations in a diverse set of driver genes increase the fitness of haematopoietic stem cells (HSCs), leading to clonal haematopoiesis(1). These lesions are precursors for blood cancers(2-6), but the basis of their fitness advantage remains largely unknown, partly owing to a paucity of large cohorts in which the clonal expansion rate has been assessed by longitudinal sampling. Here, to circumvent this limitation, we developed a method to infer the expansion rate from data from a single time point. We applied this method to 5,071 people with clonal haematopoiesis. A genome-wide association study revealed that a common inherited polymorphism in the TCL1A promoter was associated with a slower expansion rate in clonal haematopoiesis overall, but the effect varied by driver gene. Those carrying this protective allele exhibited markedly reduced growth rates or prevalence of clones with driver mutations in TET2, ASXL1, SF3B1 and SRSF2, but this effect was not seen in clones with driver mutations in DNMT3A. TCL1A was not expressed in normal or DNMT3A-mutated HSCs, but the introduction of mutations in TET2 or ASXL1 led to the expression of TCL1A protein and the expansion of HSCs in vitro. The protective allele restricted TCL1A expression and expansion of mutant HSCs, as did experimental knockdown of TCL1A expression. Forced expression of TCL1A promoted the expansion of human HSCs in vitro and mouse HSCs in vivo. Our results indicate that the fitness advantage of several commonly mutated driver genes in clonal haematopoiesis may be mediated by TCL1A activation.

Center for Individualized and Genomic Medicine Research

Weinstock JS, Laurie CA, **Gui H, Xiao S, Williams LK**, et al. The genetic determinants of recurrent somatic mutations in 43,693 blood genomes. *Sci Adv* 2023; 9(17):eabm4945. PMID: 37126548. [Full Text](#)

Nononcogenic somatic mutations are thought to be uncommon and inconsequential. To test this, we analyzed 43,693 National Heart, Lung and Blood Institute Trans-Omics for Precision Medicine blood whole genomes from 37 cohorts and identified 7131 non-missense somatic mutations that are recurrently mutated in at least 50 individuals. These recurrent non-missense somatic mutations (RNMSMs) are not clearly explained by other clonal phenomena such as clonal hematopoiesis. RNMSM prevalence increased with age, with an average 50-year-old having 27 RNMSMs. Inherited germline variation associated with RNMSM acquisition. These variants were found in genes involved in adaptive immune function, proinflammatory cytokine production, and lymphoid lineage commitment. In addition, the presence of eight specific RNMSMs associated with blood cell traits at effect sizes comparable to Mendelian genetic mutations. Overall, we found that somatic mutations in blood are an unexpectedly common phenomenon with ancestry-specific determinants and human health consequences.

Dermatology

Ceresnie MS, Gonzalez S, and Hamzavi IH. Diagnosing Disorders of Hypopigmentation and Depigmentation in Patients with Skin of Color. *Dermatol Clin* 2023. PMID: Not assigned. [Full Text](#)

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Dermatology

Ceresnie MS, Warbasse E, Gonzalez S, Pourang A, and Hamzavi IH. Implementation of the vitiligo area scoring index in clinical studies of patients with vitiligo: a scoping review. *Arch Dermatol Res* 2023; Epub ahead of print. PMID: 37029284. [Full Text](#)

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The vitiligo area scoring index (VASI) is a validated, reliable clinician-reported outcome measure widely used to assess the extent of skin depigmentation seen in patients with vitiligo and to measure patient responses to therapies for vitiligo in clinical trials. However, its implementation in studies is inconsistent and makes comparing results across different studies difficult. The aim of this scoping review is to summarize interventional clinical studies that applied the VASI to measure vitiligo and identify variability in VASI implementation. A systematic search of Ovid Medline, Embase, Web of Science, Cochrane, and ClinicalTrials.gov was performed. Interventional studies published between January 1946 and October 2020 that used the VASI as an outcome measure for assessing vitiligo response were reviewed for methodological approach. Great heterogeneity was found within the 55 included interventional studies that used VASI as an outcome measure. A total of 9 VASI subtypes were described by the authors within 10 intervention categories. VASI determined study eligibility in one study. Body surface area was most frequently established using inconsistent methods. We found unclear or ambiguously scaled assessments of depigmentation. Most VASI outcomes were reported as mean absolute difference, percentage VASI improvement, and percentage of patients who achieved the VASI endpoint. The VASI score was over 100 in one study. Our scoping review revealed many VASI methodology variations in interventional clinical studies of vitiligo. While VASI is a standard method to measure vitiligo changes, substantial heterogeneity in methodology limits reliable comparison and interpretation of findings from different clinical trials. Our findings may be used as a foundation to standardize the VASI outcome measure methodology, allowing for improved clinician training and rigorous data analysis across vitiligo research groups worldwide.

Dermatology

De DR, Rick JW, Shih T, Hsiao JL, **Hamzavi I**, and Shi VY. COVID-19 Infection in Hidradenitis Suppurativa Patients: A Retrospective Study. *Skin Appendage Disord* 2023. PMID: Not assigned. [Full Text](#)

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Introduction: Hidradenitis suppurativa (HS) is associated with comorbidities that are risk factors for severe COVID-19 infection. We evaluated demographics and COVID-19 outcomes in HS patients. Methods: HS patients with COVID-19 (HS+/COVID+) and a randomized age-, race-, and sex-matched control population of patients without HS with COVID-19 (HS-/COVID+) were selected through a retrospective chart review. Data were collected on demographics, medications, comorbidities, vaccination status, and COVID-19 treatment/outcomes. Fisher's exact test was used to analyze the relationship between risk factors and COVID-19 outcomes. A p value of <0.05 was considered statistically significant. Results: There were 58 HS+/COVID+ patients, primarily African American (83%, n = 48) and female (88%, n = 51). Compared to HS+/COVID+ patients, HS-/COVID+ patients were significantly more likely to have cardiovascular disease (51% vs. 24%; p = 0.0029) and be pregnant (23% vs. 4%; p = 0.0093). HS+/COVID+ and HS-/COVID+ patients did not vary significantly in vaccination rate at time of COVID-19 diagnosis (6% vs. 5%; p = 0.78). HS-/COVID+ patients were significantly more likely to have COVID-19 complications (35% vs. 7%; p = 0.001) and receive COVID-19 treatment (37% vs. 7%; p = 0.0001) when compared to HS+/COVID+ patients. Conclusion: Our findings support the growing evidence that having HS itself may not be a risk factor for severe COVID-19 outcomes.

Dermatology

Strahan AG, Lubov JE, Prasad S, Fox LP, McMahon DE, Singh R, Rosenbach M, Desai SR, **Lim HW**, Thiers BH, Hruza GJ, French LE, and Freeman EE. The impact of the American Academy of Dermatology/International League of Dermatological Societies COVID-19 registry during the pandemic: 2500 cases across 72 countries. *J Am Acad Dermatol* 2023; Epub ahead of print. PMID: 37120029. [Full Text](#)

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Dermatology

Wang P, Gilbert M, Lim HW, McHargue C, Friedman BJ, Veenstra JJ, and Siddiqui F. Single-fraction Radiation Therapy for Localized Cutaneous T-cell Lymphoma. *Pract Radiat Oncol* 2023; Epub ahead of print. PMID: 37040819. [Full Text](#)

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BACKGROUND: Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL). Single-fraction radiation therapy has been used as a skin-targeted therapy to treat localized CTCL lesions. **OBJECTIVE:** To investigate the treatment outcomes associated with single-fraction radiation therapy for CTCL. **METHODS:** We retrospectively studied the outcomes among patients with CTCL treated with single fraction radiation therapy at our institution between October 2013 and August 2022. Clinical response including complete response (CR), partial response (PR) or no response (NR) and re-treatment response were evaluated. **RESULTS:** A total of 242 lesions from 46 patients were analyzed, for an average of 5.3 lesions treated per patient. The majority of lesions presented with a plaque morphology (n = 145, 60.0%). All lesions were treated to a dose of 8 Gy in 1 fraction. Median follow-up was 24.6 months (range, 1-88 months). Of the 242 lesions, 36 (14.8%) had an initial PR or NR; all were re-treated with the same regimen to the same site at a median interval of 8 weeks. 50% of re-treated lesions (n = 18) went on to have a CR. Thus, the overall CR rate for CTCL lesions was 92.6%. No recurrences were noted in the treated areas after achieving CR. **CONCLUSION:** Single-fraction radiation therapy to a dose of 8 Gy in 1 fraction to localized areas provided a high rate of complete and durable responses in the affected sites.

Dermatology

Zhang J, Peng Y, Hu Y, Guo H, Sun Y, Zhang X, **Mi QS**, and Xu Y. TFAM Deficiency–Mediated Mitochondrial Disorder Affects Langerhans Cell Maintenance and Function. *J Invest Dermatol* 2023; 143(3):508-513.e502. PMID: 36049540. [Full Text](#)

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Dermatology

Zolghadri S, Beygi M, **Mohammad TF**, Alijanianzadeh M, Pillaiyar T, Garcia-Molina P, Garcia-Canovas F, Luis Munoz-Munoz J, and Akbar Saboury A. Targeting Tyrosinase in Hyperpigmentation: Current Status, Limitations and Future Promises. *Biochem Pharmacol* 2023;115574. Epub ahead of print. PMID: 37127249. [Request Article](#)

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Hyperpigmentation is a common and distressing dermatologic condition. Since tyrosinase (TYR) plays an essential role in melanogenesis, its inhibition is considered a logical approach along with other therapeutic methods to prevent the accumulation of melanin in the skin. Thus, TYR inhibitors are a tempting target as the medicinal and cosmetic active agents of hyperpigmentation disorder. Among TYR inhibitors, hydroquinone is a traditional lightening agent that is commonly used in clinical practice. However, despite good efficacy, prolonged use of hydroquinone is associated with side effects. To overcome these shortcomings, new approaches in targeting TYR and treating hyperpigmentation are desperately required. In line with this purpose, several non-hydroquinone lightening agents have been developed and suggested as hydroquinone alternatives. In addition to traditional approaches, nanomedicine and nanotheranostic platforms have been recently proposed in the treatment of hyperpigmentation. In this review, we discuss the available strategies for the management of hyperpigmentation with a focus on TYR inhibition. In addition, alternative treatment options to hydroquinone are discussed. Finally, we present nano-based strategies to improve the therapeutic effect of drugs prescribed to patients with skin disorders.

Diagnostic Radiology

Karandikar A, Solberg A, Fung A, **Scher C**, **Leschied JR**, **Ledbetter K**, **Mandava S**, et al. Radiologists staunchly support patient safety and autonomy, in opposition to the SCOTUS decision to overturn Roe v Wade. *Clin Imaging* 2023; 93:117-121. PMID: 36064645. [Full Text](#)

Diagnostic Radiology

Kauffman N, Morrison J, **O'Brien K**, Fan J, and Zinn KR. Intra-Arterial Delivery of Radiopharmaceuticals in Oncology: Current Trends and the Future of Alpha-Particle Therapeutics. *Pharmaceutics* 2023; 15(4). PMID: 37111624. [Full Text](#)

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A paradigm shift is underway in cancer diagnosis and therapy using radioactivity-based agents called radiopharmaceuticals. In the new strategy, diagnostic imaging measures the tumor uptake of radioactive agent "X" in a patient's specific cancer, and if uptake metrics are realized, the patient can be selected for therapy with radioactive agent "Y". The X and Y represent different radioisotopes that are optimized for each application. X-Y pairs are known as radiotheranostics, with the currently approved route of therapy being intravenous administration. The field is now evaluating the potential of intra-arterial dosing of radiotheranostics. In this manner, a higher initial concentration can be achieved at the cancer site, which could potentially enhance tumor-to-background targeting and lead to improved imaging and therapy. Numerous clinical trials are underway to evaluate these new therapeutic approaches that can be performed via interventional radiology. Of further interest is changing the therapeutic radioisotope that provides radiation therapy by β - emission to radioisotopes that also decay by α -particle emissions. Alpha (α)-particle emissions provide high energy transfer to the tumors and have distinct advantages. This review discusses the current landscape of intra-arterially delivered radiopharmaceuticals and the future of α -particle therapy with short-lived radioisotopes.

Diagnostic Radiology

Silbergleit AK, Isabell K, Turnbull J, Patel N, Boettcher E, Konnai R, Collins D, Sidiropoulos C, and **Schultz L**. Comparison of Oropharyngeal Dysphagia Before and After Botulinum Toxin Injection in Cervical Dystonia. *Dysphagia* 2023; Epub ahead of print. PMID: 37071189. [Full Text](#)

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Cervical dystonia (CD) is the most common form of focal dystonia with Botulinum neurotoxin (BoNT) being a frequent method of treatment. Dysphagia is a common side effect of BoNT treatment for CD. Instrumental evaluation of swallowing in CD using standardized scoring for the videofluoroscopic swallowing study (VFSS) and validated and reliable patient-reported outcomes measures is lacking in the literature. (1) to determine if BoNT injections change instrumental findings of swallowing function using

the Modified Barium Swallow Impairment Profile (MBSImP) in individuals with CD; (2) to determine if BoNT injections change self-perception of the psychosocial handicapping effects of dysphagia in individuals with CD, using the Dysphagia Handicap Index (DHI); (3) to determine the effect of BoNT dosage on instrumental swallowing evaluation and self-reported swallowing outcomes measures. 18 subjects with CD completed a VFSS and the DHI before and after BoNT injection. There was a significant increase in pharyngeal residue for pudding consistency after BoNT injection, $p = 0.015$. There were significant positive associations between BoNT dosage and self-perception of the physical attributes of the handicapping effect of dysphagia, the grand total score and patient self-reported severity of dysphagia on the DHI; $p = 0.022$; $p = 0.037$; $p = 0.035$ respectively. There were several significant associations between changes in MBSImP scores and BoNT dose. Pharyngeal efficiency of swallowing may be affected by BoNT for thicker consistencies. Individuals with CD perceive greater physical handicapping effects of dysphagia with increased amounts of BoNT units and have greater self-perceptions of dysphagia severity with increased amounts of BoNT units.

Emergency Medicine

Ball M, Powell JR, Gage CB, Kapalo KA, Kurth JD, Collard L, Miller MG, and Panchal AR. Paramedic educational program attrition accounts for significant loss of potential EMS workforce. *J Am Coll Emerg Physicians Open* 2023; 4(2):e12917. PMID: 37034493. [Full Text](#)

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OBJECTIVE: Recent concerns for the strength and stability of the emergency medical services (EMS) workforce have fueled interest in enhancing the entry of EMS clinicians into the workforce. However, the educational challenges associated with workforce entry remain unclear. Our objective was to evaluate the educational pathway of entry into the EMS workforce and to identify factors that lead to the loss of potential EMS clinicians. **METHODS:** This is a cross-sectional evaluation of all US paramedic educational programs, with enrolled students, in the 2019 Committee on Accreditation of Educational Programs for the EMS Professions annual report survey. This data set includes detailed program characteristics and metrics including program attrition rate (leaving before completion), and certifying exam pass rates. Descriptive statistics were calculated, and multivariable logistic regression analysis was conducted to evaluate the association between high program attrition rates (>30%) and program specific characteristics. **RESULTS:** In 2019, 640 accredited programs met inclusion with 17,457 students enrolled in paramedic educational programs. Of these, 13,884 students successfully graduated (lost to attrition, 3,573/17,457 [21%]) and 12,002 passed the certifying exam on the third attempt (lost to unable to certify, 1,882/17,457 [11%]). High program attrition rates were associated with longer programs (>12 months), small class sizes (<12 students), and regional locations. **CONCLUSIONS:** Nearly 1 in 3 paramedic students were lost from the potentially available workforce either owing to attrition during the educational program or failure to certify after course completion. Attrition represented the largest loss, providing an avenue for future targeted research and interventions to improve EMS workforce stability.

Emergency Medicine

Hanson CG, and **Chopra A**. A Case of Neuroleptic Malignant Syndrome Presenting as Anxiety. *Cureus* 2023; 15(3):e35892. PMID: 37033557. [Full Text](#)

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Neuroleptic malignant syndrome (NMS) is a rare but potentially lethal complication of dopamine antagonist use. A 34-year-old male presented to the emergency department with a chief complaint of feeling anxious for the past several days. He presented with his family who helped provide history as he had become less communicative over the preceding two days. It was revealed that the patient had a

recent psychiatric hospitalization for suspected new-onset psychosis and was discharged six days prior to his presentation. It was reported that the patient was discharged with unknown psychiatric medications but stopped taking them two days prior because he felt they were increasing his anxiety. On physical examination, the patient was found to have upper extremity rigidity and appeared tremulous. A review of records revealed that the patient was discharged from inpatient psychiatric treatment on dual antipsychotic therapy. With this information, the patient met the diagnostic criteria for NMS. He was hospitalized and his symptoms resolved following treatment. Without the knowledge of antipsychotic use, the diagnosis of a serious, life-threatening condition may have been missed. Our case highlights an important but occasionally overlooked aspect of evaluating a patient in the emergency department, namely, outside chart and documentation reviewing.

Emergency Medicine

Horiuchi Y, Wettersten N, van Veldhuisen DJ, Mueller C, **Nowak R**, Hogan C, Kontos MC, Cannon CM, Birkhahn R, Vilke GM, Mahon N, Nuñez J, Briguori C, Duff S, Murray PT, and Maisel A. The influence of body mass index on clinical interpretation of established and novel biomarkers in acute heart failure. *J Card Fail* 2023; Epub ahead of print. PMID: 37127240. [Full Text](#)

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BACKGROUND: Body mass index (BMI) is a known confounder for natriuretic peptides but its influence on other biomarkers is less well described. We investigated whether BMI interacts with biomarkers association with prognosis in patients with acute heart failure (AHF). **METHODS AND RESULTS:** B-type natriuretic peptide (BNP), high-sensitivity cardiac troponin I (hs-cTnI), galectin-3, serum neutrophil gelatinase associated lipocalin (sNGAL) and urine NGAL were measured serially in AHF patients during hospitalization in the AKINESIS study. Cox regression analysis was used to determine the association of biomarkers and their interaction with BMI for 30-day, 90-day and 1-year composite outcome of death or HF readmission. Among 866 patients, 21.2%, 29.7%, and 46.8% had normal (18.5-24.9 kg/m²), overweight (25-29.9 kg/m²), and obese (≥ 30 kg/m²) BMIs on admission, respectively. Admission values of BNP and hs-cTnI were negatively associated with BMI, while galectin-3 and sNGAL were positively associated with BMI. Admission BNP and hs-cTnI were associated with the composite outcome within 30-day, 90-day and 1-year. Only BNP had a significant interaction with BMI. When BNP was analyzed by BMI category, its association with the composite outcome attenuated at higher BMIs and was no longer significant in obese individuals. Findings were similar when evaluated by the last measured biomarkers and BMI. **CONCLUSIONS:** In patients with AHF, only BNP had a significant interaction with BMI for the outcomes with its association attenuating as BMI increased. hs-cTnI was prognostic regardless of BMI.

Emergency Medicine

Jones CW, An X, **Lewandowski C**, et al. Derivation and Validation of a Brief Emergency Department-Based Prediction Tool for Posttraumatic Stress After Motor Vehicle Collision. *Ann Emerg Med* 2023; 81(3):249-261. PMID: 36328855. [Full Text](#)

STUDY OBJECTIVE: To derive and initially validate a brief bedside clinical decision support tool that identifies emergency department (ED) patients at high risk of substantial, persistent posttraumatic stress symptoms after a motor vehicle collision. **METHODS:** Derivation (n=1,282, 19 ED sites) and validation (n=282, 11 separate ED sites) data were obtained from adults prospectively enrolled in the Advancing Understanding of Recovery after Trauma study who were discharged from the ED after motor vehicle collision-related trauma. The primary outcome was substantial posttraumatic stress symptoms at 3 months (Posttraumatic Stress Disorder Checklist for Diagnostic and Statistical Manual of Mental Disorders-5 ≥ 38). Logistic regression derivation models were evaluated for discriminative ability using the area under the curve and the accuracy of predicted risk probabilities (Brier score). Candidate posttraumatic stress predictors assessed in these models (n=265) spanned a range of sociodemographic, baseline health, peritraumatic, and mechanistic domains. The final model selection was based on performance and ease of administration. **RESULTS:** Significant 3-month posttraumatic stress symptoms were common in the derivation (27%) and validation (26%) cohort. The area under the curve and Brier score of the final 8-question tool were 0.82 and 0.14 in the derivation cohort and 0.76 and 0.17 in the validation cohort. **CONCLUSION:** This simple 8-question tool demonstrates promise to risk-stratify individuals with substantial posttraumatic stress symptoms who are discharged to home after a motor vehicle collision. Both external validation of this instrument, and work to further develop more accurate tools, are needed. Such tools might benefit public health by enabling the conduct of preventive intervention trials and assisting the growing number of EDs that provide services to trauma survivors aimed at promoting psychological recovery.

Emergency Medicine

Rowland GE, Roeckner A, **Lewandowski C**, et al. Prior Sexual Trauma Exposure Impacts Posttraumatic Dysfunction and Neural Circuitry Following a Recent Traumatic Event in the AURORA Study. *Biol Psychiatry Glob Open Sci* 2023. PMID: Not assigned. [Full Text](#)

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Background: Prior sexual trauma (ST) is associated with greater risk for posttraumatic stress disorder after a subsequent traumatic event; however, the underlying neurobiological mechanisms remain opaque. We investigated longitudinal posttraumatic dysfunction and amygdala functional dynamics following admission to an emergency department for new primarily nonsexual trauma in participants with and without previous ST. **Methods:** Participants (N = 2178) were recruited following acute trauma exposure (primarily motor vehicle collision). A subset (n = 242) completed magnetic resonance imaging that included a fearful faces task and a resting-state scan 2 weeks after the trauma. We investigated associations between prior ST and several dimensions of posttraumatic symptoms over 6 months. We further assessed amygdala activation and connectivity differences between groups with or without prior ST. **Results:** Prior ST was associated with greater posttraumatic depression ($F_{1,1120} = 28.35, p = 1.22 \times 10^{-7}, \eta^2 = 0.06$), anxiety ($F_{1,1113} = 17.43, p = 3.21 \times 10^{-5}, \eta^2 = 0.05$), and posttraumatic stress disorder ($F_{1,1027} = 11.34, p = 7.85 \times 10^{-4}, \eta^2 = 0.04$) severity and more maladaptive beliefs about pain ($F_{1,1113} = 8.51, p = .004, \eta^2 = 0.02$) but was not related to amygdala reactivity to fearful versus neutral faces (all p s > .05). A secondary analysis revealed an interaction between ST and lifetime trauma load on the left amygdala to visual cortex connectivity (peak Z value: -4.41, corrected $p < .02$). **Conclusions:** Findings suggest that prior ST is associated with heightened posttraumatic dysfunction following a new trauma exposure but not increased amygdala activity. In addition, ST may interact with lifetime trauma load to alter neural circuitry in visual processing regions following acute trauma exposure. Further research should probe the relationship between trauma type and visual circuitry in the acute aftermath of trauma.

Emergency Medicine

Stewart CR, Hanson CG, and Cronovich HA. Spontaneous Arterial Thrombus and Dissection Associated With Exercise and Exogenous Testosterone Use. *Cureus* 2023; 15(3):e35936. PMID: 37038590. [Full Text](#)

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Spontaneous lower extremity arterial dissection has been linked to atherosclerotic and non-atherosclerotic causes. A 55-year-old male presented to the emergency department via emergency medical services for a chief complaint of right leg pain. He stated that he was performing leg exercises when he felt a sudden pop in his right leg followed by severe pain. His exam was remarkable for lack of ipsilateral distal popliteal or dorsalis pedis pulse by palpation or doppler. The patient was admitted to a three-year history of non-prescription testosterone injection use along with a history of prior portal vein thrombosis two years prior with anticoagulation noncompliance after one month of therapy. A computed tomography angiography of the lower extremity was performed which demonstrated complete acute occlusion of the right common iliac, and right external iliac, along with right femoral artery dissection. The patient was emergently taken to the operating room with vascular surgery where a thrombectomy with stent placement was performed. After three days in the surgical intensive care unit and nine days in the hospital, the patient was subsequently discharged from the hospital in good condition. A post-operative follow-up appointment three weeks after discharge revealed mild residual pain; however, no issues ambulating or residual weakness, and normal ankle-brachial indexes. This case highlights a unique presentation of acute limb ischemia associated with exogenous testosterone use.

Emergency Medicine

Vuong L, Kenney RM, Thomson JM, Faison DJ, Church BM, McCollom R, Gunaga S, Cahill MM, Slezak MA, Davis SL, and Veve MP. Implementation of indication-based antibiotic order sentences improves antibiotic use in emergency departments. *Am J Emerg Med* 2023; 69:5-10. PMID: 37027958. [Full Text](#)

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INTRODUCTION: Prior data have suggested that suboptimal antibiotic prescribing in the emergency department (ED) is common for uncomplicated lower respiratory tract infections (LRTI), urinary tract infections (UTI), and acute bacterial skin and skin structure infections (ABSSSI). The objective of this study was to measure the effect of indication-based antibiotic order sentences (AOS) on optimal antibiotic prescribing in the ED. **METHODS:** This was an IRB-approved quasi-experiment of adults prescribed antibiotics in EDs for uncomplicated LRTI, UTI, or ABSSSI from January to June 2019 (pre-implementation) and September to December 2021 (post-implementation). AOS implementation occurred in July 2021. AOS are lean process, electronic discharge prescriptions retrievable by name or indication within the discharge order field. The primary outcome was optimal prescribing, defined as correct antibiotic selection, dose, and duration per local and national guidelines. Descriptive and bivariate statistics were performed; multivariable logistic regression was used to determine variables associated with optimal prescribing. **RESULTS:** A total of 294 patients were included: 147 pre-group and 147 post-group. Overall optimal prescribing improved from 12 (8%) to 34 (23%) ($P < 0.001$). Individual components of optimal prescribing were optimal selection at 90 (61%) vs 117 (80%) ($P < 0.001$), optimal dose at 99 (67%) vs 115 (78%) ($P = 0.036$), and optimal duration at 38 (26%) vs 50 (34%) ($P = 0.13$) for pre- and

post-group, respectively. AOS was independently associated with optimal prescribing after multivariable logistic regression analysis (adjOR, 3.6; 95%CI,1.7-7.2). A post-hoc analysis showed low uptake of AOS by ED prescribers. CONCLUSIONS: AOS are an efficient and promising strategy to enhance antimicrobial stewardship in the ED.

Endocrinology and Metabolism

Isaacs D, **Kruger DF**, Shoger E, and Chawla H. Patient Perceptions of Satisfaction and Quality of Life Regarding Use of a Novel Insulin Delivery Device. *Clin Diabetes* 2023; 41(2):198-207. PMID: 37092165. [Full Text](#)

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Advances in insulin delivery technologies have led to the development of tubeless "patch" systems; however, these devices still involve a level of complexity. We surveyed individuals with type 1 or type 2 diabetes to explore their attitudes and satisfaction after using the CeQur Simplicity insulin patch (SIP) for 2 months. Transition to the SIP yielded significant increases in respondents' overall treatment satisfaction, less diabetes burden, and improvements in psychological well-being compared with respondents' prior insulin delivery method.

Family Medicine

Larrabee K, Meeks N, Williams AM, Springer K, Siddiqui F, Chang SS, Ghanem T, Wu VF, Momin S, and Tam S. Cognitive Function and Postoperative Outcomes in Patients with Head and Neck Cancer. *Laryngoscope* 2023; Epub ahead of print. PMID: 37017269. [Full Text](#)

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OBJECTIVE: Determine the relationship between cognitive function and postoperative outcomes.

METHODS: This IRB-approved retrospective cohort study included all patients treated between August 2015 and March 2020 undergoing major surgery for aerodigestive cancer or cutaneous/thyroid cancer that required free-flap reconstruction at Henry Ford Hospital. Routine administration of the Montreal Cognitive Assessment (MoCA) was completed as part of preoperative psychosocial evaluation. Outcomes included postoperative diagnosis of delirium, discharge disposition, return to the emergency department within 30 days of surgery, and readmission within 30 days of surgery. Univariate and multivariate logistic regression were used to determine the associations between preoperative MoCA score and each outcome measure. RESULTS: One hundred thirty-five patients with HNC were included in the study (mean [SD] age, 60.7 [\pm 10.8] years; 70.4% [n = 95] male; 83.0% [n = 112] White, 16.3% [n = 22] Black). The average preoperative MoCA score was 23.4 (SD \pm 4.5). Based on the MoCA score, 35% (n = 47) scored \geq 26 (i.e., normal cognitive status), 55.6% (n = 75) scored between 18 and 25 (i.e., mild impairment), 8.1% (n = 11) scored between 10 and 17 (i.e., moderate impairment), and 1.5% (n = 2) scored <10 (i.e., severe impairment). After adjusting for other variables, a lower MoCA score was associated with discharge disposition to a location other than home and prolonged length of hospital stay. CONCLUSIONS: Preoperative cognitive function in patients undergoing major head and neck surgery for head and neck cancer was associated with discharge destination and length of stay. LEVEL OF EVIDENCE: 3 *Laryngoscope*, 2023.

Gastroenterology

Blach S, **Brown KA**, Brown RS, Gholam PM, Terrault NA, Estes C, and Razavi HA. Modeling HCV elimination recovery following the COVID-19 pandemic in the United States: Pathways to regain progress. *J Infect Public Health* 2023; 16(1):64-70. PMID: 36473359. [Full Text](#)

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BACKGROUND: As of 2019, the United States (US) was not on track to achieve targets for elimination, due to increasing incidence and treatment barriers. In 2020, the COVID-19 pandemic disrupted HCV services globally and in the US. As healthcare services normalize, there is an urgent need to reassess progress and evaluate scenarios that restore a pathway toward HCV elimination. **METHODS:** We updated a validated Markov model to estimate HCV-related morbidity and mortality in the US. Five scenarios were developed to bookend possible HCV outcomes in the wake of the pandemic. These included 1) return to pre-COVID-19 treatment forecasts; 2) achieve elimination targets through treatment and harm reduction; 3) long-term treatment disruptions; 4/5) achieve elimination targets through increased treatment without increased harm reduction, starting in either 2022 or 2025. **FINDINGS:** From 2014-2019, more than 1.2 million patients were treated for HCV in the US. Elimination targets in 2030 could be achieved in the US by treating an additional 3.2-3.3 million patients from 2020 to 2030, or by preventing new infections through expanded harm reduction programs and treating up to 2.7 million patients. Intervention scenarios could prevent over 30,000 HCC cases and over 29,000 liver-related deaths. **INTERPRETATION:** The US has made strides toward HCV elimination, but gains could be lost in the wake of the pandemic. However, it is still possible to avert nearly 30,000 deaths through increased harm reduction and increased treatment rates. This requires a coordinated effort from the entire HCV community.

Gastroenterology

Ichkhanian Y, Al-Haddad MA, Jacobs CC, Schlachterman A, Yang J, Canakis A, Kim R, Guerson-Gil A, D'Souza LS, **Alsheik E**, **Ginnebaugh BD**, Khashab MA, **Zuchelli T**, **Kellie M**, and **Piraka C**. Gastric Peroral Endoscopic Myotomy for Management of Refractory Gastroparesis in Patients with Gastric Neurostimulator Devices: A Multicenter Retrospective Case Control Study. *Gastrointest Endosc* 2023; Epub ahead of print. PMID: 37121364. [Full Text](#)

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BACKGROUND AND AIMS: Gastric neurostimulation (GNS) and gastric peroral myotomy (G-POEM), therapies for refractory gastroparesis, are associated with suboptimal outcomes. We studied the role of G-POEM as a salvage therapy in patients with refractory symptoms after GNS implantation. **METHODS:** This was a multicenter, retrospective, matched-case control study. Consecutive patients with GNS device and underwent G-POEM as a salvage therapy for clinical failure (cases) and patients without GNS implantation and underwent G-POEM for refractory gastroparesis (control) between 10-2018 and 08-2021 were included. The primary outcome was clinical success after G-POEM. **RESULTS:** A total of 123 patients (mean age 45.7 ± 14.7 years; 88 females [72%]) underwent G-POEM therapy during the duration of the study: 41 cases and 82 controls. Clinical success was achieved in 66% in the case group and 65% in the control, ($P=0.311$), during a median total clinical follow-up time of 11.8 (IQR: 2.4-6.3) months. In the case group, the mean Gastroparesis Cardinal Symptom Index (GCSI) decreased from 2.8 ± 1.8 to $1.5 \pm$

1.9, (P=0.024), and gastric retention at 4 hours improved from 45% ± 25.8 to 16.6% ± 13.1, (P=0.06). The mean delta improvement in the subscales of nausea/vomiting (1.3 ± 0.6 vs. 0.9 ± 1.1; P=0.044) and bloating (1.6 ± 1.3 vs. 1.2 ± 1.4; P=0.041) were significantly higher in cases than in controls. CONCLUSIONS: Among patients with refractory symptoms after GNS, G-POEM can be a reasonable salvage therapy to provide further symptomatic relief with evidence of a potential additive effect of both G-POEM and GNS.

Hematology-Oncology

Abu Rous F, Li P, Carskadon S, Singh SR, Chacko R, Abushukair H, Gadgeel S, and Palanisamy N. Brief Report: Prognostic Relevance of 3q Amplification in Squamous Cell Carcinoma of the Lung. *JTO Clin Res Rep* 2023; 4(4):100486. PMID: 37025118. [Full Text](#)

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INTRODUCTION: Amplification of 3q is the most common genetic alteration identified in squamous cell carcinoma of the lung (LUSC), with the most frequent amplified region being 3q26 to 3q28. METHODS: In this analysis, we aim to describe the prognostic relevance of 3q amplification by focusing on a minimal common region (MCR) of amplification constituted of 25 genes. We analyzed 511 cases of LUSC from The Cancer Genome Atlas and included 476 in the final analysis. RESULTS: We identified a 25-gene MCR that was amplified in 221 (44.3%) cases and was associated with better disease-specific survival (not reported [NR] versus 9.25 y, 95% confidence interval [CI]: 5.24-NR, log-rank p = 0.011) and a progression-free interval of 8 years (95% CI: 5.1-NR) versus 4.9 years (95% CI: 3.5-NR, log-rank p = 0.020). Multivariable analysis revealed that MCR amplification was associated with improved disease-specific survival and progression-free interval. CONCLUSIONS: Amplification of the 25-gene MCR within 3q was present in 44% of this cohort, consisting mainly of Caucasian patients with early stage LUSC. This analysis strongly indicates the prognostic relevance of the 25-gene MCR within 3q. We are further evaluating its prognostic and predictive relevance in a racially diverse patient population with advanced LUSC.

Hematology-Oncology

Khan HY, Kamgar M, Aboukameel A, Bannoura S, Chung BY, Li Y, Hallak MNA, Philip PA, Tsai S, Luther S, Hall WA, and Azmi AS. Targeting Cellular Metabolism With CPI-613 Sensitizes Pancreatic Cancer Cells to Radiation Therapy. *Adv Radiat Oncol* 2023; 8(1):101122. PMID: 36479231. [Full Text](#)

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PURPOSE: Local tumor progression is a cause of significant morbidity and mortality in patients with pancreatic ductal adenocarcinoma (PDAC) with surgically unresectable disease. Novel and effective approaches to accomplish durable local control are urgently needed. We tested whether CPI-613 (devimistat), a first-in-class investigational small molecule inhibitor of mitochondrial metabolism, was capable of altering cancer cell energy metabolism and sensitizing PDAC cells to radiation therapy (RT). METHODS AND MATERIALS: The effect of a combined treatment of RT with CPI-613 on the viability of, clonogenic potential of, and cell death induction in PDAC cells (MiaPaCa-2 and Panc-1) was determined using a trypan blue dye exclusion assay, a colony formation assay, and a 7-amino-actinomycin D assay, respectively. The synergistic effects of CPI-613-RT and chemotherapeutic agents (gemcitabine or 5-fluorouracil) were measured in MiaPaCa-2 cells using a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide and spheroid formation assay. Changes in energy metabolism were

determined by profiling metabolites treated with either RT, CPI-613, or both using liquid chromatography-mass spectrometry. RESULTS: This study demonstrates that a combination of single-fraction RT (2 and 10 Gy) with CPI-613 significantly inhibits PDAC cell growth compared with RT alone. Molecular analysis revealed inhibition of α -ketoglutarate dehydrogenase at the protein level. In addition, we demonstrate enhanced cell death of PDAC cells when treated with RT-CPI-613 combination. Targeted metabolomic analysis on PDAC cells post-CPI-613-RT treatment revealed alterations in key mitochondrial metabolites, with broader target engagement by the combination treatment, indicating the sensitization of CPI-613-treated PDAC cells to RT. Furthermore, a combination treatment of CPI-613 with either gemcitabine or 5-fluorouracil in the presence of 2 Gy RT synergistically inhibits PDAC cell proliferation. CONCLUSIONS: Our results support a novel combination of CPI-613-RT that warrants further preclinical and early-phase clinical investigations. A phase 1 trial designed to identify the maximum tolerated dose of CPI-613 in combination with chemo-RT in patients with PDAC was recently initiated (NCT05325281).

Hospital Medicine

Sattar Y, Taha A, Patel N, Victor V, Titus A, Aziz S, Gonuguntla K, Thyagaturu H, Atti L, **Micho T**, Almas T, Tarun T, Alraies MC, and Balla S. Cardiovascular outcomes of type 2 myocardial infarction among COVID-19 patients: a propensity matched national study. *Expert Rev Cardiovasc Ther* 2023; 1-7. Epub ahead of print. PMID: 37038300. [Request Article](#)

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BACKGROUND: Myocardial infarction Type II (T2MI) is a prevalent cause of troponin elevation secondary to a variety of conditions causing stress/demand mismatch. The impact of T2MI on outcomes in patients hospitalized with COVID-19 is not well studied. METHODS: The Nationwide Inpatient Sample database from the year 2020 was queried to identify COVID-19 patients with T2MI during the index hospitalization. Clinical Modification (ICD-10-CM) codes 'U07.1' and 'I21.A1' were used as disease identifiers for COVID-19 and T2MI respectively. Multivariate adjusted Odds ratio (aOR) and propensity score matching (PSM) was done to compare outcomes among COVID patients with and without T2MI. The primary outcome was in-hospital mortality. RESULTS: A total of 1,678,995 COVID-19-weighted hospitalizations were identified in the year 2020, of which 41,755 (2.48%) patients had T2MI compared to 1,637,165 (97.5%) without T2MI. Patients with T2MI had higher adjusted odds of in-hospital mortality (aOR 1.44, PSM 32.27%, 95% CI 1.34-1.54) sudden cardiac arrest (aOR 1.29, PSM 6.6%, 95% CI 1.17-1.43) and CS (aOR 2.16, PSM 2.73%, 95% CI 1.85-2.53) compared to patients without T2MI. The rate of coronary angiography (CA) in T2MI with COVID was 1.19%, with significant use of CA among patients with T2MI complicated by CS compared to those without CS (4% vs 1.1%, $p < 0.001$). Additionally, COVID-19 patients with T2MI had an increased prevalence of sepsis compared to COVID-19 without T2MI (48% vs 24.1%, $p < 0.001$). CONCLUSION: COVID-19 patients with T2MI had worse cardiovascular outcomes with significantly higher in-hospital mortality, SCA, and CS compared to those without T2MI. Long-term mortality and morbidity among COVID-19 patients who had T2MI will need to be clarified in future studies.

Hypertension and Vascular Research

Arkhipov SN, Potter DL, Sultanova RF, Ilatovskaya DV, Harris PC, and **Pavlov TS**. Probenecid slows disease progression in a murine model of autosomal dominant polycystic kidney disease. *Physiol Rep* 2023; 11(7):e15652. PMID: 37024297. [Full Text](#)

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Development of autosomal dominant polycystic kidney disease (ADPKD) involves renal epithelial cell abnormalities. Cystic fluid contains a high level of ATP that, among other effects, leads to a reduced reabsorption of electrolytes in cyst-lining cells, and thus results in cystic fluid accumulation. Earlier, we demonstrated that Pkd1(RC/RC) mice, a hypomorphic model of ADPKD, exhibit increased expression of pannexin-1, a membrane channel capable of ATP release. In the current study, we found that human ADPKD cystic epithelia have higher pannexin-1 abundance than normal collecting ducts. We hypothesized that inhibition of pannexin-1 function with probenecid can be used to attenuate ADPKD development. Renal function in male and female Pkd1(RC/RC) and control mice was monitored between 9 and 20 months of age. To test the therapeutic effects of probenecid (a uricosuric agent and a pannexin-1 blocker), osmotic minipumps were implanted in male and female Pkd1(RC/RC) mice, and probenecid or vehicle was administered for 42 days until 1 year of age. Probenecid treatment improved glomerular filtration rates and slowed renal cyst formation in male mice (as shown in histopathology). The mechanistic effects of probenecid on sodium reabsorption and fluid transport were tested on polarized mpkCCD(c14) cells subjected to short-circuit current measurements, and in 3D cysts grown in Matrigel. In the mpkCCD(c14) epithelial cell line, probenecid elicited higher ENaC currents and attenuated in vitro cyst formation, indicating lower sodium and less fluid retention in the cysts. Our studies open new avenues of research into targeting pannexin-1 in ADPKD pathology.

Hypertension and Vascular Research

Man Y, Li W, Yap YT, Kearney A, Yee SP, Strauss JF, 3rd, **Harding P**, Song S, Zhang L, and Zhang Z. Generation of floxed Spag6l mice and disruption of the gene by crossing to a Hrpt-Cre line. *Genesis* 2023; e23512. Epub ahead of print. PMID: 37058328. [Full Text](#)

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Mouse sperm-associated antigen 6 like (SPAG6L) is an axoneme central apparatus protein, essential for the normal function of the ependymal cell and lung cilia, and sperm flagella. Accumulated evidence has disclosed multiple biological functions of SPAG6L, including ciliary/flagellar biogenesis and polarization, neurogenesis, and neuronal migration. Conventional Spag6l knockout mice died of hydrocephalus, which impedes further investigation of the function of the gene in vivo. To overcome the limitation of the short lifespan of conventional knockout mice, we developed a conditional allele by inserting two loxP sites in the genome flanking exon 3 of the Spag6l gene. By crossing the floxed Spag6l mice to a Hrpt-Cre line which expresses Cre recombinase ubiquitously in vivo, mutant mice that are missing SPAG6L globally were obtained. Homozygous mutant Spag6l mice showed normal appearance within the first week after birth, but reduced body size was observed after 1 week, and all developed hydrocephalus and died within 4 weeks of age. The phenotype mirrored that of the conventional Spag6l knockout mice. The newly established floxed Spag6l model provides a powerful tool to further investigate the role of the Spag6l gene in individual cell types and tissues.

Infectious Diseases

Adeyemo A, Montgomery S, Chancey RJ, Annambhotla P, Barba L, Clarke T, **Williams J, Malilay A**, and Coyle J. Investigation of donor-derived *Strongyloides stercoralis* infection in multiple solid organ transplant recipients-California, Michigan, Ohio, 2022. *Transpl Infect Dis* 2023; e14059. Epub ahead of print. PMID: 37005911. [Full Text](#)

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BACKGROUND: The Centers for Disease Control and Prevention led an investigation to determine if *Strongyloides* infection in a right kidney recipient was an existing chronic infection, or if the infection was transmitted from an infected organ donor. **METHODS:** Evidence regarding the organ donor and organ recipients *Strongyloides* testing, treatment, and risk factors were gathered and evaluated. The case classification algorithm created by the Disease Transmission Advisory Committee was utilized.

RESULTS: The organ donor had risk factors for *Strongyloides* infection; the banked donor specimen, submitted for serology testing 112 days post-donor death, was positive. The right kidney recipient was negative for *Strongyloides* infection pretransplant. *Strongyloides* infection was diagnosed via small bowel and stomach biopsies. The left kidney recipient had risk factors for *Strongyloides* infection. Two posttransplant *Strongyloides* antibody tests were negative at 59 and 116 days posttransplant; repeat antibody tests returned positive at 158 and 190 days posttransplant. Examination of bronchial alveolar lavage fluid collected 110 days posttransplant from the heart recipient showed a parasite morphologically consistent with *Strongyloides* species. She subsequently developed complications from *Strongyloides* infection, including hyperinfection syndrome and disseminated strongyloidiasis. Based on the evidence from our investigation, donor-derived strongyloidiasis was suspected in one recipient and proven in two recipients. **CONCLUSION:** The results of this investigation support the importance of preventing donor-derived *Strongyloides* infections by laboratory-based serology testing of solid organ donors. Donor positive testing results would direct the monitoring and treatment of recipients to avoid severe complications.

Infectious Diseases

Birk NK, Monday L, Singh T, Cherabuddi M, Hojeij M, Ho B, Chen A, Brar I, and Alangaden G.

Vaccine coverage and factors associated with vaccine adherence in persons with HIV at an urban infectious disease clinic. *Hum Vaccin Immunother* 2023; 2204785. Epub ahead of print. PMID: 37106506.

[Full Text](#)

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Information on vaccination rates and factors associated with adherence in persons with HIV (PWH) is limited. We report vaccine adherence in 653 adult PWH attending an urban Infectious Disease Clinic from January 2015 to December 2021. Vaccines evaluated included influenza, pneumococcal, tetanus, hepatitis A virus (HAV) and hepatitis B virus (HBV), human papillomavirus (HPV), and zoster vaccines. Vaccine reminders were triggered at every visit, and all vaccines were accessible in the clinic. The mean age was 50 y (\pm SD 13), male gender was 78.6%, and black race was 74.3%. The overall adherence to all recommended vaccines was 63.6%. Vaccine adherence was >90% for influenza, pneumococcal, and tetanus, >80% for HAV and HBV, and \geq 60% for HPV and zoster vaccines. The main predictor of adherence to all vaccines was \geq 2 annual clinic visits (odds ratio [OR] 3.45; 95% confidence interval [CI] 2.36-5.05; $p < .001$). Other predictors included an assigned primary care provider within the system (OR 2.89 [95% CI 1.71-5.00, $p < .001$]) and CD4 >200 cell/mm³ at entry into care (OR 1.91 [95% CI 1.24-2.94, $p = .0003$]). Retention in care combined with vaccine reminders and accessibility of vaccines in the clinic can achieve high vaccine uptake in PWH.

Infectious Diseases

de Oca JEM, Veve MP, Zervos MJ, and Kenney RM. Aminopenicillins versus Non-aminopenicillins for Treatment of Enterococcal Lower Urinary Tract Infections. *Int J Antimicrob Agents* 2023; 106800. Epub ahead of print. PMID: 37004756. [Full Text](#)

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Aminopenicillins achieve urinary concentrations that exceed typical minimum inhibitory concentrations for enterococcal lower urinary tract infection (UTI). Our clinical microbiology laboratory discontinued routine susceptibilities on enterococcal urine isolates and reports "aminopenicillins are predictably reliable for uncomplicated enterococcal UTI". The study objective was to compare outcomes of aminopenicillins (AP) to non-aminopenicillins (NAP) for enterococcal lower UTIs. This was an IRB approved, retrospective cohort of adults hospitalized with symptomatic enterococcal lower UTIs from 2013-2021. Primary endpoint: composite clinical success at 14-days, defined as resolution of symptoms without new symptoms and no repeat culture growth of index organism. A non-inferiority analysis was utilized with a 15% margin, and logistic regression evaluated characteristics associated with 14-day failure. 178 subjects were included: 89 AP, 89 NAP. VRE was identified in 73 (82%) AP and 76 (85%) NAP patients (P=0.54); a total of 34 (38.2%) AP and 66 (74.2%) NAP patients had confirmed *E. faecium* (P<0.001). Amoxicillin (36, 40.5%) and ampicillin (36, 40.5%) were the most frequent AP utilized; linezolid (41, 46%) and fosfomycin (30, 34%) were the most frequent NAP. 14-day clinical success for AP and NAP was 83.1% and 82.0% (1.1% difference, 97.5%CI, -0.117-0.139). Among the *E. faecium* subgroup, 14-day clinical success was observed in 27/34 (79.4%) of AP and 53/66 (80.3%) of NAP patients (P=0.916). In logistic regression, APs were not associated with 14-day clinical failure (adjOR 0.84; 95%CI, 0.38-1.86). Aminopenicillins were noninferior to non-aminopenicillins for treating enterococcal lower UTIs and may be considered irrespective of susceptibility results.

Infectious Diseases

Morales Junior R, Telles JP, **Kwiatkowski SY**, Juodinis VD, de Souza DC, and Santos SRCJ. Pharmacokinetic and pharmacodynamic considerations of antibiotics and antifungals in liver transplantation recipients. *Liver Transpl* 2023; 29(1):91-102. PMID: 35643926. [Full Text](#)

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The liver plays a major role in drug metabolism. Liver transplantation impacts the intrinsic metabolic capability and extrahepatic mechanisms of drug disposition and elimination. Different levels of inflammation and oxidative stress during transplantation, the process of liver regeneration, and the characteristics of the graft alter the amount of functional hepatocytes and activity of liver enzymes. Binding of drugs to plasma proteins is affected by the hyperbilirubinemia status and abnormal synthesis of albumin and alpha-1-acid glycoproteins. Postoperative intensive care complications such as biliary, circulatory, and cardiac also impact drug distribution. Renally eliminated antimicrobials commonly present reduced clearance due to hepatorenal syndrome and the use of nephrotoxic immunosuppressants. In addition, liver transplantation recipients are particularly susceptible to multidrug-resistant infections due to frequent manipulation, multiple hospitalizations, invasive devices, and frequent use of empiric broad-spectrum therapy. The selection of appropriate anti-infective therapy must consider the pathophysiological changes after transplantation that impact the pharmacokinetics and pharmacodynamics of antibiotics and antifungal drugs.

Internal Medicine

Almajed MR, Mahmood S, Obri M, Nona P, Gonzalez PE, Chiang M, Wang DD, Frisoli T, Lee J, Basir M, O'Neill B, O'Neill W, and Villablanca P. Application of Impella mechanical circulatory support devices in transcatheter aortic valve replacement and balloon aortic valvuloplasty: A single center experience. *Cardiovasc Revasc Med* 2023; Epub ahead of print. PMID: 37012106. [Full Text](#)

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BACKGROUND/PURPOSE: Percutaneous valve interventions for aortic stenosis (AS) include transcatheter aortic valve replacement (TAVR) and balloon aortic valvuloplasty (BAV). Intraprocedural mechanical circulatory support (MCS) with Impella devices (Abiomed, Danvers, MA) is used in select high-risk patients, although data regarding its efficacy is limited. This study sought to evaluate the clinical outcomes of Impella use in patients with AS who underwent TAVR and BAV at a quaternary-care center. **METHODS/MATERIALS:** All patients with severe AS who underwent TAVR and BAV with Impella between 2013 and 2020 were included. Patient demographics, outcomes, complications, and 30-day mortality data was analyzed. **RESULTS:** Over the study period 2680 procedures were performed, 1965 TAVR and 715 BAV. 120 utilized Impella support, 26 TAVR and 94 BAV. Among TAVR Impella cases, justifications for MCS included cardiogenic shock (53.9 %), cardiac arrest (19.2 %), and coronary occlusion (15.4 %). Among BAV Impella cases, justifications for MCS included cardiogenic shock (55.3 %) and protected percutaneous coronary intervention (43.6 %). The 30-day mortality rate in TAVR Impella was 34.6 % and in BAV Impella was 28 %. BAV Impella cases involving cardiogenic shock had a higher rate of 45 %. Impella remained in-use past 24 h from the procedure in 32.2 % cases. Vascular access-related complications occurred in 4.8 % cases and bleeding complications occurred in 1.5 % cases. Conversion to open-heart surgery occurred in 0.7 % cases. **CONCLUSIONS:** MCS is an option for high-risk patients with severe AS who require TAVR and BAV. Despite hemodynamic support, the 30-day mortality rate remained high especially in cases where support was employed for cardiogenic shock.

Internal Medicine

Gupta K, Balachandran I, Foy J, Hermel M, Latif A, Krittanawong C, Slipczuk L, Baloch F, Samad Z, and Virani SS. Highlights of Cardiovascular Disease Prevention Studies Presented at the 2023 American College of Cardiology Conference. *Curr Atheroscler Rep* 2023; Epub ahead of print. PMID: 37086374.

[Full Text](#)

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PURPOSE OF REVIEW: To summarize selected late-breaking science on cardiovascular (CV) disease prevention presented at the 2023 American College of Cardiology (ACC) conference. **RECENT FINDINGS:** The CLEAR outcomes randomized control trial (RCT) compared bempedoic acid to placebo in patients at high-risk of cardiovascular disease (CVD) or prevalent CVD and statin intolerance for CV outcomes. The YELLOW III was a single-arm study that evaluated the effect of Evolocumab on coronary plaque characteristics in patients with stable coronary artery disease (CAD). A cohort evaluated the

association between a self-reported low-carbohydrate high-fat (ketogenic) diet and serum lipid levels as compared to a standard diet. The LOADSTAR trial compared CV outcomes with targeted low-density lipoprotein cholesterol (LDL-C) approach vs. high-intensity statin in patients with CAD. The PCDS statin cluster randomized trial compared the effectiveness of an electronic reminder to the clinician on a high-intensity statin use among patients with a history of ASCVD as compared to no reminder. A prospective cohort study compared the extent of coronary atherosclerosis among lifelong endurance athletes and healthy non-athletes. A causal artificial intelligence study combined polygenic risk scores with data from large CV prevention RCTs to guide systolic blood pressure and LDL-C reduction targets to reach average CV risk. The ACCESS trial evaluated the impact of eliminating copayment for low-income older adults in Canada with chronic CV diseases on composite CV outcomes. A pooled analysis of 3 large RCTs evaluated the association between residual inflammatory risk and CV outcomes, as compared to residual elevated cholesterol risk in patients receiving statin therapy. A Phase 2B RCT compared the efficacy of an oral PCSK9i, MK-0616, in reducing LDL-C as compared to a placebo. The late-breaking clinical science presented at the 2023 conference of the ACC paves the way for an evidence-based alternative to statin therapy and provides data on several common clinical scenarios encountered in daily practice.

Internal Medicine

Ichkhanian Y, Al-Haddad MA, Jacobs CC, Schlachterman A, Yang J, Canakis A, Kim R, Guerson-Gil A, D'Souza LS, **Alsheik E**, **Ginnebaugh BD**, Khashab MA, **Zuchelli T**, **Kellie M**, and **Piraka C**. Gastric Peroral Endoscopic Myotomy for Management of Refractory Gastroparesis in Patients with Gastric Neurostimulator Devices: A Multicenter Retrospective Case Control Study. *Gastrointest Endosc* 2023; Epub ahead of print. PMID: 37121364. [Full Text](#)

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BACKGROUND AND AIMS: Gastric neurostimulation (GNS) and gastric peroral myotomy (G-POEM), therapies for refractory gastroparesis, are associated with suboptimal outcomes. We studied the role of G-POEM as a salvage therapy in patients with refractory symptoms after GNS implantation. **METHODS:** This was a multicenter, retrospective, matched-case control study. Consecutive patients with GNS device and underwent G-POEM as a salvage therapy for clinical failure (cases) and patients without GNS implantation and underwent G-POEM for refractory gastroparesis (control) between 10-2018 and 08-2021 were included. The primary outcome was clinical success after G-POEM. **RESULTS:** A total of 123 patients (mean age 45.7 ± 14.7 years; 88 females [72%]) underwent G-POEM therapy during the duration of the study: 41 cases and 82 controls. Clinical success was achieved in 66% in the case group and 65% in the control, ($P=0.311$), during a median total clinical follow-up time of 11.8 (IQR: 2.4-6.3) months. In the case group, the mean Gastroparesis Cardinal Symptom Index (GCSI) decreased from 2.8 ± 1.8 to 1.5 ± 1.9 , ($P=0.024$), and gastric retention at 4 hours improved from $45\% \pm 25.8$ to $16.6\% \pm 13.1$, ($P=0.06$). The mean delta improvement in the subscales of nausea/vomiting (1.3 ± 0.6 vs. 0.9 ± 1.1 ; $P=0.044$) and bloating (1.6 ± 1.3 vs. 1.2 ± 1.4 ; $P=0.041$) were significantly higher in cases than in controls. **CONCLUSIONS:** Among patients with refractory symptoms after GNS, G-POEM can be a reasonable salvage therapy to provide further symptomatic relief with evidence of a potential additive effect of both G-POEM and GNS.

Internal Medicine

Jamil M, Salam A, Joseph Benher B, **Nasiri N**, and **Chaudhary AJ**. A Case of Acute Liver Failure Due to Artemisinin-Derived Herbal Supplements. *Cureus* 2023; 15(3):e36582. PMID: 37095792. [Full Text](#)

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A 49-year-old female presented with malaise, nausea, vomiting, and discolored urine. She was found to have an acute liver failure with labs significant for aspartate aminotransferase (AST) of 2164, alanine aminotransferase (ALT) of 2425, alkaline phosphatase (ALP) of 106, total bilirubin of 3.6, and lactate dehydrogenase (LDH) of 2269. The international normalized ratio (INR) was also elevated at 1.9. All workup for acute liver failure was negative and it was found that she had started taking a new supplement called "Gut Health", which contained artemisinin, for weight loss and menopausal symptoms. After discontinuing the supplements and symptomatically treating her for acute liver failure, her transaminitis resolved.

Internal Medicine

Obeidat L, Albusoul L, Maki M, Ibrahim H, and Parikh S. Infliximab-Induced Lupus in a Patient With Psoriatic Arthritis Who Presented With Cardiac Tamponade: A Case Report. *Cureus* 2023; 15(3):e36424. PMID: 37090269. [Full Text](#)

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Psoriatic arthritis (PsA) is a chronic, immune-mediated inflammatory condition, and the proinflammatory cytokine tumor necrosis factor- α (TNF- α) plays a major pathogenic role in the development and progression of PsA. Anti-TNF- α therapies, such as the monoclonal antibody infliximab, are used to treat patients whose PsA has not responded favorably to conventional anti-rheumatic drugs. However, exposure to anti-TNF- α therapeutics can lead to drug-induced lupus erythematosus (DILE), which may rarely be accompanied by cardiac manifestations. Here, we describe a rare case of drug-induced lupus erythematosus secondary to infliximab therapy for PsA and psoriasis in a patient who presented with life-threatening acute pericarditis and cardiac tamponade. Newly developed skin rashes, newly elevated autoimmune indicators, and punch biopsy results indicating subacute cutaneous lupus collectively supported a DILE diagnosis within the context of infliximab use. Pericardiocentesis, colchicine, and corticosteroids alleviated symptoms, and infliximab was replaced with alternate therapy. This case highlights the importance of early recognition of the possible serious and uncommon adverse reactions from infliximab therapy. Prompt initiation of appropriate treatment and discontinuation of the offending agent are critical in cases of drug-induced lupus erythematosus, particularly when rare cardiac complications occur.

Internal Medicine

Prathivadhi-Bhayankaram S, Abbasi MA, Ismayl M, Marar RI, Al-Abcha A, El-Am E, Ahmad A, Acevedo AD, **Ellauzi R**, Villarraga H, Paludo J, and Anavekar N. Cardiotoxicities of Novel Therapies in Hematological Malignancies: Monoclonal Antibodies and Enzyme Inhibitors. *Curr Probl Cardiol* 2023; 101757. Epub ahead of print. PMID: 37094764. [Full Text](#)

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Monoclonal antibodies (mAB) selectively target leukemia surface antigens and work by either blocking cell surface receptors or triggering the target cell's destruction. Similarly, enzyme inhibitors bind to complex molecular platforms and induce downstream mechanisms that trigger cell death. These are used in a variety of hematologic malignancies. Yet, they also elicit severe immune-mediated reactions as biological agents that require careful monitoring. Cardiovascular effects include cardiomyopathy, ventricular dysfunction, cardiac arrest, and acute coronary syndrome. While there have been scattered reviews of mAB and enzyme inhibitors, a consolidated resource regarding their cardiovascular risk profile is lacking. We provide general recommendations for initial screening and serial monitoring based on the literature.

Internal Medicine

Robinson C, Ramanan S, Singh H, Minhas JS, and Zebda H. A Case of T-Cell Large Granulocyte Lymphocytic Leukemia in Rheumatoid Arthritis. *Cureus* 2023; 15(3):e36266. PMID: 37065388. [Full Text](#)

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T-cell large granulocyte lymphocytic (TLGL) leukemia is a lymphoproliferative disorder involving clonal expansion of cytotoxic T-cells and subsequent cytopenia, most notably neutropenia, as well as splenomegaly. TLGL leukemia is commonly associated with autoimmune disorders, most commonly rheumatoid arthritis (RA). We present a case of a 54-year-old female with a past medical history of seropositive RA who was lost to follow-up and thus was not on any active treatment for RA for several years. She returned to the clinic with worsening joint pain, swelling, and stiffness involving multiple joints. Screen laboratory work revealed an absolute neutrophil count (ANC) of 0.19 K/uL, indicating severe neutropenia. This finding prompted further workup, for which our patient was ultimately diagnosed with TLGL leukemia. Proper treatment and control of inflammation in RA are important not only to preserve joint function and vitality but also to prevent rare sequela of untreated autoimmune disorders, as was the case in our patient.

Nephrology

Chu CD, Lenoir KM, Rai NK, **Soman S**, Dwyer JP, Rocco MV, Agarwal AK, Beddhu S, Powell JR, Suarez MM, Lash JP, McWilliams A, Whelton PK, Drawz PE, Pajewski NM, Ishani A, and Tuot DS. Concordance between clinical outcomes in the systolic blood pressure intervention trial and in the electronic health record. *Contemp Clin Trials* 2023; 128:107172. PMID: 37004812. [Full Text](#)

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BACKGROUND: Randomized trials are the gold standard for generating clinical practice evidence, but follow-up and outcome ascertainment are resource-intensive. Electronic health record (EHR) data from routine care can be a cost-effective means of follow-up, but concordance with trial-ascertained outcomes is less well-studied. **METHODS:** We linked EHR and trial data for participants of the Systolic Blood Pressure Intervention Trial (SPRINT), a randomized trial comparing intensive and standard blood pressure targets. Among participants with available EHR data concurrent to trial-ascertained outcomes, we calculated sensitivity, specificity, positive predictive value, and negative predictive value for EHR-recorded cardiovascular disease (CVD) events, using the gold standard of SPRINT-adjudicated outcomes (myocardial infarction (MI)/acute coronary syndrome (ACS), heart failure, stroke, and composite CVD events). We additionally compared the incidence of non-CVD adverse events (hyponatremia, hypernatremia, hypokalemia, hyperkalemia, bradycardia, and hypotension) in trial versus EHR data. **RESULTS:** 2468 SPRINT participants were included (mean age 68 (SD 9) years; 26% female). EHR data demonstrated $\geq 80\%$ sensitivity and specificity, and $\geq 99\%$ negative predictive value for MI/ACS, heart failure, stroke, and composite CVD events. Positive predictive value ranged from 26% (95% CI; 16%, 38%) for heart failure to 52% (95% CI; 37%, 67%) for MI/ACS. EHR data uniformly identified more non-CVD adverse events and higher incidence rates compared with trial ascertainment. **CONCLUSIONS:** These results support a role for EHR data collection in clinical trials, particularly for capturing laboratory-based adverse events. EHR data may be an efficient source for CVD outcome ascertainment, though there is clear benefit from adjudication to avoid false positives.

Neurology

Huber B, Pellumbi N, Davoodi-Bojd E, and Soltanian-Zadeh H. Inter- and intra-operator variations in manual segmentation of hippocampus from MRI. *Inform Med Unlocked* 2023; 39. PMID: Not assigned.

[Full Text](#)

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Purpose: We evaluate inter- and intra-operator variations in manual segmentation of hippocampus and present their potential sources. Hippocampal atrophy is common in mesial temporal lobe epilepsy (mTLE). Effective diagnosis and treatment of mTLE depends on accurate and efficient segmentation of hippocampus from magnetic resonance imaging (MRI) data. Manual segmentation by expert radiologists remains the gold standard, although automated segmentation methods exist. **Methods:** Hippocampus was segmented in MRI of 118 unilateral mTLE patients and 25 non-epileptic subjects (65 males, 78 females; mean age 39 years) by three operators (M1, M2, M3) manually and by three software tools (FreeSurfer, LocalInfo, ABSS) automatically. Segmentation results were evaluated using 7 volume-, voxel-, and distance-based performance measures. Inter-operator variation was evaluated by comparing the segmentation results of the three operators. Intra-operator variation was evaluated by comparing manual and automatic segmentation results. Segmentation results were used to lateralize epileptogenicity in mTLE patients. **Results:** Ranking of performance measures differed when using M3 segmentations as ground truth rather than M1 or M2 segmentations. The standard deviation tended to be higher when using M3 as ground truth and M1 or M2 as test segmentation. Variation in performance measures and increased standard deviation when using M3 as ground truth are indicative of inter-operator variability. Standard deviations were larger when using M2 segmentations as ground truth and automated segmentations as test segmentation, rather than M1 or M3. Large standard deviations between M2 segmentations and automated segmentations are indicative of intra-operator variation. Among automated segmentation methods, ABSS produced segmentations most similar to manual segmentations, but FreeSurfer and LocalInfo lateralized epileptogenicity more accurately. **Conclusions:** Part of inter-operator

variation might be due to temporal separation of M3 segmentations from M1 and M2 segmentations (M3 performed segmentations a few years before operators M1 and M2). Inter-operator variation will likely reduce if all operators segment within the same time frame, reducing discrepancies in training of operators. Intra-operator variation can likely be mitigated with additional oversight by a neuroradiologist. Inter- and intra-operator variability may generate inconsistencies in outcomes. Future automated segmentation techniques may integrate neural-network-based (ABSS) and atlas-based (FreeSurfer and LocalInfo) segmentation techniques for optimal performance.

Neurology

Jost WH, Kulisevsky J, and **LeWitt PA**. Inhaled levodopa for threatening impending OFF episodes in managing Parkinson's disease. *J Neural Transm (Vienna)* 2023; Epub ahead of print. PMID: 37087697. [Full Text](#)

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Parkinson's disease (PD) is a neurodegenerative disorder that leads to the degeneration of dopaminergic neurons resulting in a widespread pathology of motor and non-motor symptoms. Oral levodopa remains the most effective symptomatic treatment of PD, but motor complications such as Off episodes occur over time. The spectrum of manifestation of OFF episodes varies, e.g., early morning akinesia, end-of-dose wearing OFF, delayed ON, suboptimal ON and dose failure. The functional disability substantially impacts the quality of life for PD patients. An innovative on-demand therapy to treat Off episodes was approved for patients receiving oral levodopa/dopa decarboxylase inhibitor: inhaled levodopa powder (Inbrija®). The pulmonary delivery of inhaled levodopa powder provides a predictable and fast treatment effect, independent of gastrointestinal dysfunctions or food intake, which could affect levodopa absorption. Levodopa is administered with a breath-actuated inhaler device and the approved dose is 84 mg per Off episode. During the pivotal SPAN-PD phase III trial, significant improvement in Unified Parkinson Disease Rating Scale III score was measured 30 min post-dose at week 12. Improvement was already seen for the first measured time point 10 min post-dose. No differences in pulmonary function was observed when using inhaled levodopa powder regularly for up to 12 months. Inhaled levodopa powder was also approved for early morning Off episodes. The aim of this review article is to give an overview of the different clinical studies of the innovative inhaled levodopa powder, a new on-demand therapy to treat Off episodes in PD.

Neurology

LeWitt P, Ellenbogen A, Burdick D, Gunzler S, Gil R, Dhall R, Banisadr G, and D'Souza R. Improving levodopa delivery: IPX203, a novel extended-release carbidopa-levodopa formulation. *Clin Park Relat Disord* 2023; 8. PMID: Not assigned. [Full Text](#)

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Introduction: IPX203 is a novel oral extended-release (ER) formulation of carbidopa (CD) and levodopa (LD) developed to address the short half-life and limited area for absorption of LD in the gastrointestinal tract. This paper presents the formulation strategy of IPX203 and its relationship to the pharmacokinetics (PK) and pharmacodynamic profile of IPX203 in Parkinson's disease (PD) patients. Methods: IPX203 was developed with an innovative technology containing immediate-release (IR) granules and ER beads that provides rapid LD absorption to achieve desired plasma concentration and maintaining it within the therapeutic range for longer than can be achieved with current oral LD formulations. The PK and pharmacodynamics of IPX203 were compared with IR CD-LD in a Phase 2, open-label, rater-blinded,

multicenter, crossover study in patients with advanced PD. Results: Pharmacokinetic data showed that on Day 15, LD concentrations were sustained above 50% of peak for 6.2 h with IPX203 vs. 3.9 h with IR CD-LD ($P = 0.0002$). Pharmacodynamic analysis demonstrated that mean MDS-UPDRS Part III scores prior to administration of the first daily dose were significantly lower among patients receiving IPX203 than IR CD-LD (LS mean difference -8.1 [25.0], $P = 0.0255$). In a study conducted in healthy volunteers, a high-fat, high-calorie meal delayed plasma LD T_{max} by 2 h, and increased C_{max} and AUC_{tau} by approximately 20% compared with a fasted state. Sprinkling capsule contents on applesauce did not affect PK parameters. Conclusion: These data confirm that the unique design of IPX203 addresses some of the limitations of oral LD delivery.

Neurosurgery

Asmaro K, Zhang M, Rodrigues AJ, Mohyeldin A, Vigo V, Nernekli K, Vogel H, Born DE, Katznelson L, and Fernandez-Miranda JC. Cytodifferentiation of pituitary tumors influences pathogenesis and cavernous sinus invasion. *J Neurosurg* 2023; 1-9. Epub ahead of print. PMID: 37119095. [Full Text](#)

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OBJECTIVE: Pituitary tumors (PTs) continue to present unique challenges given their proximity to the cavernous sinus, whereby invasive behavior can limit the extent of resection and surgical outcome, especially in functional tumors. The aim of this study was to elucidate patterns of cavernoinvasive behavior by PT subtype. **METHODS:** A total of 169 consecutive first-time surgeries for PTs were analyzed; 45% of the tumors were functional. There were 64 pituitary transcription factor-1 (PIT-1)-expressing, 62 steroidogenic factor-1 (SF-1)-expressing, 38 T-box transcription factor (TPIT)-expressing, and 5 nonstaining PTs. The gold standard for cavernous sinus invasion (CSI) was based on histopathological examination of the cavernous sinus medial wall and intraoperative exploration. **RESULTS:** Cavernous sinus disease was present in 33% of patients. Of the Knosp grade 3 and 4 tumors, 12 (19%) expressed PIT-1, 7 (11%) expressed SF-1, 8 (21%) expressed TPIT, and 2 (40%), were nonstaining ($p = 0.36$). PIT-1 tumors had a significantly higher predilection for CSI: 53% versus 24% and 18% for TPIT and SF-1 tumors, respectively (OR 6.08, 95% CI 2.86-13.55; $p < 0.001$). Microscopic CSI-defined as Knosp grade 0-2 tumors with confirmed invasion-was present in 44% of PIT-1 tumors compared with 7% and 13% of TPIT and SF-1 tumors, respectively (OR 11.72, 95% CI 4.35-35.50; $p < 0.001$). Using the transcavernous approach to excise cavernous sinus disease, surgical biochemical remission rates for patients with acromegaly, prolactinoma, and Cushing disease were 88%, 87%, and 100%, respectively. The granule density of PIT-1 tumors and corticotroph functional status did not influence CSI. **CONCLUSIONS:** The likelihood of CSI differed by transcription factor expression; PIT-1-expressing tumors had a higher predilection for invading the cavernous sinus, particularly microscopically, compared with the other tumor subtypes. This elucidates a unique cavernoinvasive behavior absent in cells from other lineages. Innovative surgical techniques, however, can mitigate tumor behavior and achieve robust, reproducible biochemical remission and gross-total resection rates. These findings can have considerable implications on the surgical management and study of PT biology and behavior.

Neurosurgery

Kazi M, Khan MF, Nasr FA, Ahmed MZ, Alqahtani AS, **Ali MM**, and Aldughaim MS. Development of Curcumin and Piperine-Loaded Bio-Active Self-Nanoemulsifying Drugs and Investigation of Their Bioactivity in Zebrafish Embryos and Human Hematological Cancer Cell Lines. *Int J Nanomedicine* 2023; 18:1793-1808. PMID: 37051315. [Full Text](#)

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PURPOSE: Curcumin (CUR) and piperine (PP) are bioactive compounds with prominent pharmacological activities that have been investigated for the treatment of various diseases. The aim of the present study is to develop Bio-SNEDDS for CUR and PP as a combined delivery system for cancer therapy.

METHODS: CUR and PP loaded Bio-SNEDDSs with varying compositions of bioactive lipid oils, surfactants, and cosolvents were prepared at room temperature. Bio-SNEDDSs were characterized using a Zetasizer Nano particle size analyzer and further examined by transmission electron microscopy (TEM) for morphology. The in vivo toxicity of the preparations of Bio-SNEDDS was investigated in wild-type zebrafish embryos and cytotoxicity in THP-1 (human leukemia monocytic cells), Jurkat (human T lymphocyte cells) and HUVEC (non-cancerous normal) cells. **RESULTS:** Bio-SNEDDSs were successfully developed with black seed oil, Imwitor 988, Transcutol P and Cremophor RH40 at a ratio of 20/20/10/50 (%w/w). The droplet size, polydispersity index and zeta potential of the optimized Bio-SNEDDS were found to be 42.13 nm, 0.59, and -19.30 mV, respectively. Bio-SNEDDS showed a spherical structure evident by TEM analysis. The results showed that Bio-SNEDDS did not induce toxicity in zebrafish embryos at concentrations between 0.40 and 30.00 µg/mL. In TG (fli1: EGFP) embryos treated with Bio-SNEDDS, there was no change in the blood vessel structure. The O-dianisidine staining of Bio-SNEDDS treated embryos at 48 h post-fertilization also showed a significant reduction in the number of blood cells compared to mock (DMSO 0.1% V/V) treated embryos. Bio-SNEDDS induced significant levels of cytotoxicity in the hematological cell lines THP-1 and Jurkat, while low toxicity in normal HUVEC cell lines was observed with IC50 values of 18.63±0.23 µg/mL, 26.03 ± 1.5 µg/mL and 17.52 ± 0.22 µg/mL, respectively. **CONCLUSION:** Bio-SNEDDS exhibited enhanced anticancer activity and could thus be an important new pharmaceutical formulation to treat leukemia.

Neurosurgery

Koekkoek JAF, van der Meer PB, and **Walbert T**. Reply to the letter regarding "Palliative care and end-of-life care in adults with malignant brain tumors". *Neuro Oncol* 2023; Epub ahead of print. PMID: 37098001.

[Full Text](#)

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Obstetrics, Gynecology and Women's Health Services

Ayyash M, Daviskiba S, Vriesen N, Yaquinto A, Roberson J, and Pitts D. High rates of "atypical" single nucleotide polymorphism-based noninvasive prenatal screening results among consanguineous Arab American patients: A single center retrospective study. *J Genet Couns* 2023; Epub ahead of print. PMID: 37066630. [Full Text](#)

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Noninvasive prenatal screening (NIPS), using placental cell-free DNA from a maternal blood sample, is currently the most sensitive and specific screening tool for detecting common fetal aneuploidies. The aim of this study was to compare the rates of "atypical" single nucleotide polymorphism (SNP)-based NIPS results and subsequent pregnancy outcomes between Arab American and non-Arab American patients. We conducted a retrospective cohort study of pregnant Arab and non-Arab American patients who had SNP-based NIPS performed between September 2018 and January 2021 at an urban health system in Michigan. The rate of "atypical" results and other perinatal outcomes were compared between groups

using descriptive statistics. "Atypical" results due to multifetal gestations, either undisclosed or unknown at time of ordering, were excluded. Five thousand eight hundred and seventy-three patients underwent SNP-based NIPS: 771 (13.1%) were identified as Arab American, 5102 (86.9%) were non-Arab American, and 49 (0.8%) patients received "atypical" results. Arab patients represented only 13.1% of patients screened (771/5873) but had a significantly higher rate of "atypical" results than non-Arab American patients (17/771 [2.2%] vs. 32/5102 [0.6%]; $p < 0.001$). Of the 17 Arab patients with "atypical" results, 9 (52.9%) were in known consanguineous relationships. No major congenital anomalies or chromosomal aberrations were identified for any patients who had "atypical" results, and no significant differences in other perinatal outcomes were observed between Arab and non-Arab American patients. A better understanding of the association between consanguinity and "atypical" SNP-based NIPS results would aid in appropriate test selection and interpretation and may help physicians and genetic counselors provide better perinatal counseling and follow-up care for patients in consanguineous relationships.

Ophthalmology and Eye Care Services

Magazin M, **Kasetty VM**, and Thomas DA. Aseptic Orbital Cellulitis as a Complication of Suprachoroidal Hemorrhage. *Cureus* 2023; 15(2):e35528. PMID: 37007350. [Full Text](#)

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Suprachoroidal hemorrhage is a rare and potentially devastating clinical entity seen in individuals on anticoagulation presenting with severe unilateral eye pain, sudden vision loss, and elevated intraocular pressures. Herein, we report the first case of aseptic orbital cellulitis caused by recurrent spontaneous suprachoroidal hemorrhage. This case highlights an example of non-infectious orbital cellulitis arising from choroidal pathology in the setting of uncontrolled intraocular pressures and recurrent intraocular bleeding. Surgical intervention with blood drainage should be considered to prevent complications and preserve the globe.

Ophthalmology and Eye Care Services

Portney DS, Berkowitz ST, Garner DC, **Qalieh A**, Tiwari V, Friedman S, Patel S, Parikh R, and Mian SI. Comparison of Incremental Costs and Medicare Reimbursement for Simple vs Complex Cataract Surgery Using Time-Driven Activity-Based Costing. *JAMA Ophthalmol* 2023; 141(4):358-364. PMID: 36892825. [Full Text](#)

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IMPORTANCE: Cataract surgery is one of the most commonly performed surgeries across medicine and an integral part of ophthalmologic care. Complex cataract surgery requires more time and resources than simple cataract surgery, yet it remains unclear whether the incremental reimbursement for complex cataract surgery, compared with simple cataract surgery, offsets the increased costs. **OBJECTIVE:** To measure the difference in day-of-surgery costs and net earnings between simple and complex cataract surgery. **DESIGN, SETTING, AND PARTICIPANTS:** This study is an economic analysis at a single academic institution using time-driven activity-based costing methodology to determine the operative-day costs of simple and complex cataract surgery. Process flow mapping was used to define the operative episode limited to the day of surgery. Simple and complex cataract surgery cases (Current Procedural Terminology codes 66984 and 66982, respectively) at the University of Michigan Kellogg Eye Center from 2017 to 2021 were included in the analysis. Time estimates were obtained using an internal anesthesia

record system. Financial estimates were obtained using a mix of internal sources and prior literature. Supply costs were obtained from the electronic health record. MAIN OUTCOMES AND MEASURES: Difference in day-of-surgery costs and net earnings. RESULTS: A total of 16 092 cataract surgeries were included, 13 904 simple and 2188 complex. Time-based day-of-surgery costs for simple and complex cataract surgery were \$1486.24 and \$2205.83, respectively, with a mean difference of \$719.59 (95% CI, \$684.09-\$755.09; P < .001). Complex cataract surgery required \$158.26 more for costs of supplies and materials (95% CI, \$117.00-\$199.60; P < .001). The total difference in day-of-surgery costs between complex and simple cataract surgery was \$877.85. Incremental reimbursement for complex cataract surgery was \$231.01; therefore, complex cataract surgery had a negative earnings difference of \$646.84 compared with simple cataract surgery. CONCLUSIONS AND RELEVANCE: This economic analysis suggests that the incremental reimbursement for complex cataract surgery undervalues the resource costs required for the procedure, failing to cover increased costs and accounting for less than 2 minutes of increased operating time. These findings may affect ophthalmologist practice patterns and access to care for certain patients, which may ultimately justify increasing cataract surgery reimbursement.

Orthopedics/Bone and Joint Center

Bell KL, King BW, and Sangeorzan BJ. Acute and Chronic Subtalar Joint Instability: Does It Really Exist? *Foot Ankle Clin* 2023; 28(2):427-444. PMID: 37137632. [Full Text](#)

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Acute and chronic subtalar instability and commonly coexistent with other hindfoot pathology but can be difficult to diagnose. A high degree of clinical suspicion is required as most imaging modalities and clinical maneuvers are poor at detecting isolated subtalar instability. The initial treatment is similar to ankle instability, and a wide variety of operative interventions have been presented in the literature for persistent instability. Outcomes are variable and limited.

Orthopedics/Bone and Joint Center

Castle JP, Cotter D, Abbas MJ, Jildeh TR, **Gaudiani MA**, Lau E, **Kadouh A**, Ziad F, and **Moutzouros V**. High Return to Play Rate and Diminished Career Longevity are Seen Following Arthroscopic Shoulder Labral Repair in Major League Baseball Players. *Arthrosc Sports Med Rehab* 2023. PMID: Not assigned. [Full Text](#)

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Purpose: To evaluate the impact of arthroscopic shoulder labral repair, not related to instability, on return to play (RTP), return to prior performance (RTPP), game utilization, and performance in Major League Baseball (MLB) pitchers and positional players. Methods: A retrospective review of all MLB athletes who underwent arthroscopic shoulder labrum repair from 2002 to 2020 was performed. Players with a history of instability events were excluded. A 2:1 control cohort of healthy MLB players were matched to the operative cohort by age, years of experience, position, height, and body mass index (BMI). Player demographics, game utilization, and performance metrics were collected for all players. Results: Twenty-six of 39 MLB pitchers (66%) and 18 of 25 (72%) positional players, who underwent arthroscopic shoulder labral repair RTP, with 46.2% of pitchers and 72% of positional players successfully RTP. At one season postsurgery, pitchers and positional players experienced a significant reduction in games played compared to their one season preinjury (44.7 ± 29.3 vs 109.5 ± 73.2 games; P < .001 and 75.7 ± 47.1 vs 98.0 ± 50.7 games; P = .04). When compared with matched controls at one season postinjury, pitchers had significantly fewer runs allowed per 9 innings (5.8 ± 2.0 vs 4.3 ± 1.4 ; P = .0061) and walk and hits per inning pitched (WHIP) (1.5 ± 0.3 vs 1.3 ± 0.2 ; P = .0035), while positional players had worse on-base percentage (0.3 ± 0.1 vs 0.3 ± 0.1 ; P = .0116). Both pitchers and positional players experienced significantly shorter career lengths after surgery (P = .002) when compared to controls. Conclusion: Following arthroscopic shoulder labral surgery, most MLB pitchers and positional players were able to RTP successfully but experienced shorter careers thereafter. These players also experienced declines in

game utilization and performance one season after surgery but were able to return to baseline at 3 seasons after surgery.

Orthopedics/Bone and Joint Center

Castle JP, Jildeh TR, **Abbas MJ**, **Hennekes ME**, **Buckley PJ**, Shabet CL, Cotter DL, and **Moutzouros V**. Patient factors influencing the choice of opioid versus non-opioid postoperative analgesia following common sports procedures: a prospective survey study. *J Orthop* 2023; 40:1-6. PMID: 37124142. [Full Text](#)

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PURPOSE: Despite established opioid-free protocols for postoperative analgesia after common orthopaedic sports procedures, many patients continue to request opioids postoperatively. The purpose of this study was to elucidate patient factors influencing preferences for opioid versus nonopioid postoperative analgesia. **METHODS:** Patients (age ≥ 15) without a history of a documented chronic pain disorder who were scheduled for one of ten sports procedure types from August 2020 to May 2021 were eligible for inclusion. Patients were excluded if undergoing revision surgery, had concomitant injuries, had opioids use >3 months preoperatively, or unable to read English. Recruitment ended after 100 patients enrolled. At the patients' preoperative visit, patients were administered a written survey assessing pain medication preferences. Participants completed the Opioid Risk Tool survey, as well as Visual Analog Scale and Patient-Reported Outcome Measurement Information System surveys. **RESULTS:** One hundred patients participated in the study. Forty-two patients preferred opioids versus 58 patients preferring nonopioid postoperative analgesia. Patients preferring opiates were more likely to have had previous surgery (90.2% vs. 69.6%, $p = 0.023$) with post-operative pain managed with opiates (87.5% vs 55.4%, $p = 0.003$), higher preoperative Visual Analog Scale score (6 ± 3.5 vs. 3 ± 2 , $p < 0.001$), reported post-operative pain as a reason for opioids preference (88.1% vs 20.0%, $p < 0.001$), and were less concerned about addiction (4.8% vs. 45.5%, $p < 0.001$) and side effects (11.9% vs. 52.7%, $p < 0.001$). For every unit increase in Visual Analog Scale score, the odds of preferring opioid pain control increased 1.41 times. **CONCLUSIONS:** Patients with a history of prior surgery utilizing opioid pain control, higher Visual Analog Scale scores preoperatively, and concern for inadequately managed postoperative pain were more likely to prefer opioid pain control following common orthopaedic sports procedures. Patients may benefit from increased preoperative education about opioid risks and the role of multimodal pain management regimens.

Orthopedics/Bone and Joint Center

Day CS, Lattanza L, Van Heest A, Templeton K, **Fore JA**, and Ode GE. AOA Critical Issues: Gender Justice in Academic Medicine: What It Might Look Like in Orthopaedic Surgery. *J Bone Joint Surg Am* 2023; Epub ahead of print. PMID: 37027484. [Full Text](#)

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As the number of women entering medicine has increased, so has the number of women entering orthopaedics; however, many orthopaedic programs struggle to create an equitable space for women, particularly in leadership. Struggles experienced by women include sexual harassment and gender bias, lack of visibility, lack of well-being, disproportionate family care responsibilities, and lack of flexibility in the criteria for promotions. Historically, sexual harassment and bias has been a problem faced by women physicians, and often the harassment continues even when the issue has been reported; many women

find that reporting it results in negative consequences for their career and training. Additionally, throughout medical training, women are less exposed to orthopaedics and lack the mentorship that is given to their colleagues who are men. The late exposure and lack of support prevent women from entering and advancing in orthopaedic training. Typical surgery culture can also result in women orthopaedic surgeons avoiding help for mental wellness. Improving well-being culture requires systemic changes. Finally, women in academics perceive decreased equality in promotional considerations and face leadership that already lacks representation of women. This paper presents solutions to assist in developing equitable work environments for all academic clinicians.

Orthopedics/Bone and Joint Center

Makhni EC, Hennekes ME, Baumhauer JF, Muh SJ, and Spindler K. AOA Critical Issues: Patient-Reported Outcome Measures: Why Every Orthopaedic Practice Should Be Collecting Them. *J Bone Joint Surg Am* 2023; 105(8):641-648. PMID: 37074301. [Full Text](#)

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Patient-centered care is essential to providing high-quality value-based care. Patient-reported outcome measures (PROMs) are arguably the best tools available to orthopaedic providers for providing patient-centered care. Many clinical opportunities exist for the implementation of PROMs into routine practice, such as shared decision-making, mental health screening, and prediction of postoperative disposition. Routine use of PROMs is also an adjunct to the streamlining of documentation, patient intake, and telemedicine visits, and hospitals can aggregate PROMs for the purpose of risk stratification. Physicians can harness the power of PROMs for quality improvement initiatives and improvement of the patient experience. Despite these numerous applications, PROMs are frequently underutilized tools. Understanding the many benefits of PROMs may allow orthopaedic practices to justify investing in these valuable tools.

Orthopedics/Bone and Joint Center

Pullen WM, Pierre K, Wong I, Aoki SK, Lynch TS, Mather RC, 3rd, Ayeni OR, Byrd JWT, and Safran MR. MRI Does Not Improve Inter- or Intrarater Reliability for Hip Arthritis Grading Systems. *Am J Sports Med* 2023; 3635465231167866. Epub ahead of print. PMID: 37103331. [Full Text](#)

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BACKGROUND: Magnetic resonance imaging (MRI) scans and radiographs are often utilized in assessing for preoperative osteoarthritis in patients undergoing hip preservation surgery. **PURPOSE:** To determine if MRI scans improve inter- or intrarater reliabilities over radiographs for findings of hip arthritis. **STUDY DESIGN:** Cohort study (Diagnosis); Level of evidence, 3. **METHODS:** Anteroposterior and cross-table lateral radiographs as well as a representative coronal and sagittal T2-weighted MRI scan were reviewed for 50 patients by 7 experienced subspecialty hip preservation surgeons, with a minimum experience of 10 years. Radiographs and MRI scans were assessed for joint space narrowing, subchondral cysts, osteophytes, subchondral sclerosis, Likert osteoarthritis grade (none, mild, moderate, or severe), and Tönnis grade. MRI scans were also evaluated for bony edema, heterogeneous articular cartilage, and chondral defects. Inter- and intrarater reliabilities were calculated utilizing the Fleiss method with a 95% CI. **RESULTS:** The scans of 50 patients (28 female and 22 male) with a mean age of 42.8

years (SD, 14.2 years; range, 19-70 years) were reviewed. Radiographs revealed fair agreement for joint space narrowing ($\kappa = 0.25$ [95% CI, 0.21-0.30]), osteophytes ($\kappa = 0.26$ [95% CI, 0.14-0.40]), Likert osteoarthritis grading ($\kappa = 0.33$ [95% CI, 0.28-0.37]) and Tönnis grade ($\kappa = 0.30$ [95% CI, 0.26-0.34]). Radiographs revealed moderate agreement for subchondral cysts ($\kappa = 0.53$ [95% CI, 0.35-0.69]). MRI scans demonstrated poor to fair agreement for joint space narrowing ($\kappa = 0.15$ [95% CI, 0.09-0.21]), subchondral sclerosis ($\kappa = 0.27$ [0.19-0.34]), heterogeneous articular cartilage ($\kappa = 0.07$ [95% CI, 0.00-0.14]), Likert osteoarthritis grade ($\kappa = 0.19$ [95% CI, 0.15-0.24]), and Tönnis grade ($\kappa = 0.20$ [95% CI, 0.15-0.24]). MRI scans demonstrated substantial agreement for subchondral cysts ($\kappa = 0.73$ [95% CI, 0.63-0.83]). Intrarater reliabilities were statistically improved compared with interrater reliabilities, but no differences were found between radiographs and MRI scans for joint space narrowing, subchondral cysts, osteophytes, osteoarthritis grade, or Tönnis grade. **CONCLUSION:** Radiographs and MRI scans had substantial limitations and inconsistency between raters in evaluating common markers of hip osteoarthritis. MRI scans demonstrated strong reliability in evaluating for subchondral cysts but did not improve the interobserver variability of grading hip arthritis.

Orthopedics/Bone and Joint Center

Shaw JH, Wesemann LD, Banka TR, North WT, Charters MA, and Davis JJ. Oral Dexamethasone Following Total Knee Arthroplasty: A Double-Blind, Randomized Controlled Trial. *J Arthroplasty* 2023; Epub ahead of print. PMID: 37105325. [Full Text](#)

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BACKGROUND: Intravenous dexamethasone has been shown to reduce pain in total joint arthroplasty. This double-blind, randomized, placebo-controlled trial investigated the postoperative effects and safety of oral dexamethasone as a potential augment to multimodal pain management in outpatient knee arthroplasty. **METHODS:** The authors prospectively randomized 109 consecutive patients undergoing primary total knee arthroplasty. Patients were assigned to Group A (57 patients) received 4 mg of dexamethasone by mouth twice per day starting postoperative day (POD) one for four days and Group B received placebo capsules. All healthcare professionals and patients were blinded to group allocation. The primary outcome was defined as postoperative pain scores. Secondary outcomes included 90-day postoperative complications, nausea and vomiting, daily opioid usage, assistance for ambulation, difficulty sleeping, and early patient reported outcomes. Demographics were similar between groups. **RESULTS:** The patients who received dexamethasone had statistically significant decrease in VAS scores when averaging POD 1 to 4 ($P=0.01$). The average VAS scores among individual days were significantly lower with dexamethasone on POD 2, 3, and 4. While taking dexamethasone, morning and mid-day VAS scores were significantly lower. There was no difference between the groups with opioid use, nausea or vomiting, 90-day complications, ability to walk with/without assistance, difficulty sleeping, and early patient reported outcomes. **CONCLUSION:** This double-blind, randomized, placebo-controlled trial demonstrated that oral dexamethasone following primary total knee arthroplasty can reduce postoperative pain. This may be a beneficial option in ambulatory surgery where intravenous limitations exist, but larger series are needed to further evaluate the safety profile in this population.

Orthopedics/Bone and Joint Center

Yedulla NR, Faraj MT, Hazime AA, Gong JH, Tang A, and Day CS. Decision Aid on Orthopedic Virtual Care: Patient Preferences in Orthopedic Hand Clinic. *Telemed J E Health* 2023; Epub ahead of print. PMID: 37074349. [Full Text](#)

Department of Orthopedic Surgery, Henry Ford Health System, Detroit, Michigan, USA.
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Introduction: The objectives of this study are to develop a decision aid for orthopedic patients to decide between virtual or in-person care and assess patient preferences for these modalities in hand clinic. **Methods:** An orthopedic virtual care decision aid was developed alongside orthopedic surgeons and a virtual care expert. Subject participation involved 5 steps: Orientation, Memory, and Concentration Test (OMCT), knowledge pretest, decision aid, postdecision aid questionnaire, and Decisional Conflict Scale (DCS) assessment. Patients presenting to hand clinic were initially provided the OMCT to assess decision-making capacity, with those failing excluded. Subjects were then administered a pretest to assess their understanding of virtual and in-person care. Subsequently, the validated decision aid was provided to patients, after which a postdecision aid questionnaire and DCS assessment were administered. **Results:** This study enrolled 124 patients. Pre- to postdecision aid knowledge test scores increased by 15.3% ($p < 0.0001$), and the average patient DCS score was 18.6. After reading the decision aid, 47.6% of patients believed that virtual and in-person care provided similar physician interaction, 46.0% felt little difference in effectiveness between the modalities, and 39.5% had no preference for either. Most patients understood their options (79.8%) and were ready to make a care modality decision (65.4%) following decision aid administration. **Conclusion:** Significant improvements in knowledge scores, strong DCS scores, and high levels of understanding and decision-making readiness support decision aid validity. Hand patients appear to have no consensus preferences for care modality, emphasizing the need for a decision aid to help determine individual care preferences.

Otolaryngology – Head and Neck Surgery

Larrabee K, Meeks N, Williams AM, Springer K, Siddiqui F, Chang SS, Ghanem T, Wu VF, Momin S, and Tam S. Cognitive Function and Postoperative Outcomes in Patients with Head and Neck Cancer. *Laryngoscope* 2023; Epub ahead of print. PMID: 37017269. [Full Text](#)

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OBJECTIVE: Determine the relationship between cognitive function and postoperative outcomes. **METHODS:** This IRB-approved retrospective cohort study included all patients treated between August 2015 and March 2020 undergoing major surgery for aerodigestive cancer or cutaneous/thyroid cancer that required free-flap reconstruction at Henry Ford Hospital. Routine administration of the Montreal Cognitive Assessment (MoCA) was completed as part of preoperative psychosocial evaluation. Outcomes included postoperative diagnosis of delirium, discharge disposition, return to the emergency department within 30 days of surgery, and readmission within 30 days of surgery. Univariate and multivariate logistic regression were used to determine the associations between preoperative MoCA score and each outcome measure. **RESULTS:** One hundred thirty-five patients with HNC were included in the study (mean [SD] age, 60.7 [± 10.8] years; 70.4% [$n = 95$] male; 83.0% [$n = 112$] White, 16.3% [$n = 22$] Black). The average preoperative MoCA score was 23.4 (SD ± 4.5). Based on the MoCA score, 35% ($n = 47$) scored ≥ 26 (i.e., normal cognitive status), 55.6% ($n = 75$) scored between 18 and 25 (i.e., mild impairment), 8.1% ($n = 11$) scored between 10 and 17 (i.e., moderate impairment), and 1.5% ($n = 2$) scored < 10 (i.e., severe impairment). After adjusting for other variables, a lower MoCA score was associated with discharge disposition to a location other than home and prolonged length of hospital stay. **CONCLUSIONS:** Preoperative cognitive function in patients undergoing major head and neck surgery for head and neck cancer was associated with discharge destination and length of stay. **LEVEL OF EVIDENCE:** 3 *Laryngoscope*, 2023.

Pathology and Laboratory Medicine

Aryal SC, Husain S, Zhang Z, and Yuan L. Gastric glomus tumor on EUS-FNA-based cytology: clinicopathologic and immunohistochemical features of 4 cases, including 1 case with associated MIR143HG-NOTCH2 fusion gene. *J Am Soc Cytopathol* 2023; Epub ahead of print. PMID: 37072283. [Full Text](#)

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INTRODUCTION: Gastric glomus tumor (GT) is a rare submucosal tumor for which the preoperative diagnosis can be challenging. We report the cytomorphologic and immunohistochemical features of 4 gastric GTs diagnosed by endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) cytology. **MATERIALS AND METHODS:** Files were searched to identify gastric GTs diagnosed by EUS-FNA between 2018 and 2021. A total of 4 cases of gastric GTs (3 men and 1 women; mean age, 60 years) were included. **RESULTS:** Three GTs were located in the gastric antrum and one in the gastric body. Their size ranged from 2 to 2.5 cm. Three patients presented with epigastric discomfort and one with chest wall discomfort. Rapid on-site evaluation was performed for 3 cases; the findings for all 3 were indeterminate. The smears were moderate to highly cellular and showed loose clusters of evenly distributed small- to medium-size bland tumor cells. The tumor cells had centrally located round to oval nuclei with inconspicuous nucleoli and scant to moderate amount of eosinophilic to clear cytoplasm. Examination of the cell blocks revealed branching small vessels surrounded by small- to medium-size cells. The neoplastic cells were positive for smooth muscle actin and synaptophysin and negative for AE1/AE3 and S-100. C-KIT and CD34 were variably positive. Ki-67 was <2% positive. In 1 case, the fusion panel-solid tumor (50 genes) revealed the MIR143HG-NOTCH2 fusion gene. **CONCLUSIONS:** Smears and cell block preparation revealed angiocentric sheets of uniform, small round to oval tumor cells with pale to eosinophilic cytoplasm, intermingled with endothelial cells. The differential diagnosis of gastric GTs on rapid on-site evaluation includes neuroendocrine tumors and epithelioid or spindled cell neoplasms. Immunohistochemical and molecular studies can be helpful in the preoperative diagnosis of gastric GT.

Pathology and Laboratory Medicine

Obaidat D, Giordo R, Kleinbrink EL, Banisad E, Grossman LI, Arshad R, **Stark A**, Maroun MC, Lipovich L, and Fernandez-Madrid F. Non-coding regions of nuclear-DNA-encoded mitochondrial genes and intergenic sequences are targeted by autoantibodies in breast cancer. *Front Genet* 2022; 13:970619. PMID: 37082114. [Full Text](#)

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Autoantibodies against mitochondrial-derived antigens play a key role in chronic tissue inflammation in autoimmune disorders and cancers. Here, we identify autoreactive nuclear genomic DNA (nDNA)-encoded mitochondrial gene products (GAPDH, PKM2, GSTP1, SPATA5, MFF, TSPOAP1, PHB2, COA4, and HAGH) recognized by breast cancer (BC) patients' sera as nonself, supporting a direct relationship of mitochondrial autoimmunity to breast carcinogenesis. Autoreactivity of multiple nDNA-encoded mitochondrial gene products was mapped to protein-coding regions, 3' untranslated regions (UTRs), as well as introns. In addition, autoantibodies in BC sera targeted intergenic sequences that may be parts of long non-coding RNA (lncRNA) genes, including LINC02381 and other putative lncRNA neighbors of the protein-coding genes ERCC4, CXCL13, SOX3, PCDH1, EDDM3B, and GRB2. Increasing evidence indicates that lncRNAs play a key role in carcinogenesis. Consistent with this, our findings suggest that lncRNAs, as well as mRNAs of nDNA-encoded mitochondrial genes, mechanistically contribute to BC progression. This work supports a new paradigm of breast carcinogenesis based on a globally dysfunctional genome with altered function of multiple mitochondrial and non-mitochondrial oncogenic pathways caused by the effects of autoreactivity-induced dysregulation of multiple genes and

their products. This autoimmunity-based model of carcinogenesis will open novel avenues for BC treatment.

Pathology and Laboratory Medicine

Xu Z, Saikia K, and Yuan L. Dedifferentiated endometrial carcinoma arising from serous carcinoma: Diagnostic challenges and recommendations. *Gynecol Oncol Rep* 2023; 47:101188. PMID: 37122437. [Full Text](#)

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•Dedifferentiated endometrial carcinoma arising from serous carcinoma (null-type P53).•Differential diagnosis including carcinosarcoma, FIGO grade 3 endometrioid carcinoma. •Also need to rule out SMARCA4-deficient uterine sarcoma and other sarcomas.

Pediatrics

Gamarel KE, Jadwin-Cakmak L, King WM, Reyes LA, Trammell R, Neilands TB, **Connolly MD**, and Jennings Mayo-Wilson L. Community-Led Response to Address Economic Vulnerability due to COVID-19 with, for, and by Transgender Women of Color: A Qualitative Pilot Evaluation. *Transgend Health* 2023; 8(2):195-199. PMID: 37013097. [Request Article](#)

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PURPOSE: Intersectional stigma fuels inequities among transgender women of color, which have been exacerbated by coronavirus disease 2019 (COVID-19). This study evaluated a community-led emergency assistance program for transgender women of color. **METHODS:** We conducted a pilot program evaluation (n=8). **RESULTS:** Retention was 87.5% over the follow-up. Funds were primarily used for bills, food, and housing. Requesting and receiving funds was described as "somewhat to extremely easy." Participants identified the need for economic empowerment components in future programming, specifically gender affirmation, skill-building for education and employment, and entrepreneurial opportunities. **CONCLUSION:** Findings highlight the need to invest in community-led strategies to address inequities experienced by transgender women of color.

Pediatrics

Straughen JK, Sitarik AR, Wegienka G, Cole Johnson C, Johnson-Hooper TM, and Cassidy-Bushrow AE. Association between prenatal antimicrobial use and offspring attention deficit hyperactivity disorder. *PLoS One* 2023; 18(5):e0285163. PMID: 37134093. [Full Text](#)

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

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BACKGROUND: Gut-brain cross-talk may play an important role in modulating neurodevelopment. Few studies have examined the association between antimicrobials that influence infant gut microbiota assemblage and attention deficit hyperactivity disorder (ADHD). **OBJECTIVE:** To examine the association between maternal prenatal antimicrobial use and ADHD in offspring at 10 years of age. **METHODS:** Data are from the Wayne County Health, Environment, Allergy and Asthma Longitudinal Study, a racially and socioeconomically diverse birth cohort in metropolitan Detroit, Michigan. Maternal antimicrobial use was extracted from the medical record. ADHD diagnoses were based on parental report at the 10-year study visit. Poisson regression models with robust error variance were used to calculate risk ratios (RR).

Cumulative frequency of exposure to antibiotics, and effect modification were also evaluated. RESULTS: Among the 555 children included in the analysis, 108 were diagnosed with ADHD. During pregnancy, 54.1% of mothers used antibiotics while 18.7% used antifungals. Overall, there was no evidence of an association between prenatal antibiotic exposure and ADHD (RR [95% CI] = 0.98 [0.75, 1.29]), but there was an increased risk of ADHD among those with mothers using 3+ courses of antibiotics (RR [95%CI] = 1.58 [1.10, 2.29]). Prenatal exposure to antifungals was associated with a 1.6 times higher risk of ADHD (RR [95% CI] = 1.60 [1.19, 2.15]). In examining effect modification by child sex for antifungal use, there was no evidence of an association among females (RR [95% CI] = 0.97 [0.42, 2.23]), but among males, prenatal antifungal use was associated with 1.82 times higher risk of ADHD (RR [95% CI] = 1.82 [1.29, 2.56]). CONCLUSIONS: Maternal prenatal antifungal use and frequent prenatal antibiotic use are associated with an increased risk of ADHD in offspring at age 10. These findings highlight the importance of the prenatal environment and the need for careful use of antimicrobials.

Pharmacy

de Oca JEM, Veve MP, Zervos MJ, and Kenney RM. Aminopenicillins versus Non-aminopenicillins for Treatment of Enterococcal Lower Urinary Tract Infections. *Int J Antimicrob Agents* 2023; 106800. Epub ahead of print. PMID: 37004756. [Full Text](#)

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Aminopenicillins achieve urinary concentrations that exceed typical minimum inhibitory concentrations for enterococcal lower urinary tract infection (UTI). Our clinical microbiology laboratory discontinued routine susceptibilities on enterococcal urine isolates and reports "aminopenicillins are predictably reliable for uncomplicated enterococcal UTI". The study objective was to compare outcomes of aminopenicillins (AP) to non-aminopenicillins (NAP) for enterococcal lower UTIs. This was an IRB approved, retrospective cohort of adults hospitalized with symptomatic enterococcal lower UTIs from 2013-2021. Primary endpoint: composite clinical success at 14-days, defined as resolution of symptoms without new symptoms and no repeat culture growth of index organism. A non-inferiority analysis was utilized with a 15% margin, and logistic regression evaluated characteristics associated with 14-day failure. 178 subjects were included: 89 AP, 89 NAP. VRE was identified in 73 (82%) AP and 76 (85%) NAP patients (P=0.54); a total of 34 (38.2%) AP and 66 (74.2%) NAP patients had confirmed *E. faecium* (P<0.001). Amoxicillin (36, 40.5%) and ampicillin (36, 40.5%) were the most frequent AP utilized; linezolid (41, 46%) and fosfomycin (30, 34%) were the most frequent NAP. 14-day clinical success for AP and NAP was 83.1% and 82.0% (1.1% difference, 97.5%CI, -0.117-0.139). Among the *E. faecium* subgroup, 14-day clinical success was observed in 27/34 (79.4%) of AP and 53/66 (80.3%) of NAP patients (P=0.916). In logistic regression, APs were not associated with 14-day clinical failure (adjOR 0.84; 95%CI, 0.38-1.86). Aminopenicillins were noninferior to non-aminopenicillins for treating enterococcal lower UTIs and may be considered irrespective of susceptibility results.

Pharmacy

Kurish HP, **Gabriel JM**, Bruck CL, and Stumpf JL. Efficacy of a Viokace Pancreatic Enzyme Protocol for Clearing Occluded Enteral Feeding Tubes: A Quality Assurance Evaluation. *J Pharm Pract* 2023; 36(2):271-275. PMID: 34340577. [Full Text](#)

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Background: A previous retrospective study documented restored patency to 48.2% of occluded enteral feeding tubes using alkalized Creon pancreatic enzyme capsules. In light of the low efficacy rate, the institutional enteral feeding tube clearance protocol was subsequently revised to incorporate a newly marketed non-enteric-coated Viokace pancreatic enzyme tablet, despite the lack of published data for this indication. **Objective:** This study aims to evaluate the effectiveness of a Viokace-based alkalized pancreatic enzyme protocol to clear occluded enteral feeding tubes in a university health system. **Methods:** This retrospective, cohort quality assurance study included adult and pediatric patients receiving a Viokace-based pancreatic enzyme protocol for enteral feeding tube occlusions in a university health system during a 12-month period. The primary outcome was effectiveness in enteral tube clearance as documented in the electronic medical record. Efficacy of the new protocol was also compared with a Creon-based alkalized solution using historical data. **Results:** The Viokace protocol successfully cleared 176 of the 277 (63.5%) occluded enteral feeding tubes occurring in 205 patients included in the analysis. The revised protocol was significantly more effective at clearing occluded enteral feeding tubes ($P = 0.0056$) than a protocol using Creon pancreatic enzyme capsules. **Conclusion:** According to this retrospective evaluation, an alkalized Viokace pancreatic enzyme protocol was effective in clearing 63.5% of occluded enteral feeding tubes. This significantly higher success rate than previously documented with a Creon-based protocol supports the change in pancreatic enzyme formulations in the institutional protocol.

Pharmacy

Vuong L, Kenney RM, Thomson JM, Faison DJ, Church BM, McCollom R, Gunaga S, Cahill MM, Slezak MA, Davis SL, and Veve MP. Implementation of indication-based antibiotic order sentences improves antibiotic use in emergency departments. *Am J Emerg Med* 2023; 69:5-10. PMID: 37027958.

[Full Text](#)

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INTRODUCTION: Prior data have suggested that suboptimal antibiotic prescribing in the emergency department (ED) is common for uncomplicated lower respiratory tract infections (LRTI), urinary tract infections (UTI), and acute bacterial skin and skin structure infections (ABSSSI). The objective of this study was to measure the effect of indication-based antibiotic order sentences (AOS) on optimal antibiotic prescribing in the ED. **METHODS:** This was an IRB-approved quasi-experiment of adults prescribed antibiotics in EDs for uncomplicated LRTI, UTI, or ABSSSI from January to June 2019 (pre-implementation) and September to December 2021 (post-implementation). AOS implementation occurred in July 2021. AOS are lean process, electronic discharge prescriptions retrievable by name or indication within the discharge order field. The primary outcome was optimal prescribing, defined as correct antibiotic selection, dose, and duration per local and national guidelines. Descriptive and bivariate statistics were performed; multivariable logistic regression was used to determine variables associated with optimal prescribing. **RESULTS:** A total of 294 patients were included: 147 pre-group and 147 post-group. Overall optimal prescribing improved from 12 (8%) to 34 (23%) ($P < 0.001$). Individual components of optimal prescribing were optimal selection at 90 (61%) vs 117 (80%) ($P < 0.001$), optimal dose at 99 (67%) vs 115 (78%) ($P = 0.036$), and optimal duration at 38 (26%) vs 50 (34%) ($P = 0.13$) for pre- and post-group, respectively. AOS was independently associated with optimal prescribing after multivariable logistic regression analysis (adjOR, 3.6; 95%CI, 1.7-7.2). A post-hoc analysis showed low uptake of AOS by ED prescribers. **CONCLUSIONS:** AOS are an efficient and promising strategy to enhance antimicrobial stewardship in the ED.

Public Health Sciences

Abu Rous F, Li P, Carskadon S, Singh SR, **Chacko R**, Abushukair H, **Gadgeel S**, and **Palanisamy N**. Brief Report: Prognostic Relevance of 3q Amplification in Squamous Cell Carcinoma of the Lung. *JTO Clin Res Rep* 2023; 4(4):100486. PMID: 37025118. [Full Text](#)

Division of Hematology/Oncology, Department of Internal Medicine, Henry Ford Health, Detroit, Michigan.
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Faculty of Medicine, Jordan University of Science and Technology, Ar-Ramtha, Jordan.

INTRODUCTION: Amplification of 3q is the most common genetic alteration identified in squamous cell carcinoma of the lung (LUSC), with the most frequent amplified region being 3q26 to 3q28. **METHODS:** In this analysis, we aim to describe the prognostic relevance of 3q amplification by focusing on a minimal common region (MCR) of amplification constituted of 25 genes. We analyzed 511 cases of LUSC from The Cancer Genome Atlas and included 476 in the final analysis. **RESULTS:** We identified a 25-gene MCR that was amplified in 221 (44.3%) cases and was associated with better disease-specific survival (not reported [NR] versus 9.25 y, 95% confidence interval [CI]: 5.24-NR, log-rank $p = 0.011$) and a progression-free interval of 8 years (95% CI: 5.1-NR) versus 4.9 years (95% CI: 3.5-NR, log-rank $p = 0.020$). Multivariable analysis revealed that MCR amplification was associated with improved disease-specific survival and progression-free interval. **CONCLUSIONS:** Amplification of the 25-gene MCR within 3q was present in 44% of this cohort, consisting mainly of Caucasian patients with early stage LUSC. This analysis strongly indicates the prognostic relevance of the 25-gene MCR within 3q. We are further evaluating its prognostic and predictive relevance in a racially diverse patient population with advanced LUSC.

Public Health Sciences

Agarwal M, Hoffman J, Ngo Tenlep SY, **Santarossa S**, Pearson KJ, **Sitarik AR**, **Cassidy-Bushrow AE**, and Petriello MC. Maternal polychlorinated biphenyl 126 (PCB 126) exposure modulates offspring gut microbiota irrespective of diet and exercise. *Reprod Toxicol* 2023; 118:108384. PMID: 37061048.

[Request Article](#)

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The gut microbiota plays an important role throughout the lifespan in maintaining host health, and several factors can modulate microbiota composition including diet, exercise, and environmental exposures. Maternal microbiota is transferred to offspring during early life; thus, environmental exposures before gestation may also modulate offspring microbiota. Here we aimed to investigate the effects of maternal exposure to dioxin-like polychlorinated biphenyls (PCBs) on the microbiota of aged offspring and to determine if lifestyle factors, including maternal exercise or offspring high-fat feeding alter these associations. To test this, dams were exposed to PCB 126 (0.5 $\mu\text{mole/kg}$ body weight) or vehicle oil by oral gavage during preconception, gestation, and during lactation. Half of each group was allowed access to running wheels for ≥ 7 days before and during pregnancy and up through day 14 of lactation. Female offspring born from the 4 maternal groups (PCB exposure or not, with/without exercise) were subsequently placed either on regular diet or switched to a high-fat diet during adulthood. Microbiota composition was quantified in female offspring at 49 weeks of age by 16 S rRNA sequencing. Maternal exposure to PCB 126 resulted in significantly reduced richness and diversity in offspring microbiota regardless of diet or exercise. Overall compositional differences were largely driven by offspring diet, but

alterations in specific taxa due to maternal PCB 126 exposure, included the depletion of Verrucomicrobiaceae and Akkermansia muciniphila, and an increase in Anaeroplasma. Perturbation of microbiota due to PCB 126 may predispose offspring to a variety of chronic diseases later in adulthood.

Public Health Sciences

Bossick AS, Painter I, Williams EC, and Katon JG. Development of a Composite Risk Index of Reproductive Autonomy Using State Laws: Association With Maternal and Neonatal Outcomes. *Womens Health Issues* 2023; Epub ahead of print. PMID: 37120364. [Full Text](#)

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OBJECTIVE: We developed a composite index to quantify state legislation related to reproductive autonomy and examined its association with maternal and neonatal outcomes. We hypothesized that greater reproductive autonomy would be associated with lower rates of severe maternal morbidity (SMM), pregnancy-related mortality (PRM), preterm birth (PTB), and low birthweight. **DESIGN:** A Delphi panel was used to inform development of the index. Restrictive policies were assigned values of -1 and enabling policies +1. Publicly available data were used to conduct a cross-sectional study among all live births in the 50 U.S. states to people aged 15 to 44 between January 1, 2016, and December 31, 2018, to examine the association between the risk index and PRM, SMM, PTB, and low birthweight. We used linear regression with state scores and quartiles, adjusted for state-level proportions of White, Black, and Hispanic live births; percent living in rural areas; percent of population foreign born; Health Resources and Services Administration spending on maternal and child health; and the Opportunity Index, a composite measure of indicators of the economy, education, and community. **RESULTS:** From 2016 to 2018, there were 11,530,785 births, 2,846 pregnancy-related deaths, and 154,384 cases of SMM. The Delphi panel resulted in a summed state measure of 106 laws in 8 categories that could affect reproductive autonomy. In adjusted analyses, states in the most enabling (most reproductive autonomy) quartile had a 44.7 per 10,000 higher rate of SMM compared with the most restrictive quartile. However, the most enabling quartile was associated with a 9.87 per 100,000 lower rate of PRM and 0.67 per 100 lower rate of PTB compared with the most restrictive quartile (least reproductive autonomy). **CONCLUSIONS:** A composite policy index of reproductive autonomy was found to be associated with higher rates of SMM but lower rates of PRM and PTB. Further research is needed to understand how reproductive autonomy in the cumulative index may influence these and other maternal and birth outcomes.

Public Health Sciences

Hecht LM, Adams R, Dutkiewicz D, Radloff D, Wales MN, Whitmer J, **Murphy D**, and **Santarossa S**. "Healing Can Be a Very Jagged Line": Reflections on Life as a COVID-19 Long Hauler. *J Patient Cent Res Rev* 2023; 10(2):77-81. PMID: 37091113. [Full Text](#)

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"Long COVID" - a term referring to COVID-19-associated symptoms and conditions (ie, sequelae) that remain or emerge after resolution of a SARS-CoV-2 infection - is a multifaceted condition about which little is known. As part of formalized patient-engaged research at a large Midwestern health system, patient stakeholders with long COVID (N=5) wrote stories based on their lived experience, as this was their preferred format for detailing their experience with the condition. These patient stakeholders reviewed one another's stories, identified relevant quotes, and provided opportunities for elaboration.

Independently, a trained researcher extracted quotes from the stories, identified themes, and wove the quotes together to share the independent, yet similar, stories. Emergent themes were that of uncertainty about the symptomatology of long COVID and its effects on patients' mental health, physical functioning, family unit, self-identity, and future outlook. Further patient-engaged research on understanding the lived experience of long COVID may serve to advance knowledge and treatment. Health care providers caring for those with long COVID can benefit from listening and validating the stories of individuals suffering from this condition.

Public Health Sciences

Katon JG, **Bossick A**, Carey C, Christy A, Doll K, Gatsby E, Gray KE, Lynch KE, Moy E, Owens S, Washington DL, and Callegari LS. Racial Disparities in Uterine Fibroid Treatment Among Veterans Using VA Health Care. *Womens Health Issues* 2023; Epub ahead of print. PMID: 37105835. [Full Text](#)

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INTRODUCTION: Uterine fibroids are common, nonmalignant tumors that disproportionately impact Black patients. We aimed to examine Black and White differences in receipt of any treatment and type of first treatment in the Department of Veterans Affairs, including effect modification by severity as approximated by anemia. **METHODS:** We used Department of Veterans Affairs administrative data to identify 5,041 Black and 3,206 White veterans with symptomatic uterine fibroids, identified by International Classification of Diseases, 9th edition, Clinical Modification, codes, between fiscal year 2010 and fiscal year 2012 and followed in the administrative data through fiscal year 2018 for outcomes. Outcomes included receipt of any treatment, hysterectomy as first treatment, and fertility-sparing treatment as first treatment. We stratified all analyses by age (<45, ≥45 years old), used generalized linear models with a log link and Poisson error distribution, included an interaction term between race and anemia, and used recycled

predictions to estimate adjusted percentages for outcomes. RESULTS: There was evidence of effect modification by anemia for receipt of any treatment but not for any other outcomes. Across age and anemia sub-groups, Black veterans were less likely to receive any treatment than White veterans. Adjusted racial differences were most pronounced among veterans with anemia (<45 years, Black-White difference = -10.3 percentage points; 95% confidence interval, -15.9 to -4.7; ≥45 years, Black-White difference = -20.3 percentage points; 95% confidence interval, -27.8 to -12.7). Across age groups, Black veterans were less likely than White veterans to have hysterectomy and more likely to have a fertility-sparing treatment as their first treatment. CONCLUSIONS: We identified significant Black-White disparities in receipt of treatment for symptomatic uterine fibroids. Additional research that centers the experiences of Black veterans with uterine fibroids is needed to inform strategies to eliminate racial disparities in uterine fibroid care.

Public Health Sciences

Larrabee K, Meeks N, Williams AM, Springer K, Siddiqui F, Chang SS, Ghanem T, Wu VF, Momin S, and Tam S. Cognitive Function and Postoperative Outcomes in Patients with Head and Neck Cancer. *Laryngoscope* 2023; Epub ahead of print. PMID: 37017269. [Full Text](#)

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OBJECTIVE: Determine the relationship between cognitive function and postoperative outcomes.

METHODS: This IRB-approved retrospective cohort study included all patients treated between August 2015 and March 2020 undergoing major surgery for aerodigestive cancer or cutaneous/thyroid cancer that required free-flap reconstruction at Henry Ford Hospital. Routine administration of the Montreal Cognitive Assessment (MoCA) was completed as part of preoperative psychosocial evaluation. Outcomes included postoperative diagnosis of delirium, discharge disposition, return to the emergency department within 30 days of surgery, and readmission within 30 days of surgery. Univariate and multivariate logistic regression were used to determine the associations between preoperative MoCA score and each outcome measure. RESULTS: One hundred thirty-five patients with HNC were included in the study (mean [SD] age, 60.7 [±10.8] years; 70.4% [n = 95] male; 83.0% [n = 112] White, 16.3% [n = 22] Black). The average preoperative MoCA score was 23.4 (SD ± 4.5). Based on the MoCA score, 35% (n = 47) scored ≥26 (i.e., normal cognitive status), 55.6% (n = 75) scored between 18 and 25 (i.e., mild impairment), 8.1% (n = 11) scored between 10 and 17 (i.e., moderate impairment), and 1.5% (n = 2) scored <10 (i.e., severe impairment). After adjusting for other variables, a lower MoCA score was associated with discharge disposition to a location other than home and prolonged length of hospital stay. CONCLUSIONS: Preoperative cognitive function in patients undergoing major head and neck surgery for head and neck cancer was associated with discharge destination and length of stay. LEVEL OF EVIDENCE: 3 *Laryngoscope*, 2023.

Public Health Sciences

Leonard-Murali S, Nathanson SD, Springer K, Baker P, and Susick L. Early breast cancer survival of black and white American women with equal diagnostic and therapeutic management. *Eur J Surg Oncol* 2023; 49(3):583-588. PMID: 36464602. [Full Text](#)

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PURPOSE: Breast cancer (BC) survival favors White versus Black Americans despite advances in screening and treatment. We hypothesized that these differences were dependent upon quality of care by analyzing long-term outcomes of 3139 early BC patients at our quaternary care center where uniform access and management of BC is provided to women irrespective of race. **METHODS:** Prospectively collected data for clinical stage I-II BC patients from our quaternary care cancer center were analyzed, focusing on disease-specific survival (DSS). Subgroup analyses included the overall cohort, triple-negative BC (TNBC), non-TNBC and HER2/neu positive patients. Multivariable analyses to evaluate associations of variables with DSS were performed for each subgroup. **RESULTS:** The overall cohort consisted of 3139 BC patients (1159 Black, 1980 White). Black and White patients did not differ by most baseline variables. Black patients had higher rates of TNBC (18% versus 10%, $p < 0.0001$). Kaplan-Meier analysis of all subgroups (overall, TNBC, non-TNBC, HER2/neu positive) did not reveal DSS differences between Black and White patients. Multivariable analysis of subgroups also did not find race to be associated with DSS. **CONCLUSION:** In this large, carefully controlled, long term, single-institution prospective cohort study DSS in Black and White early BC patients with equal access to high quality care, did not differ. While BC patients with adverse molecular markers did slightly worse than those with more favorable markers, there is no observable difference between Black and White women with the same markers. These observations support the conclusion that equal access to, and quality, of BC care abolishes racial disparities in DSS.

Public Health Sciences

Lokhandwala T, Aly A, Farrelly E, Willey JP, **Lamerato LE**, Healey M, Coutinho AD, and Seal BS. Management of hepatocellular carcinoma from diagnosis in routine clinical practice. *Hepat Oncol* 2023; 9(4):Hep45. PMID: 37009420. [Full Text](#)

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AIM: To assess real-world management of patients diagnosed with hepatocellular carcinoma (HCC) within an integrated delivery network. **MATERIALS & METHODS:** A retrospective cohort analysis of adults newly diagnosed with HCC from January 2014 to March 2019. Overall survival and treatment journey were assessed over the entire available follow-up period per patient. **RESULTS:** Of the 462 patients, 85% had ≥ 1 treatment. The 24-month overall survival rate (95% CI) from first treatment was 77% (72-82%). Majority of Child-Pugh class A (71%) and B (60%) patients received locoregional therapy first. Half (53.6%) of the patients with liver transplantation first were Child-Pugh class C patients. Sorafenib was the predominant systemic therapy. **CONCLUSION:** This integrated delivery network data analysis offers a comprehensive insight into the real-world management of HCC.

Public Health Sciences

O'Leary BF, Hill AB, Linn C, **Lu M**, Miller CJ, Newman A, Sperone FG, and **Zhang Q**. Exploring the association of Brownfield remediation status with socioeconomic conditions in Wayne County, MI. *Environ Sci Pollut Res Int* 2023; Epub ahead of print. PMID: 37039917. [Full Text](#)

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Urban neighborhoods with locations of environmental contamination, known as brownfields, impact entire neighborhoods, but corrective environmental remedial action on brownfields is often tracked on an individual property basis, neglecting the larger neighborhood-level impact. This study addresses this

impact by examining spatial differences between brownfields with unmitigated environmental concerns (open site) and sites that are considered fully mitigated or closed in urban neighborhoods (closed site) on the US census tract scale in Wayne County, MI. Michigan's Department of Environment, Great Lakes, and Energy's leaking underground storage tank (LUST) database provided brownfield information for Wayne County. Local indicators of spatial association (LISA) produced maps of spatial clustering and outliers. A McNemar's test demonstrated significant discordances in LISA categories between LUST open and closed sites ($p < 0.001$). Geographically weighted regressions (GWR) evaluated the association between open and closed site spatial density (open-closed) with socioeconomic variables (population density, proportion of White or Black residents, proportion of college educated populations, the percentage of owner-occupied units, vacant units, rented units, and median household value). Final multivariate GWR showed that population density, being Black, college education, vacant units, and renter occupied units were significantly associated ($p < 0.05$) with open-closed, and that those associations varied across Wayne County. Increases in Black population was associated with increased open-closed. Increases in vacant units, renter-occupied units, and college education were associated with decreased open-closed. These results provide input for environmental justice research to identify inequalities and discover the distribution of environmental hazards among urban neighborhoods.

Public Health Sciences

Silbergleit AK, Isabell K, Turnbull J, Patel N, Boettcher E, Konnai R, Collins D, Sidiropoulos C, and Schultz L. Comparison of Oropharyngeal Dysphagia Before and After Botulinum Toxin Injection in Cervical Dystonia. *Dysphagia* 2023; Epub ahead of print. PMID: 37071189. [Full Text](#)

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Cervical dystonia (CD) is the most common form of focal dystonia with Botulinum neurotoxin (BoNT) being a frequent method of treatment. Dysphagia is a common side effect of BoNT treatment for CD. Instrumental evaluation of swallowing in CD using standardized scoring for the videofluoroscopic swallowing study (VFSS) and validated and reliable patient-reported outcomes measures is lacking in the literature. (1) to determine if BoNT injections change instrumental findings of swallowing function using the Modified Barium Swallow Impairment Profile (MBSImP) in individuals with CD; (2) to determine if BoNT injections change self-perception of the psychosocial handicapping effects of dysphagia in individuals with CD, using the Dysphagia Handicap Index (DHI); (3) to determine the effect of BoNT dosage on instrumental swallowing evaluation and self-reported swallowing outcomes measures. 18 subjects with CD completed a VFSS and the DHI before and after BoNT injection. There was a significant increase in pharyngeal residue for pudding consistency after BoNT injection, $p = 0.015$. There were significant positive associations between BoNT dosage and self-perception of the physical attributes of the handicapping effect of dysphagia, the grand total score and patient self-reported severity of dysphagia on the DHI; $p = 0.022$; $p = 0.037$; $p = 0.035$ respectively. There were several significant associations between changes in MBSImP scores and BoNT dose. Pharyngeal efficiency of swallowing may be affected by BoNT for thicker consistencies. Individuals with CD perceive greater physical handicapping effects of dysphagia with increased amounts of BoNT units and have greater self-perceptions of dysphagia severity with increased amounts of BoNT units.

Public Health Sciences

Straughen JK, Sitarik AR, Wegienka G, Cole Johnson C, Johnson-Hooper TM, and Cassidy-Bushrow AE. Association between prenatal antimicrobial use and offspring attention deficit hyperactivity disorder. *PLoS One* 2023; 18(5):e0285163. PMID: 37134093. [Full Text](#)

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BACKGROUND: Gut-brain cross-talk may play an important role in modulating neurodevelopment. Few studies have examined the association between antimicrobials that influence infant gut microbiota assemblage and attention deficit hyperactivity disorder (ADHD). **OBJECTIVE:** To examine the association between maternal prenatal antimicrobial use and ADHD in offspring at 10 years of age. **METHODS:** Data are from the Wayne County Health, Environment, Allergy and Asthma Longitudinal Study, a racially and socioeconomically diverse birth cohort in metropolitan Detroit, Michigan. Maternal antimicrobial use was extracted from the medical record. ADHD diagnoses were based on parental report at the 10-year study visit. Poisson regression models with robust error variance were used to calculate risk ratios (RR). Cumulative frequency of exposure to antibiotics, and effect modification were also evaluated. **RESULTS:** Among the 555 children included in the analysis, 108 were diagnosed with ADHD. During pregnancy, 54.1% of mothers used antibiotics while 18.7% used antifungals. Overall, there was no evidence of an association between prenatal antibiotic exposure and ADHD (RR [95% CI] = 0.98 [0.75, 1.29]), but there was an increased risk of ADHD among those with mothers using 3+ courses of antibiotics (RR [95%CI] = 1.58 [1.10, 2.29]). Prenatal exposure to antifungals was associated with a 1.6 times higher risk of ADHD (RR [95% CI] = 1.60 [1.19, 2.15]). In examining effect modification by child sex for antifungal use, there was no evidence of an association among females (RR [95% CI] = 0.97 [0.42, 2.23]), but among males, prenatal antifungal use was associated with 1.82 times higher risk of ADHD (RR [95% CI] = 1.82 [1.29, 2.56]). **CONCLUSIONS:** Maternal prenatal antifungal use and frequent prenatal antibiotic use are associated with an increased risk of ADHD in offspring at age 10. These findings highlight the importance of the prenatal environment and the need for careful use of antimicrobials.

Pulmonary and Critical Care Medicine

Villanueva-Villegas R, **Diaz-Mendoza J**, Salas-Lopez J, and Espiche C. Paragonimiasis Misdiagnosed as Pulmonary Tuberculosis: A Case Report. *Cureus* 2023; 15(3):e36169. PMID: 37065342. [Full Text](#)

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Paragonimiasis is a zoonosis caused by the ingestion of raw or undercooked crustaceans parasitized with metacercaria of *Paragonimus* spp. In Peru, Cajamarca is considered an endemic region for paragonimiasis. A 29-year-old man from the department of San Martín, Peru presented with a three-year history of cough, chest pain, fever, and hemoptysis. Treatment for tuberculosis (TB) was initiated even with negative results for sputum acid-fast bacillus (AFB), due to the patient's clinical characteristics and the high prevalence of the condition in the region. After eight months, due to the lack of any clinical improvement, he was referred to a regional hospital, where *Paragonimus* eggs were evidenced in direct sputum cytology. The patient received treatment with triclabendazole and showed clinical and radiological improvement. It is important to consider eating habits, even in non-endemic areas, for diagnosing paragonimiasis in patients with TB symptoms who do not respond to a specific treatment.

Radiation Oncology

Allen SG, Dragovic AF, Yin HM, Bryant AK, Paximadis PA, Matuszak MM, Schipper MJ, Dess RT, Hayman JA, Dominello MM, Kestin LL, **Movsas B**, Jolly S, and Bergsma DP. Prospective Evaluation of Limited-Stage Small Cell Lung Cancer Radiotherapy Fractionation Regimen Usage and Acute Toxicity in a Large Statewide Quality Collaborative. *Pract Radiat Oncol* 2023; Epub ahead of print. PMID: 37100388. [Full Text](#)

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PURPOSE: National guidelines on limited stage small cell lung cancer (LS-SCLC) treatment give preference to a hyperfractionated regimen of 45 Gy/30 fractions delivered twice-daily, however use of this regimen is uncommon compared to once-daily regimens. The purpose of this study was to characterize the LS-SCLC fractionation regimens used throughout a statewide collaborative, analyze patient and treatment factors associated with these regimens, and describe real-world acute toxicity profiles of once- and twice-daily RT regimens. **METHODS AND MATERIALS:** Demographic, clinical, and treatment data along with physician toxicity and patient-reported outcomes were prospectively collected by 29 institutions within the [quality consortium] between 2012 and 2021 for patients with LS-SCLC. We modeled the influence of RT fractionation and other patient-level variables clustered by treatment site on the odds of a treatment break specifically due to toxicity with multilevel logistic regression. Common Terminology Criteria for Adverse Events, version 4.0, incident Grade 2 or worse toxicity was longitudinally compared between regimens. **RESULTS:** There were 78 patients (15.6% overall) treated with twice-daily RT and 421 patients treated with once-daily RT. Patients receiving twice-daily RT were more likely to be married/living with someone (65% vs 51%, $p=0.019$) and to have no major comorbidities (24% vs 10%, $p=0.017$). Once-daily RT fractionation toxicity peaked during RT and twice-daily toxicity peaked within 1 month after RT. After stratifying by treatment site and adjusting for patient-level variables, once-daily treated patients had a 4.11 (95% confidence interval 1.31-12.87) higher odds of treatment break specifically due to toxicity than twice-daily treated patients. **CONCLUSION:** Hyperfractionation for LS-SCLC remains infrequently prescribed despite the lack of evidence demonstrating superior efficacy or lower toxicity of once-daily RT. With peak acute toxicity after RT and lower likelihood of a treatment break with twice-daily fractionation in real-world practice, providers may start utilizing hyperfractionated RT more frequently.

Radiation Oncology

Chuong MD, Clark MA, Henke LE, Kishan AU, Portelance L, **Parikh PJ**, Bassetti MF, Nagar H, Rosenberg SA, Mehta MP, Refaat T, Rineer JM, Smith A, Seung S, Zaki BI, Fuss M, and Mak RH. Patterns of utilization and clinical adoption of 0.35 Tesla MR-guided radiation therapy in the United States - Understanding the transition to adaptive, ultra-hypofractionated treatments. *Clin Transl Radiat Oncol* 2023; 38:161-168. PMID: 36466748. [Full Text](#)

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PURPOSE/OBJECTIVE: Magnetic resonance-guided radiation therapy (MRgRT) utilization is rapidly expanding worldwide, driven by advanced capabilities including continuous intrafraction visualization, automatic triggered beam delivery, and on-table adaptive replanning (oART). Our objective was to describe patterns of 0.35Tesla(T)-MRgRT (MRIdian) utilization in the United States (US) among early adopters of this novel technology. **MATERIALS/METHODS:** Anonymized administrative data from all US MRIdian treatment systems were extracted for patients completing treatment from 2014 to 2020. Detailed treatment information was available for all MRIdian linear accelerator (linac) systems and some cobalt systems. **RESULTS:** Seventeen systems at 16 centers delivered 5736 courses and 36,389 fractions (fraction details unavailable for 1223 cobalt courses), of which 21.1% were adapted. Ultra-hypofractionation (UHfx) (1-5 fractions) was used in 70.3% of all courses. At least one adaptive fraction was used for 38.5% of courses (average 1.7 adapted fractions/course), with higher oART use in UHfx dose schedules (47.7% of courses, average 1.9 adapted fractions per course). The most commonly treated organ sites were pancreas (20.7%), liver (16.5%), prostate (12.5%), breast (11.5%), and lung (9.4%). Temporal trends show a compounded annual growth rate (CAGR) of 59.6% in treatment courses delivered, with a dramatic increase in use of UHfx to 84.9% of courses in 2020 and similar increase in use of oART to 51.0% of courses. **CONCLUSIONS:** This is the first comprehensive study reporting patterns of utilization among early adopters of MRIdian in the US. Intrafraction MR image-guidance, advanced motion management, and increasing adoption of adaptive radiation therapy has led to a substantial transition to ultra-hypofractionated regimens. 0.35 T-MRgRT has been predominantly used to treat abdominal and pelvic tumors with increasing use of on-table adaptive replanning, which represents a paradigm shift in radiation therapy.

Radiation Oncology

Krauss DJ, Karrison T, Martinez AA, Morton G, Yan D, Bruner DW, **Movsas B, Elshaikh M**, Citrin D, Hershatter B, Michalski JM, Efstathiou JA, Currey A, Kavadi VS, Cury FL, Lock M, Raben A, Seaward SA, El-Gayed A, Rodgers JP, and Sandler HM. Dose-Escalated Radiotherapy Alone or in Combination With Short-Term Androgen Deprivation for Intermediate-Risk Prostate Cancer: Results of a Phase III Multi-Institutional Trial. *J Clin Oncol* 2023; Jco2202390. Epub ahead of print. PMID: 37104748. [Full Text](#)

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PURPOSE: It remains unknown whether or not short-term androgen deprivation (STAD) improves survival among men with intermediate-risk prostate cancer (IRPC) treated with dose-escalated radiotherapy (RT). **METHODS:** The NRG Oncology/Radiation Therapy Oncology Group 0815 study randomly assigned 1,492 patients with stage T2b-T2c, Gleason score 7, or prostate-specific antigen (PSA) value >10 and ≤20 ng/mL to dose-escalated RT alone (arm 1) or with STAD (arm 2). STAD was 6 months of luteinizing hormone-releasing hormone agonist/antagonist therapy plus antiandrogen. RT modalities were external-beam RT alone to 79.2 Gy or external beam (45 Gy) with brachytherapy boost. The primary end point was overall survival (OS). Secondary end points included prostate cancer-specific mortality (PCSM), non-PCSM, distant metastases (DMs), PSA failure, and rates of salvage therapy. **RESULTS:** Median follow-up was 6.3 years. Two hundred nineteen deaths occurred, 119 in arm 1 and 100 in arm 2. Five-year OS estimates were 90% versus 91%, respectively (hazard ratio [HR], 0.85; 95% CI, 0.65 to 1.11; P = .22). STAD resulted in reduced PSA failure (HR, 0.52; P <.001), DM (HR, 0.25; P <.001), PCSM (HR, 0.10; P = .007), and salvage therapy use (HR, 0.62; P = .025). Other-cause deaths were not significantly different (P = .56). Acute grade ≥3 adverse events (AEs) occurred in 2% of patients in arm 1 and in 12% for arm 2 (P <.001). Cumulative incidence of late grade ≥3 AEs was 14% in arm 1 and 15% in arm 2 (P = .29). **CONCLUSION:** STAD did not improve OS rates for men with IRPC treated with dose-escalated RT. Improvements in metastases rates, prostate cancer deaths, and PSA failures should be weighed against the risk of adverse events and the impact of STAD on quality of life.

Radiation Oncology

Larrabee K, Meeks N, Williams AM, Springer K, Siddiqui F, Chang SS, Ghanem T, Wu VF, Momin S, and Tam S. Cognitive Function and Postoperative Outcomes in Patients with Head and Neck Cancer. *Laryngoscope* 2023; Epub ahead of print. PMID: 37017269. [Full Text](#)

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OBJECTIVE: Determine the relationship between cognitive function and postoperative outcomes. **METHODS:** This IRB-approved retrospective cohort study included all patients treated between August 2015 and March 2020 undergoing major surgery for aerodigestive cancer or cutaneous/thyroid cancer that required free-flap reconstruction at Henry Ford Hospital. Routine administration of the Montreal Cognitive Assessment (MoCA) was completed as part of preoperative psychosocial evaluation. Outcomes included postoperative diagnosis of delirium, discharge disposition, return to the emergency department within 30 days of surgery, and readmission within 30 days of surgery. Univariate and multivariate logistic regression were used to determine the associations between preoperative MoCA score and each outcome measure. **RESULTS:** One hundred thirty-five patients with HNC were included in the study (mean [SD] age, 60.7 [±10.8] years; 70.4% [n = 95] male; 83.0% [n = 112] White, 16.3% [n = 22] Black). The average preoperative MoCA score was 23.4 (SD ± 4.5). Based on the MoCA score, 35% (n = 47) scored ≥26 (i.e., normal cognitive status), 55.6% (n = 75) scored between 18 and 25 (i.e., mild impairment), 8.1% (n = 11) scored between 10 and 17 (i.e., moderate impairment), and 1.5% (n = 2) scored <10 (i.e., severe impairment). After adjusting for other variables, a lower MoCA score was associated with discharge disposition to a location other than home and prolonged length of hospital stay. **CONCLUSIONS:** Preoperative cognitive function in patients undergoing major head and neck surgery for head and neck cancer was associated with discharge destination and length of stay. **LEVEL OF EVIDENCE:** 3 *Laryngoscope*, 2023.

Radiation Oncology

Movsas B, Rodgers JP, **Elshaikh MA**, Martinez AA, Morton GC, Krauss DJ, Yan D, Citrin DE, Hershatter BW, Michalski JM, Ellis RJ, Kavadi VS, Gore EM, Gustafson GS, Schulz CA, Velker VM, Olson AC, Cury FL, Papagikos MA, Karrison TG, Sandler HM, and Bruner DW. Dose-Escalated Radiation Alone or in Combination With Short-Term Total Androgen Suppression for Intermediate-Risk Prostate Cancer: Patient-Reported Outcomes From NRG/Radiation Therapy Oncology Group 0815 Randomized Trial. *J Clin Oncol* 2023; Jco2202389. Epub ahead of print. PMID: 37104723. [Full Text](#)

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William Beaumont Hospital, Royal Oak, MI.

Center for Cancer Research, National Cancer Institute, Bethesda, MD.

Emory University Hospital/Winship Cancer Institute, Atlanta, GA.

Washington University School of Medicine, Saint Louis, MO.

Penn State Milton Hershey Medical Center, Hershey, PA.

Case Western Reserve University, Cleveland, OH.

The US Oncology Network, Sugar Land, TX.

Froedtert and the Medical College of Wisconsin and Zablocki VAMC, Milwaukee, WI.

Beaumont NCI Community Oncology Research Program, Troy, MI.

Columbia Saint Mary's Water Tower Medical Commons, Milwaukee, WI.

London Regional Cancer Program, London, ON, Canada.

University of Pittsburgh Cancer Institute, Pittsburgh, PA.

The Research Institute of the McGill University Health Centre (MUHC), Montreal, QC, Canada.

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PURPOSE: To report patient-reported outcomes (PROs) of a phase III trial evaluating total androgen suppression (TAS) combined with dose-escalated radiation therapy (RT) for patients with intermediate-risk prostate cancer. **METHODS:** Patients with intermediate-risk prostate cancer were randomly assigned to dose-escalated RT alone (arm 1) or RT plus TAS (arm 2) consisting of luteinizing hormone-releasing hormone agonist/antagonist with oral antiandrogen for 6 months. The primary PRO was the validated Expanded Prostate Cancer Index Composite (EPIC-50). Secondary PROs included Patient-Reported Outcome Measurement Information System (PROMIS)-fatigue and EuroQOL five-dimensions scale questionnaire (EQ-5D). PRO change scores, calculated for each patient as the follow-up score minus baseline score (at the end of RT and at 6, 12, and 60 months), were compared between treatment arms using a two-sample t test. An effect size of 0.50 standard deviation was considered clinically meaningful. **RESULTS:** For the primary PRO instrument (EPIC), the completion rates were $\geq 86\%$ through the first year of follow-up and 70%-75% at 5 years. For the EPIC hormonal and sexual domains, there were clinically meaningful ($P < .0001$) deficits in the RT + TAS arm. However, there were no clinically meaningful differences by 1 year between arms. There were also no clinically meaningful differences at any time points between arms for PROMIS-fatigue, EQ-5D, and EPIC bowel/urinary scores. **CONCLUSION:** Compared with dose-escalated RT alone, adding TAS demonstrated clinically meaningful declines only in EPIC hormonal and sexual domains. However, even these PRO differences were transient, and there were no clinically meaningful differences between arms by 1 year.

Radiation Oncology

Puckett LL, Titi M, Kujundzic K, Dawes SL, Gore E, Katsoulakis E, Park JH, Solanki AA, Kapoor R, Kelly M, Palta J, **Chetty IJ**, Jabbour SK, Liao Z, **Movsas B**, Thomas CR, Timmerman RD, Werner-Wasik M, Kudner R, Wilson E, and Simone CB. Consensus Quality Measures and Dose Constraints for Lung Cancer from the Veterans Affairs Radiation Oncology Quality Surveillance Program and American Society for Radiation Oncology (ASTRO) Expert Panel. *Pract Radiat Oncol* 2023; Epub ahead of print. PMID: 37075838. [Full Text](#)

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INTRODUCTION: For patients with lung cancer, it is critical to provide evidence-based radiation therapy to ensure high quality care. The VA National Radiation Oncology Program (VA NROP) partnered with the American Society for Radiation Oncology (ASTRO) as part of the VA Radiation Oncology Quality Surveillance (VA ROQS) to develop lung cancer quality metrics and assess quality of care as a pilot program in 2016. Herein, we present recently updated consensus quality measures and dose-volume histogram (DVH) constraints. **METHODS:** A series of measures and performance standards were reviewed and developed by a Blue-Ribbon Panel of lung cancer experts in conjunction with ASTRO in 2022. As part of this initiative, quality, surveillance, and aspirational metrics were developed for a) Initial Consultation and Work Up, b) Simulation, Treatment Planning, and Treatment Delivery, and c) Follow Up. DVH metrics for target and organ at risk treatment planning dose constraints were also reviewed and defined. **RESULTS:** Altogether, a total of 19 lung cancer quality metrics were developed. There were 121 DVH constraints developed for various fractionation regimens including ultrahypofractionated (1,3,4,5 fraction[s]), hypofractionated (10 and 15 fractionations), and conventional fractionation (30-35 fractions). **CONCLUSIONS:** The devised measures will be implemented for quality surveillance for Veterans both inside and outside of the VA system, as well as provide a resource for lung cancer specific quality metrics. The recommended DVH constraints serve as a unique, comprehensive resource for evidence and expert-consensus based constraints across multiple fractionation schemas.

Radiation Oncology

Quinn TJ, **Chapman D**, Parzen J, Wahl DR, McNamara A, Dess R, Chan J, Feng F, Jackson WC, and Hamstra D. Validation of the Combination Gleason Score as an Independent Favorable Prognostic Factor in Prostate Cancer Treated With Dose-Escalated Radiation Therapy. *Pract Radiat Oncol* 2023; 13(2):e166-e175. PMID: 36503624. [Full Text](#)

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PURPOSE: Prognostic factors for prostate cancer include tumor, node, metastases stage, pretreatment prostate-specific antigen, and pathology (via Gleason score [GS] or grade group). Of these, GS yields the largest effect on prostate cancer specific mortality. It was previously determined that those with cores with a mix of higher and lower GS at biopsy (which was termed a "ComboGS") had decreased risk for prostate cancer specific mortality after either surgical or radiation treatment. We validate the effect of ComboGS in an independent cohort of patients with prostate cancer treated with definitive dose-escalated radiation therapy (DE-RT) at 2 institutions. **METHODS AND MATERIALS:** DE-RT was administered to 2539 men, of which 687 men had a ComboGS. To further ascertain the ComboGS effect we employed the modified Cancer of the Prostate Risk Assessment (mCAPRA) score. Rates of biochemical event-free survival and distant metastasis-free survival were compared across CAPRA scores, with and without modification, and the prognostic value of the CAPRA scores was compared using Harrel's concordance index. **RESULTS:** On univariate analysis in Gleason 7 to 10 patients the presence of ComboGS improved 10-year biochemical event-free survival from 76.6% to 82.4% (hazard ratio [HR], 0.75; confidence interval [CI], 0.59-0.96; P = .021), 10-year distant metastasis-free survival from 89.3% to 93.2% (HR, 0.57; CI, 0.39-0.85; P = .005), 10-year prostate cancer specific survival from 93.9% to 97.4% (HR, 0.39; CI, 0.21-0.7; P = .001), and 10-year overall survival from 65.7% to 75.6% (HR, 0.69; CI, 0.57-0.83; P < .001). Multivariable analysis also supported that ComboGS is protective for biochemical failure (HR, 0.64; CI, 0.50-0.83; P < .001), distant metastasis (HR, 0.42; CI, 0.28-0.63; P < .001), death from prostate cancer (HR, 0.32; CI, 0.17-0.58; P < .001), and overall mortality (HR, 0.65; CI, 0.54-0.79; P < .001). Additionally, adjusting the mCAPRA score for ComboGS decreased the risk of biochemical failure by nearly 30% (HR, 0.70; 95% CI, 0.55-0.88; P = .003) and by 50% (HR, 0.54; 95% CI, 0.37-0.80; P = .002) for distant metastasis. **CONCLUSIONS:** ComboGS is a useful and readily available independent prognostic factor for all clinical endpoints evaluated. Moreover, the ComboGS can be used in conjunction with the extensively validated CAPRA scoring to better risk stratify patients being treated with definitive DE-RT for GS 7 to 10 disease.

Radiation Oncology

Ryu S, Deshmukh S, Timmerman RD, **Movsas B**, Gerszten P, Yin FF, Dicker A, Abraham CD, Zhong J, Shiao SL, Tuli R, Desai A, Mell LK, Iyengar P, Hitchcock YJ, Allen AM, Burton S, Brown D, Sharp HJ, Dunlap NE, Siddiqui MS, Chen TH, Pugh SL, and Kachnic LA. Stereotactic Radiosurgery vs Conventional Radiotherapy for Localized Vertebral Metastases of the Spine: Phase 3 Results of NRG Oncology/RTOG 0631 Randomized Clinical Trial. *JAMA Oncol* 2023; Epub ahead of print. PMID: 37079324. [Request Article](#)

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Washington University School of Medicine, Saint Louis, Missouri.

Emory University Hospital, Atlanta, Georgia.

Cedars-Sinai Medical Center, Los Angeles, California.

University of South Florida, Tampa.

Summa Akron City Hospital/Cooper Cancer Center, Akron, Ohio.

University of California San Diego Moores Cancer Center, La Jolla.

Huntsman Cancer Institute/University of Utah, Salt Lake City.

Rabin Medical Center, Tikvah, Illinois.

Wake Forest University Health Sciences, Winston Salem, North Carolina.

Levine Cancer Institute, Charlotte, North Carolina.

The James Graham Brown Cancer Center at University of Louisville, Louisville, Kentucky.

Capital Health Medical Center, Pennington, New Jersey.

Columbia University Irving Medical Center, New York, New York.

IMPORTANCE: Spine metastasis can be treated with high-dose radiation therapy with advanced delivery technology for long-term tumor and pain control. **OBJECTIVE:** To assess whether patient-reported pain relief was improved with stereotactic radiosurgery (SRS) as compared with conventional external beam radiotherapy (cEBRT) for patients with 1 to 3 sites of vertebral metastases. **DESIGN, SETTING, AND PARTICIPANTS:** In this randomized clinical trial, patients with 1 to 3 vertebral metastases were randomized 2:1 to the SRS or cEBRT groups. This NRG 0631 phase 3 study was performed as multi-institutional enrollment within NRG Oncology. Eligibility criteria included the following: (1) solitary vertebral metastasis, (2) 2 contiguous vertebral levels involved, or (3) maximum of 3 separate sites. Each site may involve up to 2 contiguous vertebral bodies. A total of 353 patients enrolled in the trial, and 339 patients were analyzed. This analysis includes data extracted on March 9, 2020. **INTERVENTIONS:** Patients randomized to the SRS group were treated with a single dose of 16 or 18 Gy (to convert to rad, multiply by 100) given to the involved vertebral level(s) only, not including any additional spine levels. Patients assigned to cEBRT were treated with 8 Gy given to the involved vertebra plus 1 additional vertebra above and below. **MAIN OUTCOMES AND MEASURES:** The primary end point was patient-reported pain response defined as at least a 3-point improvement on the Numerical Rating Pain Scale (NRPS) without worsening in pain at the secondary site(s) or the use of pain medication. Secondary end points included treatment-related toxic effects, quality of life, and long-term effects on vertebral bone and spinal cord. **RESULTS:** A total of 339 patients (mean [SD] age of SRS group vs cEBRT group, respectively, 61.9 [13.1] years vs 63.7 [11.9] years; 114 [54.5%] male in SRS group vs 70 [53.8%] male in cEBRT group) were analyzed. The baseline mean (SD) pain score at the index vertebra was 6.06 (2.61) in the SRS group and 5.88 (2.41) in the cEBRT group. The primary end point of pain response at 3 months favored cEBRT (41.3% for SRS vs 60.5% for cEBRT; difference, -19 percentage points; 95% CI, -32.9 to -5.5; 1-sided P = .99; 2-sided P = .01). Zubrod score (a measure of performance status ranging from 0 to 4, with 0 being fully functional and asymptomatic, and 4 being bedridden) was the significant factor influencing pain response. There were no differences in the proportion of acute or late adverse effects. Vertebral compression fracture at 24 months was 19.5% with SRS and 21.6% with cEBRT (P = .59). There were no spinal cord complications reported at 24 months. **CONCLUSIONS AND RELEVANCE:** In this randomized clinical trial, superiority of SRS for the primary end point of patient-reported pain response at 3 months was not found, and there were no spinal cord complications at 2 years after SRS. This finding may inform further investigation of using spine radiosurgery in the setting of oligometastases, where durability of cancer control is essential. **TRIAL REGISTRATION:** ClinicalTrials.gov Identifier: NCT00922974.

Radiation Oncology

Thoidingjam S, Sriramulu S, Freytag S, Brown SL, Kim JH, Chetty IJ, Siddiqui F, Movsas B, and Nyati S. Oncolytic virus-based suicide gene therapy for cancer treatment: a perspective of the clinical trials conducted at Henry Ford Health. *Transl Med Commun* 2023; 8(1):11. PMID: 37065938. [Full Text](#)

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Gene therapy manipulates or modifies a gene that provides a new cellular function to treat or correct a pathological condition, such as cancer. The approach of using gene manipulation to modify patient's cells to improve cancer therapy and potentially find a cure is gaining popularity. Currently, there are 12 gene therapy products approved by US-FDA, EMA and CFDA for cancer management, these include Rixin-G, Gencicine, Oncorine, Provange among other. The Radiation Biology Research group at Henry Ford Health has been actively developing gene therapy approaches for improving clinical outcome in cancer patients. The team was the first to test a replication-competent oncolytic virus armed with a therapeutic gene in humans, to combine this approach with radiation in humans, and to image replication-competent adenoviral gene expression/activity in humans. The adenoviral gene therapy products developed at Henry Ford Health have been evaluated in more than 6 preclinical studies and evaluated in 9 investigator initiated clinical trials treating more than 100 patients. Two phase I clinical trials are currently following patients long term and a phase I trial for recurrent glioma was initiated in November 2022. This systematic

review provides an overview of gene therapy approaches and products employed for treating cancer patients including the products developed at Henry Ford Health.

Radiation Oncology

Wang P, Gilbert M, Lim HW, McHargue C, Friedman BJ, Veenstra JJ, and Siddiqui F. Single-fraction Radiation Therapy for Localized Cutaneous T-cell Lymphoma. *Pract Radiat Oncol* 2023; Epub ahead of print. PMID: 37040819. [Full Text](#)

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BACKGROUND: Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL). Single-fraction radiation therapy has been used as a skin-targeted therapy to treat localized CTCL lesions. **OBJECTIVE:** To investigate the treatment outcomes associated with single-fraction radiation therapy for CTCL. **METHODS:** We retrospectively studied the outcomes among patients with CTCL treated with single fraction radiation therapy at our institution between October 2013 and August 2022. Clinical response including complete response (CR), partial response (PR) or no response (NR) and re-treatment response were evaluated. **RESULTS:** A total of 242 lesions from 46 patients were analyzed, for an average of 5.3 lesions treated per patient. The majority of lesions presented with a plaque morphology (n = 145, 60.0%). All lesions were treated to a dose of 8 Gy in 1 fraction. Median follow-up was 24.6 months (range, 1-88 months). Of the 242 lesions, 36 (14.8%) had an initial PR or NR; all were re-treated with the same regimen to the same site at a median interval of 8 weeks. 50% of re-treated lesions (n = 18) went on to have a CR. Thus, the overall CR rate for CTCL lesions was 92.6%. No recurrences were noted in the treated areas after achieving CR. **CONCLUSION:** Single-fraction radiation therapy to a dose of 8 Gy in 1 fraction to localized areas provided a high rate of complete and durable responses in the affected sites.

Research Administration

Huber B, Pellumbi N, Davoodi-Bojd E, and Soltanian-Zadeh H. Inter- and intra-operator variations in manual segmentation of hippocampus from MRI. *Inform Med Unlocked* 2023; 39. PMID: Not assigned. [Full Text](#)

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Purpose: We evaluate inter- and intra-operator variations in manual segmentation of hippocampus and present their potential sources. Hippocampal atrophy is common in mesial temporal lobe epilepsy (mTLE). Effective diagnosis and treatment of mTLE depends on accurate and efficient segmentation of hippocampus from magnetic resonance imaging (MRI) data. Manual segmentation by expert radiologists remains the gold standard, although automated segmentation methods exist. **Methods:** Hippocampus was segmented in MRI of 118 unilateral mTLE patients and 25 non-epileptic subjects (65 males, 78 females; mean age 39 years) by three operators (M1, M2, M3) manually and by three software tools (FreeSurfer, LocalInfo, ABSS) automatically. Segmentation results were evaluated using 7 volume-, voxel-, and distance-based performance measures. Inter-operator variation was evaluated by comparing the segmentation results of the three operators. Intra-operator variation was evaluated by comparing manual and automatic segmentation results. Segmentation results were used to lateralize epileptogenicity in mTLE patients. **Results:** Ranking of performance measures differed when using M3 segmentations as ground truth rather than M1 or M2 segmentations. The standard deviation tended to be higher when using M3 as ground truth and M1 or M2 as test segmentation. Variation in performance measures and increased standard deviation when using M3 as ground truth are indicative of inter-operator variability. Standard deviations were larger when using M2 segmentations as ground truth and automated

segmentations as test segmentation, rather than M1 or M3. Large standard deviations between M2 segmentations and automated segmentations are indicative of intra-operator variation. Among automated segmentation methods, ABSS produced segmentations most similar to manual segmentations, but FreeSurfer and LocalInfo lateralized epileptogenicity more accurately. Conclusions: Part of inter-operator variation might be due to temporal separation of M3 segmentations from M1 and M2 segmentations (M3 performed segmentations a few years before operators M1 and M2). Inter-operator variation will likely reduce if all operators segment within the same time frame, reducing discrepancies in training of operators. Intra-operator variation can likely be mitigated with additional oversight by a neuroradiologist. Inter- and intra-operator variability may generate inconsistencies in outcomes. Future automated segmentation techniques may integrate neural-network-based (ABSS) and atlas-based (FreeSurfer and LocalInfo) segmentation techniques for optimal performance.

Research Administration

Verhaegen F, Butterworth KT, Chalmers AJ, Coppes RP, de Ruyscher D, Dobiasch S, Fenwick JD, Granton PV, Heijmans SHJ, Hill MA, Koumenis C, Lauber K, Marples B, Parodi K, Persoon L, Staut N, Subiel A, Vaes RDW, van Hoof S, Verginadis IL, Wilkens JJ, Williams KJ, **Wilson GD**, and Dubois LJ. Roadmap for precision preclinical x-ray radiation studies. *Phys Med Biol* 2023; 68(6). PMID: 36584393.

[Full Text](#)

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This Roadmap paper covers the field of precision preclinical x-ray radiation studies in animal models. It is mostly focused on models for cancer and normal tissue response to radiation, but also discusses other

disease models. The recent technological evolution in imaging, irradiation, dosimetry and monitoring that have empowered these kinds of studies is discussed, and many developments in the near future are outlined. Finally, clinical translation and reverse translation are discussed.

Rheumatology

Obeidat L, Albusoul L, Maki M, Ibrahim H, and Parikh S. Infliximab-Induced Lupus in a Patient With Psoriatic Arthritis Who Presented With Cardiac Tamponade: A Case Report. *Cureus* 2023; 15(3):e36424. PMID: 37090269. [Full Text](#)

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Psoriatic arthritis (PsA) is a chronic, immune-mediated inflammatory condition, and the proinflammatory cytokine tumor necrosis factor- α (TNF- α) plays a major pathogenic role in the development and progression of PsA. Anti-TNF- α therapies, such as the monoclonal antibody infliximab, are used to treat patients whose PsA has not responded favorably to conventional anti-rheumatic drugs. However, exposure to anti-TNF- α therapeutics can lead to drug-induced lupus erythematosus (DILE), which may rarely be accompanied by cardiac manifestations. Here, we describe a rare case of drug-induced lupus erythematosus secondary to infliximab therapy for PsA and psoriasis in a patient who presented with life-threatening acute pericarditis and cardiac tamponade. Newly developed skin rashes, newly elevated autoimmune indicators, and punch biopsy results indicating subacute cutaneous lupus collectively supported a DILE diagnosis within the context of infliximab use. Pericardiocentesis, colchicine, and corticosteroids alleviated symptoms, and infliximab was replaced with alternate therapy. This case highlights the importance of early recognition of the possible serious and uncommon adverse reactions from infliximab therapy. Prompt initiation of appropriate treatment and discontinuation of the offending agent are critical in cases of drug-induced lupus erythematosus, particularly when rare cardiac complications occur.

Rheumatology

Robinson C, Ramanan S, Singh H, Minhas JS, and Zebda H. A Case of T-Cell Large Granulocyte Lymphocytic Leukemia in Rheumatoid Arthritis. *Cureus* 2023; 15(3):e36266. PMID: 37065388. [Full Text](#)

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T-cell large granulocyte lymphocytic (TLGL) leukemia is a lymphoproliferative disorder involving clonal expansion of cytotoxic T-cells and subsequent cytopenia, most notably neutropenia, as well as splenomegaly. TLGL leukemia is commonly associated with autoimmune disorders, most commonly rheumatoid arthritis (RA). We present a case of a 54-year-old female with a past medical history of seropositive RA who was lost to follow-up and thus was not on any active treatment for RA for several years. She returned to the clinic with worsening joint pain, swelling, and stiffness involving multiple joints. Screen laboratory work revealed an absolute neutrophil count (ANC) of 0.19 K/uL, indicating severe neutropenia. This finding prompted further workup, for which our patient was ultimately diagnosed with TLGL leukemia. Proper treatment and control of inflammation in RA are important not only to preserve joint function and vitality but also to prevent rare sequela of untreated autoimmune disorders, as was the case in our patient.

Sleep Medicine

Reffi AN, Kalmbach DA, Cheng P, and Drake CL. The sleep response to stress: how sleep reactivity can help us prevent insomnia and promote resilience to trauma. *J Sleep Res* 2023; e13892. Epub ahead of print. PMID: 37020247. [Full Text](#)

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Sleep reactivity is a predisposition to sleep disturbance during environmental perturbations, pharmacological challenges, or stressful life events. Consequently, individuals with highly reactive sleep systems are prone to insomnia disorder after a stressor, engendering risk of psychopathology and potentially impeding recovery from traumatic stress. Thus, there is tremendous value in ameliorating sleep reactivity to foster a sleep system that is robust to stress exposure, ultimately preventing insomnia and its downstream consequences. We reviewed prospective evidence for sleep reactivity as a predisposition to insomnia since our last review on the topic in 2017. We also reviewed studies investigating pre-trauma sleep reactivity as a predictor of adverse post-traumatic sequelae, and clinical trials that reported the effect of behavioural treatments for insomnia on mitigating sleep reactivity. Most studies measured sleep reactivity via self-report using the Ford Insomnia Response to Stress Test (FIRST), demonstrating high scores on this scale reliably indicate a sleep system with a lower capacity to tolerate stress. Nascent evidence suggests elevated sleep reactivity prior to trauma increases the risk of negative posttraumatic outcomes, namely acute stress disorder, depression, and post-traumatic stress disorder. Lastly, sleep reactivity appears most responsive to behavioural insomnia interventions when delivered early during the acute phase of insomnia. Overall, the literature strongly supports sleep reactivity as a premorbid vulnerability to incident acute insomnia disorder when faced with an array of biopsychosocial stressors. The FIRST identifies individuals at risk of insomnia a priori, thereby guiding early interventions toward this vulnerable population to prevent insomnia and promote resilience to adversity.

Sleep Medicine

Uygur OF, Ahmed O, Bahar A, Hursitoglu O, Aydın EF, Chung S, Ozcan H, and **Drake CL**. Adaptation and Validation of the Turkish Version of the Ford Insomnia Response to Stress Test in University Students. *Nat Sci Sleep* 2023; 15:139-149. PMID: 37008595. [Full Text](#)

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OBJECTIVE: We adapted the Ford Insomnia Response to Stress Test to Turkish (FIRST-T) and validated it. **METHODS:** We randomly divided 774 Turkish university students into two equal groups for exploratory (EFA) and confirmatory factor analysis (CFA). McDonald's omega and Cronbach's alpha values were utilized for reliability analyses. Item response theory (IRT) approach also used for psychometric properties on the full sample. For discriminant validity, study sample were classified into high and low sleep reactivity groups, and their sociodemographic and sleep data were compared. **RESULTS:** EFA results suggested a one-factor structure of the FIRST-T, which was confirmed by CFA results. The FIRST-T had solid internal reliability. Item analysis results showed that all the items could distinguish between low and high scorers. This scale showed the same construct (clinical insomnia vs good sleepers) across the sexes in multi-group CFA and differential item functioning results. In the high FIRST-T score group, sleep quality, severity of insomnia, and anxiety scores were higher. In this group, more participants had clinical insomnia according to the Insomnia Severity Index (ISI) and were poor sleepers according to the Pittsburg Sleep Quality Index (PSQI) ($p < 0.01$). **CONCLUSION:** The FIRST-T has robust psychometric properties that assesses sleep reactivity among university students.

Sleep Medicine

Uygur OF, Ahmed O, Uygur H, Bahar A, Hursitoglu O, Chung S, and **Drake CL**. Type D personality to insomnia: Sleep reactivity, sleep effort, and sleep hygiene as mediators. *Front Psychiatry* 2023; 14:1160772. PMID: 37113537. [Full Text](#)

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BACKGROUND: Insomniacs are heterogeneous group with very diverse personalities. We aimed to investigate the mediating role of sleep reactivity (SR), sleep hygiene (SH), and sleep effort (SE) in the relationship between Type D personality and insomnia. **MATERIALS AND METHODS:** We conducted a cross-sectional survey among 474 participants. The survey comprised the sociodemographic data form, Insomnia Severity Index (ISI), D Type Personality Scale (DS-14), Ford Insomnia Response to Stress Test (FIRST), Glasgow Sleep Effort Scale (GSES), and Sleep Hygiene Index (SHI). We conducted hierarchical multiple regression analysis to identify the associations between age, sex, SR, Type D personality traits, SE, SH, and insomnia severity. We subsequently conducted mediation analyses to examine whether SR, SH, and SE mediated the relationship between Type D personality and insomnia. **RESULTS:** ISI, DS-14, FIRST, SHI, and GSES scores were significantly higher in individuals with Type D personality. Female sex, SR, Type D personality traits, SE, and SH explained 45% of the variance in insomnia severity. When age, sex, insomnia response to stress, and Type D personality traits were controlled, SE and SH significantly explained 25% of the variance in insomnia severity ($R(2) = 0.45$, $R(2) \text{ change} = 0.25$, $F(6.474) = 65.58$, $p < 0.001$). SR, SE, and SH each played a partial mediating role between Type D personality and insomnia. **CONCLUSION:** The findings showed that individuals with Type D personality had high SR and that individuals with a higher number of these personality traits exhibited more severe insomnia symptoms through high SR, greater SE, and worse SH.

Sleep Medicine

Yang R, Takarae Y, Adney H, Swineford C, Walker JC, **Cheng P**, Negash S, and Wiggins JL. Neural correlates of irritability symptom relief in adolescents pre- and post-trauma-focused cognitive behavioral therapy: A pilot study on reward processing. *Psychiatry Res Neuroimaging* 2023; 332:111645. PMID: 37087811. [Full Text](#)

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Despite that Trauma-Focused Cognitive Behavioral Therapy (TF-CBT) is a first-line, evidence-based treatment for youths experiencing trauma-related symptoms, treatment responses vary and it remains unclear for whom and how this treatment works. In this context, we examined pre-treatment neural reward processing and pre- vs. post-treatment changes in neural reward processing, in relation to irritability - a transdiagnostic and dimensional feature present in multiple trauma-related syndromes, following TF-CBT. Adolescents ($N = 22$) with childhood trauma history completed a child-friendly monetary incentive delay task during fMRI acquisition, prior to and after the treatment, and irritability symptoms were assessed at five time points over the course of the treatment. Individual irritability slopes (i.e., irritability change rate) and intercepts (i.e., initial irritability level), generated by linear growth curve modeling, were integrated with fMRI data. Repeated ANCOVAs demonstrated that both pre-treatment neural response to reward and pre- vs. post-treatment changes in neural reward processing correlated with irritability symptom relief, such that opposite baseline neural reward processing profiles and differential changing patterns were observed in individuals showing irritability symptom relief vs. not. Together, our findings provide proof of

concept that integrating brain information with clinical information has the potential to identify predictors and mechanisms of symptom relief.

Surgery

Adeyemo A, Montgomery S, Chancey RJ, Annambhotla P, Barba L, Clarke T, **Williams J, Malilay A**, and Coyle J. Investigation of donor-derived *Strongyloides stercoralis* infection in multiple solid organ transplant recipients-California, Michigan, Ohio, 2022. *Transpl Infect Dis* 2023; e14059. Epub ahead of print. PMID: 37005911. [Full Text](#)

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BACKGROUND: The Centers for Disease Control and Prevention led an investigation to determine if *Strongyloides* infection in a right kidney recipient was an existing chronic infection, or if the infection was transmitted from an infected organ donor. **METHODS:** Evidence regarding the organ donor and organ recipients *Strongyloides* testing, treatment, and risk factors were gathered and evaluated. The case classification algorithm created by the Disease Transmission Advisory Committee was utilized.

RESULTS: The organ donor had risk factors for *Strongyloides* infection; the banked donor specimen, submitted for serology testing 112 days post-donor death, was positive. The right kidney recipient was negative for *Strongyloides* infection pretransplant. *Strongyloides* infection was diagnosed via small bowel and stomach biopsies. The left kidney recipient had risk factors for *Strongyloides* infection. Two posttransplant *Strongyloides* antibody tests were negative at 59 and 116 days posttransplant; repeat antibody tests returned positive at 158 and 190 days posttransplant. Examination of bronchial alveolar lavage fluid collected 110 days posttransplant from the heart recipient showed a parasite morphologically consistent with *Strongyloides* species. She subsequently developed complications from *Strongyloides* infection, including hyperinfection syndrome and disseminated strongyloidiasis. Based on the evidence from our investigation, donor-derived strongyloidiasis was suspected in one recipient and proven in two recipients. **CONCLUSION:** The results of this investigation support the importance of preventing donor-derived *Strongyloides* infections by laboratory-based serology testing of solid organ donors. Donor positive testing results would direct the monitoring and treatment of recipients to avoid severe complications.

Surgery

Dennis A, Deng C, Yang P, Bonham AJ, **Carlin AM**, and **Varban OA**. Evaluating the impact of metabolic surgery on patients with prior opioid use. *Surg Obes Relat Dis* 2023; Epub ahead of print. PMID: 36872158. [Full Text](#)

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BACKGROUND: Metabolic surgery is the most effective treatment for obesity and may improve obesity-related pain syndromes. However, the effect of surgery on the persistent use of opioids in patients with a history of prior opioid use remains unclear. **OBJECTIVE:** To determine the effect of metabolic surgery on opioid use behaviors in patients with prior opioid use. **SETTING:** A consortium of public and private hospitals in Michigan. **METHODS:** Using a statewide metabolic-specific data registry, we identified 16,820 patients who self-reported opioid use before undergoing metabolic surgery between 2006 and 2020 and analyzed the 8506 (50.6%) patients who responded to 1-year follow-up. We compared patient characteristics, risk-adjusted 30-day postoperative outcomes, and weight loss between patients who self-reported discontinuing opioid use 1 year after surgery and those who did not. **RESULTS:** Among patients who self-reported using opioids before metabolic surgery, 3864 (45.4%) discontinued use 1 year after

surgery. Predictors of persistent opioid use included an annual income of <\$10,000 (odds ratio [OR] = 1.24; 95% confidence interval [CI], 1.06-1.44; P = .006), Medicare insurance (OR = 1.48; 95% CI, 1.32-1.66; P < .0001), and preoperative tobacco use (OR = 1.36; 95% CI, 1.16-1.59; P = .0001). Patients with persistent use were more likely to have a surgical complication (9.6% versus 7.5%, P = .0328) and less percent excess weight loss (61.6% versus 64.4%, P < .0001) than patients who discontinued opioids after surgery. There were no differences in the morphine milligram equivalents prescribed within the first 30 days following surgery between groups (122.3 versus 126.5, P = .3181). CONCLUSIONS: Nearly half of patients who reported taking opioids before metabolic surgery discontinued use at 1 year. Targeted interventions aimed at high-risk patients may increase the number of patients who discontinue opioid use after metabolic surgery.

Surgery

Ichkhanian Y, Al-Haddad MA, Jacobs CC, Schlachterman A, Yang J, Canakis A, Kim R, Guerson-Gil A, D'Souza LS, **Alsheik E**, **Ginnebaugh BD**, Khashab MA, **Zuchelli T**, **Kellie M**, and **Piraka C**. Gastric Peroral Endoscopic Myotomy for Management of Refractory Gastroparesis in Patients with Gastric Neurostimulator Devices: A Multicenter Retrospective Case Control Study. *Gastrointest Endosc* 2023; Epub ahead of print. PMID: 37121364. [Full Text](#)

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BACKGROUND AND AIMS: Gastric neurostimulation (GNS) and gastric peroral myotomy (G-POEM), therapies for refractory gastroparesis, are associated with suboptimal outcomes. We studied the role of G-POEM as a salvage therapy in patients with refractory symptoms after GNS implantation. **METHODS:** This was a multicenter, retrospective, matched-case control study. Consecutive patients with GNS device and underwent G-POEM as a salvage therapy for clinical failure (cases) and patients without GNS implantation and underwent G-POEM for refractory gastroparesis (control) between 10-2018 and 08-2021 were included. The primary outcome was clinical success after G-POEM. **RESULTS:** A total of 123 patients (mean age 45.7 ± 14.7 years; 88 females [72%]) underwent G-POEM therapy during the duration of the study: 41 cases and 82 controls. Clinical success was achieved in 66% in the case group and 65% in the control, (P=0.311), during a median total clinical follow-up time of 11.8 (IQR: 2.4-6.3) months. In the case group, the mean Gastroparesis Cardinal Symptom Index (GCSI) decreased from 2.8 ± 1.8 to 1.5 ± 1.9 , (P=0.024), and gastric retention at 4 hours improved from $45\% \pm 25.8$ to $16.6\% \pm 13.1$, (P=0.06). The mean delta improvement in the subscales of nausea/vomiting (1.3 ± 0.6 vs. 0.9 ± 1.1 ; P=0.044) and bloating (1.6 ± 1.3 vs. 1.2 ± 1.4 ; P=0.041) were significantly higher in cases than in controls. **CONCLUSIONS:** Among patients with refractory symptoms after GNS, G-POEM can be a reasonable salvage therapy to provide further symptomatic relief with evidence of a potential additive effect of both G-POEM and GNS.

Surgery

Leonard-Murali S, **Nathanson SD**, **Springer K**, **Baker P**, and **Susick L**. Early breast cancer survival of black and white American women with equal diagnostic and therapeutic management. *Eur J Surg Oncol* 2023; 49(3):583-588. PMID: 36464602. [Full Text](#)

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PURPOSE: Breast cancer (BC) survival favors White versus Black Americans despite advances in screening and treatment. We hypothesized that these differences were dependent upon quality of care by analyzing long-term outcomes of 3139 early BC patients at our quaternary care center where uniform access and management of BC is provided to women irrespective of race. **METHODS:** Prospectively collected data for clinical stage I-II BC patients from our quaternary care cancer center were analyzed, focusing on disease-specific survival (DSS). Subgroup analyses included the overall cohort, triple-negative BC (TNBC), non-TNBC and HER2/neu positive patients. Multivariable analyses to evaluate associations of variables with DSS were performed for each subgroup. **RESULTS:** The overall cohort consisted of 3139 BC patients (1159 Black, 1980 White). Black and White patients did not differ by most baseline variables. Black patients had higher rates of TNBC (18% versus 10%, $p < 0.0001$). Kaplan-Meier analysis of all subgroups (overall, TNBC, non-TNBC, HER2/neu positive) did not reveal DSS differences between Black and White patients. Multivariable analysis of subgroups also did not find race to be associated with DSS. **CONCLUSION:** In this large, carefully controlled, long term, single-institution prospective cohort study DSS in Black and White early BC patients with equal access to high quality care, did not differ. While BC patients with adverse molecular markers did slightly worse than those with more favorable markers, there is no observable difference between Black and White women with the same markers. These observations support the conclusion that equal access to, and quality, of BC care abolishes racial disparities in DSS.

Surgery

Nagai S. Transplant oncology: multivisceral transplantation for neuroendocrine tumor and liver metastasis. *Curr Opin Organ Transplant* 2023; Epub ahead of print. PMID: 37040627. [Full Text](#)

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PURPOSE OF REVIEW: Neuroendocrine tumor (NET) liver metastatic lesions are often multiple and found to be unresectable. Rationale of multivisceral transplantation (MVT: liver-pancreas-intestine transplantation) include radical and complete resection of primary, visible and invisible metastatic tumors by removing all abdominal organs and the lymphatic system. This review aims to describe the concept of MVT for NET and neuroendocrine liver metastasis (NELM), patient selection, timing of MVT, and posttransplant outcomes and management. **RECENT FINDINGS:** Although indication criteria of MVT for NET vary between transplant centers, the Milan-NET criteria for liver transplant are often applied to MVT candidates. Extra-abdominal tumors such as lung and/or bone lesions should be ruled out prior to MVT. Histology should be confirmed as low-grade (G1/G2). Ki-67 should be also checked to confirm biologic features. Timing of MVT remains controversial, whereas many experts recommend 6 months of disease stability prior to MVT. **SUMMARY:** Although MVT would not be a standard therapy because of limited access to MVT centers, benefit of MVT should be recognized, which includes its potential ability to better achieve curative resection of disseminated tumors in the abdominal cavity. Early referral of difficult cases to MVT centers should be considered before palliative best supportive cares.

Surgery

Peshel EC, Blaisdell RB, **Lehrberg AV**, and Kiran S. Lessons learned in severe axillary gestational gigantomastia. *Int J Gynaecol Obstet* 2023; Epub ahead of print. PMID: 37002929. [Full Text](#)

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Surgery

Schwarze E, Chang DD, Cleary CJ, and Rakitin I. Spontaneous resolution of traumatic bronchial tear after thoracic crush injury. *J Surg Case Rep* 2023; 2023(3):rjac627. PMID: 37016700. [Full Text](#)

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Traumatic bronchial tears are rare life-threatening injuries. Here, we report a 28-year old male who presented after sustaining a crush injury to his thoracic cavity, resulting in a spiral left mainstem bronchial tear secondary to high intraluminal pressure. While preparing for surgery, a preoperative bronchoscopy found that the bronchial tear had re-approximated and effectively sealed the laceration. No operative intervention was performed and the patient subsequently underwent a full recovery. While most bronchial tears undergo surgical intervention, our report describes the successful management of a bronchial tear injury with a non-operative approach and supportive care.

Surgery

Shamaa TM, Kitajima T, Ivanics T, Shimada S, Mohamed A, Yeddula S, Rizzari M, Collins K, Yoshida A, Abouljoud M, and Nagai S. Variation of Liver Transplant Practice and Outcomes During Public Holidays in the United States: Analysis of United Network for Organ Sharing Registry. *Transplant Direct* 2023; 9(4):e1463. PMID: 37009167. [Full Text](#)

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It has been reported that patients hospitalized outside regular working hours have worse outcomes. This study aims to compare outcomes following liver transplantation (LT) performed during public holidays and nonholidays. METHODS: We analyzed the United Network for Organ Sharing registry data for 55 200 adult patients who underwent an LT between 2010 and 2019. Patients were grouped according to LT receipt during public holidays ± 3 d (n = 7350) and nonholiday periods (n = 47 850). The overall post-LT mortality hazard was analyzed using multivariable Cox regression models. RESULTS: LT recipient characteristics were similar between public holidays and nonholidays. Compared with nonholidays, deceased donors during public holidays had a lower donor risk index (median [interquartile range]: holidays 1.52 [1.29-1.83] versus nonholidays 1.54 [1.31-1.85]; P = 0.001) and shorter cold ischemia time (median [interquartile range]: holidays 5.82 h [4.52-7.22] versus nonholidays 5.91 h [4.62-7.38]; P < 0.001). Propensity score matching 4-to-1 was done to adjust for donor and recipient confounders (n = 33 505); LT receipt during public holidays (n = 6701) was associated with a lower risk of overall mortality (hazard ratio 0.94 [95% confidence interval, 0.86-0.99]; P = 0.046). The number of livers that were not recovered for transplant was higher during public holidays compared with nonholidays (15.4% versus 14.5%, respectively; P = 0.03). CONCLUSIONS: Although LT performed during public holidays was associated with improved overall patient survival, liver discard rates were higher during public holidays compared with nonholidays.

Surgery

Sturdevant M, Ganesh S, Samstein B, Verna EC, Rodriguez-Davalos M, Kumar V, **Abouljoud M**, Andacoglu O, Askar M, Broering D, Emamaullee J, Emond JC, Haugen CE, **Jesse MT**, Kasahara M, Liapakis A, Mandelbrot D, Pillai A, Roll GR, Selzner N, and Emre S. Advances and innovations in living donor liver transplant techniques, matching and surgical training: Meeting report from the living donor liver transplant consensus conference. *Clin Transplant* 2023; e14968. Epub ahead of print. PMID: 37039541. [Full Text](#)

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The practice of LDLT currently delivers limited impact in western transplant centers. The American Society of Transplantation organized a virtual consensus conference in October 2021 to identify barriers and gaps to LDLT growth, and to provide evidence-based recommendations to foster safe expansion of LDLT in the United States. This article reports the findings and recommendations regarding innovations and advances in approaches to donor-recipient matching challenges, the technical aspects of the donor and recipient operations, and surgical training. Among these themes, the barriers deemed most influential/detrimental to LDLT expansion in the United States included: (1) prohibitive issues related to donor age, graft size, insufficient donor remnant, and ABO incompatibility; (2) lack of acknowledgment and awareness of the excellent outcomes and benefits of LDLT; (3) ambiguous messaging regarding LDLT to patients and hospital leadership; and (4) a limited number of proficient LDLT surgeons across the United States. Donor-recipient mismatching may be circumvented by way of liver paired exchange. The creation of a national registry to generate granular data on donor-recipient matching will guide the practice of liver paired exchange. The surgical challenges to LDLT are addressed herein and focuses on the development of robust training pathways resulting in proficiency in donor and recipient surgery. Utilizing strong mentorship/collaboration programs with novel training practices under the auspices of established training and certification bodies will add to the breadth and depth of training.

Urology

Abou Zeinab M, Ramos R, Ferguson EL, Okhawere KE, Iarajuli T, **Wilder S**, Calvo RS, Chavali JS, Saini I, De La Rosa RS, Nguyen J, Crivellaro S, **Rogers C**, Stifelman M, Ahmed M, Badani K, and Kaouk J. Single Port Versus Multiport Robot-assisted Simple Prostatectomy: A Multi-institutional Study From the Single-port Advanced Research Consortium (SPARC). *Urology* 2023; Epub ahead of print. PMID: 37001822. [Full Text](#)

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OBJECTIVE: To compare robot-assisted simple prostatectomy intraoperative and postoperative outcomes between single-port (SP) and multiport (MP) robotic systems in a multi-institutional setting. **METHODS:** We analyzed all-consecutive robot-assisted simple prostatectomy cases done in 5 centers from January 2017 to October 2022. Data were analyzed with descriptive statistics and compared with appropriate tests depending on the type of variable and distribution. Statistical significance was considered when $P < .05$. **RESULTS:** A total of 405 cases were analyzed: 249 and 156 were MP and SP, respectively. Operative times were similar between groups ($P = .62$). Estimated blood loss during surgery was significantly lower with the SP robot ($P < .001$). Postoperatively, the SP approach required a significantly shorter hospital stay, less use of opioids, and a shorter duration of Foley catheter ($P < .001$). There was no significant difference between the post-operative Clavien-Dindo ≥ 3 complication rate

($P = .30$). The 30-day readmission rate of MP (10.8%) was significantly higher than for SP (0%) ($P < .001$). De novo urge incontinence was more common in the MP group ($P = .02$). **CONCLUSION:** The SP robotic approach to simple prostatectomy is advantageous when it comes to postoperative comfort for patients. Specifically, it requires a shorter hospital stay, less use of opioids, and a shorter Foley catheter duration.

Urology

Abu Rous F, Li P, Carskadon S, Singh SR, Chacko R, Abushukair H, Gadgeel S, and Palanisamy N. Brief Report: Prognostic Relevance of 3q Amplification in Squamous Cell Carcinoma of the Lung. *JTO Clin Res Rep* 2023; 4(4):100486. PMID: 37025118. [Full Text](#)

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INTRODUCTION: Amplification of 3q is the most common genetic alteration identified in squamous cell carcinoma of the lung (LUSC), with the most frequent amplified region being 3q26 to 3q28. **METHODS:** In this analysis, we aim to describe the prognostic relevance of 3q amplification by focusing on a minimal common region (MCR) of amplification constituted of 25 genes. We analyzed 511 cases of LUSC from The Cancer Genome Atlas and included 476 in the final analysis. **RESULTS:** We identified a 25-gene MCR that was amplified in 221 (44.3%) cases and was associated with better disease-specific survival (not reported [NR] versus 9.25 y, 95% confidence interval [CI]: 5.24-NR, log-rank $p = 0.011$) and a progression-free interval of 8 years (95% CI: 5.1-NR) versus 4.9 years (95% CI: 3.5-NR, log-rank $p = 0.020$). Multivariable analysis revealed that MCR amplification was associated with improved disease-specific survival and progression-free interval. **CONCLUSIONS:** Amplification of the 25-gene MCR within 3q was present in 44% of this cohort, consisting mainly of Caucasian patients with early stage LUSC. This analysis strongly indicates the prognostic relevance of the 25-gene MCR within 3q. We are further evaluating its prognostic and predictive relevance in a racially diverse patient population with advanced LUSC.

Urology

Agarwal A, Cannarella R, **Rambhatla A**, et al. Impact of Varicocele Repair on Semen Parameters in Infertile Men: A Systematic Review and Meta-Analysis. *World J Mens Health* 2023; 41(2):289-310. PMID: 36326166. [Full Text](#)

PURPOSE: Despite the significant role of varicocele in the pathogenesis of male infertility, the impact of varicocele repair (VR) on conventional semen parameters remains controversial. Only a few systematic reviews and meta-analyses (SRMAs) have evaluated the impact of VR on sperm concentration, total motility, and progressive motility, mostly using a before-after analytic approach. No SRMA to date has evaluated the change in conventional semen parameters after VR compared to untreated controls. This study aimed to evaluate the effect of VR on conventional semen parameters in infertile patients with clinical varicocele compared to untreated controls. **MATERIALS AND METHODS:** A literature search was performed using Scopus, PubMed, Embase, and Cochrane databases following the Population Intervention Comparison Outcome (PICOS) model (Population: infertile patients with clinical varicocele; Intervention: VR [any technique]; Comparison: infertile patients with clinical varicocele that were untreated; Outcome: sperm concentration, sperm total count, progressive sperm motility, total sperm motility, sperm morphology, and semen volume; Study type: randomized controlled trials and observational studies). **RESULTS:** A total of 1,632 abstracts were initially assessed for eligibility. Sixteen studies were finally included with a total of 2,420 infertile men with clinical varicocele (1,424 patients treated with VR vs. 996 untreated controls). The analysis showed significantly improved post-operative semen parameters in patients compared to controls with regards to sperm concentration (standardized mean difference [SMD] 1.739; 95% CI 1.129 to 2.349; $p < 0.001$; $I^2 = 97.6\%$), total sperm count (SMD 1.894; 95% CI 0.566 to 3.222; $p < 0.05$; $I^2 = 97.8\%$), progressive sperm motility (SMD 3.301; 95% CI 2.164 to 4.437; $p < 0.01$; $I^2 = 98.5\%$), total sperm motility (SMD 0.887; 95% CI 0.036 to 1.738; $p = 0.04$; $I^2 = 97.3\%$) and

normal sperm morphology (SMD 1.673; 95% CI 0.876 to 2.470; $p < 0.05$; $I^2 = 98.5\%$). All the outcomes showed a high inter-study heterogeneity, but the sensitivity analysis showed that no study was sensitive enough to change these results. Publication bias was present only in the analysis of the sperm concentration and progressive motility. No significant difference was found for the semen volume (SMD 0.313; 95% CI -0.242 to 0.868; $I^2 = 89.7\%$). **CONCLUSIONS:** This study provides a high level of evidence in favor of a positive effect of VR to improve conventional semen parameters in infertile men with clinical varicocele. To the best of our knowledge, this is the first SRMA to compare changes in conventional semen parameters after VR with changes in parameters of a control group over the same period. This is in contrast to other SRMAs which have compared semen parameters before and after VR, without reference to a control group. Our findings strengthen the available evidence and have a potential to upgrade professional societies' practice recommendations favoring VR to improve conventional semen parameters in infertile men.

Urology

Agarwal A, Farkouh A, **Rambhatla A**, et al. Controversy and Consensus on Indications for Sperm DNA Fragmentation Testing in Male Infertility: A Global Survey, Current Guidelines, and Expert Recommendations. *World J Mens Health* 2023; Epub ahead of print. PMID: 37118960. [Full Text](#)

PURPOSE: Sperm DNA fragmentation (SDF) testing was recently added to the sixth edition of the World Health Organization laboratory manual for the examination and processing of human semen. Many conditions and risk factors have been associated with elevated SDF; therefore, it is important to identify the population of infertile men who might benefit from this test. The purpose of this study was to investigate global practices related to indications for SDF testing, compare the relevant professional society guideline recommendations, and provide expert recommendations. **MATERIALS AND METHODS:** Clinicians managing male infertility were invited to take part in a global online survey on SDF clinical practices. This was conducted following the CHERRIES checklist criteria. The responses were compared to professional society guideline recommendations related to SDF and the appropriate available evidence. Expert recommendations on indications for SDF testing were then formulated, and the Delphi method was used to reach consensus. **RESULTS:** The survey was completed by 436 experts from 55 countries. Almost 75% of respondents test for SDF in all or some men with unexplained or idiopathic infertility, 39% order it routinely in the work-up of recurrent pregnancy loss (RPL), and 62.2% investigate SDF in smokers. While 47% of reproductive urologists test SDF to support the decision for varicocele repair surgery when conventional semen parameters are normal, significantly fewer general urologists (23%; $p = 0.008$) do the same. Nearly 70% would assess SDF before assisted reproductive technologies (ART), either always or for certain conditions. Recurrent ART failure is a common indication for SDF testing. Very few society recommendations were found regarding SDF testing. **CONCLUSIONS:** This article presents the largest global survey on the indications for SDF testing in infertile men, and demonstrates diverse practices. Furthermore, it highlights the paucity of professional society guideline recommendations. Expert recommendations are proposed to help guide clinicians.

Urology

DiBianco JM, Daignault-Newton S, Dupati A, Hiller S, **Kachroo N**, Seifman B, Wenzler D, Daww CA, and Ghani KR. Stent Omission in Pre-stented Patients Undergoing Ureteroscopy Decreases Unplanned Health Care Utilization. *Urol Pract* 2023; 10(2):163-169. PMID: 37103404. [Full Text](#)

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INTRODUCTION: Despite AUA guidelines providing criteria for ureteral stent omission after ureteroscopy for nephrolithiasis, stenting rates in practice remain high. Because pre-stenting may be associated with improved patient outcomes, we assessed the impact of stent omission vs placement in pre-stented and non-pre-stented patients undergoing ureteroscopy on postoperative health care utilization in Michigan.

METHODS: Using the MUSIC (Michigan Urological Surgery Improvement Collaborative) registry (2016-2019), we identified pre-stented and non-pre-stented patients with low comorbidity undergoing single-stage ureteroscopy for ≤ 1.5 cm stones with no intraoperative complications. We assessed variation in stent omission for practices/urologists with ≥ 5 cases. Using multivariable logistic regression, we evaluated whether stent placement in pre-stented patients was associated with emergency department visits and hospitalizations within 30 days of ureteroscopy. **RESULTS:** We identified 6,266 ureteroscopies from 33 practices and 209 urologists, of which 2,244 (35.8%) were pre-stented. Pre-stented cases had higher rates of stent omission vs non-pre-stented cases (47.3% vs 26.3%). Among the 17 urology practices with ≥ 5 cases, stent omission rates in pre-stented patients varied widely (0%-77.8%). Among the 156 urologists with ≥ 5 cases, stent omission rates in pre-stented patients varied substantially (0%-100%); 34/152 (22.4%) never performed stent omission. Adjusting for risk factors, stent placement in pre-stented patients was associated with increased emergency department visits (OR 2.24, 95% CI:1.42-3.55) and hospitalizations (OR 2.19, 95% CI:1.12-4.26). **CONCLUSIONS:** Pre-stented patients undergoing stent omission after ureteroscopy have lower unplanned health care utilization. Stent omission is underutilized in these patients, making them an ideal group for quality improvement efforts to avoid routine stent placement after ureteroscopy.

Urology

Farkouh A, Agarwal A, **Rambhatla A**, et al. Controversy and Consensus on the Management of Elevated Sperm DNA Fragmentation in Male Infertility: A Global Survey, Current Guidelines, and Expert Recommendations. *World J Mens Health* 2023; Epub ahead of print. PMID: 37118965. [Full Text](#)

PURPOSE: Sperm DNA fragmentation (SDF) has been associated with male infertility and poor outcomes of assisted reproductive technology (ART). The purpose of this study was to investigate global practices related to the management of elevated SDF in infertile men, summarize the relevant professional society recommendations, and provide expert recommendations for managing this condition. **MATERIALS AND METHODS:** An online global survey on clinical practices related to SDF was disseminated to reproductive clinicians, according to the CHERRIES checklist criteria. Management protocols for various conditions associated with SDF were captured and compared to the relevant recommendations in professional society guidelines and the appropriate available evidence. Expert recommendations and consensus on the management of infertile men with elevated SDF were then formulated and adapted using the Delphi method. **RESULTS:** A total of 436 experts from 55 different countries submitted responses. As an initial approach, 79.1% of reproductive experts recommend lifestyle modifications for infertile men with elevated SDF, and 76.9% prescribe empiric antioxidants. Regarding antioxidant duration, 39.3% recommend 4-6 months and 38.1% recommend 3 months. For men with unexplained or idiopathic infertility, and couples experiencing recurrent miscarriages associated with elevated SDF, most respondents refer to ART 6 months after failure of conservative and empiric medical management. Infertile men with clinical varicocele, normal conventional semen parameters, and elevated SDF are offered varicocele repair immediately after diagnosis by 31.4%, and after failure of antioxidants and conservative measures by 40.9%. Sperm selection techniques and testicular sperm extraction are also management options for couples undergoing ART. For most questions, heterogeneous practices were demonstrated. **CONCLUSIONS:** This paper presents the results of a large global survey on the management of infertile men with elevated SDF and reveals a lack of consensus among clinicians. Furthermore, it demonstrates the scarcity of professional society guidelines in this regard and attempts to highlight the relevant evidence. Expert recommendations are proposed to help guide clinicians.

Urology

Gupta R, Chopra D, Hemal AK, Mukherjee S, **Rogers CG**, Sundaram CP, and Tewari AK. The first SURS World Congress of Robotic Surgery at Mount Sinai Hospital in New York City: A tribute to the past and the future of robotic urologic surgery. *BJUI Compass* 2023; 4(3):243-245. PMID: 37025466. [Full Text](#)

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Urology

Hijazi MA, Prebay ZJ, Johnson A, **Wilder S, Patel A**, Mehra R, Montie JE, Noyes SL, Mirza M, Jafri M, Weizer A, Sarle R, Ghani KR, **Rogers C**, and Lane BR. Utilization of a Virtual Tumor Board for the Care of Patients With Renal Masses: Experience From a Quality Improvement Collaborative. *Urol Pract* 2023; Epub ahead of print. PMID: 37103551. [Full Text](#)

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INTRODUCTION: Multidisciplinary tumor board (MDTB) meetings are useful sources of insight and collaboration when establishing treatment approaches for oncologic cases. However, such meetings can be time intensive and inconvenient. We implemented a Virtual Tumor Board (VTB) within Michigan Urological Surgery Improvement Collaborative (MUSIC) to discuss and improve the management of complicated renal masses (RMs). **METHODS:** Urologists were invited to discuss decision-making for RMs through voluntary engagement. Communication was performed exclusively through email. Case details were collected and responses were tabulated. All participants were surveyed about their perceptions of the VTB. **RESULTS:** 50 RM cases were reviewed in a VTB that included 53 urologists. Patients ranged from 20-90 years old and 94% had localized RM. The cases generated 355 messages, ranging from 2-16 (median 7) per case; 144 responses (40.6%) were sent via smart-phone. All urologists (100%) who submitted to the VTB had their questions answered. The VTB provided suggestions to those with no stated treatment plan in 42% of cases, confirmed the physician's initial approach to their case in 36%, and offered alternative approaches in 16% of cases. 83% of survey respondents felt the experience was "Beneficial" or "Very Beneficial" and 93% stated increased confidence in their case management. **CONCLUSIONS:** MUSIC's initial experience with a VTB showed good engagement. The format reduced barriers to multi-institutional and multi-disciplinary discussions and improved the quality of care for selected patients with complex RMs.

Urology

Semerjian A, Ginsburg K, Qi J, Johnson A, Noyes S, **Rogers C**, and Lane BR. Guideline Compliance Regarding Chest Imaging of Suspicious cT1 Renal Masses in MUSIC-KIDNEY. *Urol Pract* 2023; Epub ahead of print. PMID: 37103883. [Full Text](#)

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INTRODUCTION: Multiple urologic societies recommend chest imaging for suspicious renal masses using chest X-ray (CXR), or computed tomography (CT) as clinically indicated. The purpose of chest imaging is to assess for thoracic metastasis at the time of renal mass (RM) diagnosis. Ideally, imaging use and type is commensurate with risk related to tumor size and clinical stage. We examined current practice patterns with chest imaging compliance in the state of Michigan and implemented clinician education and VBR (value-based reimbursement) incentivization on guideline adherence. **MATERIALS AND METHODS:** MUSIC-KIDNEY is a statewide initiative focusing on quality improvement for patients

with cT1 RM. Data regarding chest imaging in MUSIC and panel discussion occurred at in-person MUSIC meeting in October 2019. Adherence to chest imaging guidelines was made a VBR metric at the tri-annual MUSIC meeting in January 2020. Adherence was defined as optional in RM <3 cm (CT not indicated), recommended in RM 3-5 cm (CXR preferred), and required in RM >5 cm (CT preferred). The MUSIC registry was queried for percentage of patients receiving chest imaging by type. Factors associated with adherence were assessed. RESULTS: There was significant practice level variation in chest imaging rates across the 14 contributing practices, ranging from 11 to 68%. Compliance with MUSIC guidelines for chest imaging during evaluation of T1RM was 81.8% overall, with only 61.8% of patients with masses >5 cm meeting the guideline requiring imaging with preference for CT. Factors associated with increased adherence included larger tumor size (T1b vs T1a) and solid (vs cystic or indeterminate) tumor (P < .05 for each). Prior to VBR introduction, 46.7% of patients underwent imaging of either type, compared to 49.0% post-intervention. Imaging rates only slightly increased in masses >5 cm (58.3% pre-VBR vs 61.2% after, P = .56) and 3-5 cm (50.0% pre-VBR vs 56.2% post-VBR, P = .0585). CONCLUSIONS: Chest imaging guideline adherence during the initial evaluation of cT1 renal masses is acceptable, particularly given that most masses are <3 cm for which metastatic risk is low. However, despite consensus from major urologic societies regarding imaging for masses >4-5 cm, imaging rates were low across MUSIC. After educational and VBR incentive initiation, rates of imaging for 3-5 cm and >5 cm masses changed only slightly. There remains significant practice variability and room for improvement.

Urology

Shah R, Agarwal A, **Rambhatla A**, et al. Consensus and Diversity in the Management of Varicocele for Male Infertility: Results of a Global Practice Survey and Comparison with Guidelines and Recommendations. *World J Mens Health* 2023; 41(1):164-197. PMID: 35791302. [Full Text](#)

PURPOSE: Varicocele is a common problem among infertile men. Varicocele repair (VR) is frequently performed to improve semen parameters and the chances of pregnancy. However, there is a lack of consensus about the diagnosis, indications for VR and its outcomes. The aim of this study was to explore global practice patterns on the management of varicocele in the context of male infertility. MATERIALS AND METHODS: Sixty practicing urologists/andrologists from 23 countries contributed 382 multiple-choice-questions pertaining to varicocele management. These were condensed into an online questionnaire that was forwarded to clinicians involved in male infertility management through direct invitation. The results were analyzed for disagreement and agreement in practice patterns and, compared with the latest guidelines of international professional societies (American Urological Association [AUA], American Society for Reproductive Medicine [ASRM], and European Association of Urology [EAU]), and with evidence emerging from recent systematic reviews and meta-analyses. Additionally, an expert opinion on each topic was provided based on the consensus of 16 experts in the field. RESULTS: The questionnaire was answered by 574 clinicians from 59 countries. The majority of respondents were urologists/uro-andrologists. A wide diversity of opinion was seen in every aspect of varicocele diagnosis, indications for repair, choice of technique, management of sub-clinical varicocele and the role of VR in azoospermia. A significant proportion of the responses were at odds with the recommendations of AUA, ASRM, and EAU. A large number of clinical situations were identified where no guidelines are available. CONCLUSIONS: This study is the largest global survey performed to date on the clinical management of varicocele for male infertility. It demonstrates: 1) a wide disagreement in the approach to varicocele management, 2) large gaps in the clinical practice guidelines from professional societies, and 3) the need for further studies on several aspects of varicocele management in infertile men.

Conference Abstracts

Administration

Willner S, Gardell S, **She R**, Li J, **Zeld N**, **Williams LK**, **Sabbah H**, Kapoor N, and **Lanfeard D**. Circulating Metabolomic Profile Predicts Change In Ejection Fraction In Heart Failure Patients. *J Card Fail* 2023; 29(4):569. [Full Text](#)

Introduction: Heart failure (HF) with reduced ejection fraction remains a major public health concern, despite multiple effective pharmacotherapies, and disease progression can be highly variable. Accumulating data indicates that HF disease severity and progression are likely influenced by impaired structure and function of the myocardial energetic apparatus. Growing interest in circulating metabolites in HF has revealed several metabolite derangements as well as the association of certain metabolomic profiles with survival. Still unclear is whether specific metabolite levels can predict disease course, and once identified, what is the mechanism of this association. This study aimed to test whether key metabolites can predict changes in ejection fraction (EF) over time. If true, this could aid in understanding the course of disease and identify the precise metabolite targets for further mechanistic study. Methods: We conducted a prospective registry of patients with HF and reduced ejection fraction, enrolling a total of 1122 patients who had a clinical EF assessed at <50%. Baseline fasting plasma samples underwent targeted metabolomic profiling for organic acids, amino acids, and acyl carnitines (108 species in all). Roughly five years later registry participants were re-contacted to undergo repeat echocardiogram and metabolite profiling. The association of 1) baseline metabolite levels and 2) change in metabolite level, with the change in EF was tested using linear regression adjusted for baseline EF. We also tested an additional model with adjustment for age, sex, race, diabetes, and creatinine. False discovery rate (FDR) was used to adjust for multiple comparisons with FDR<0.05 being considered statistically significant. Results: A total of 268 patients underwent EF and metabolite reassessment. Of these patients 97 were female (36.2%), 140 were African American (52.5%), the mean age was 63.6 (SD 10.2), and baseline EF was 36.5% (SD 10.8). The median follow-up time was 5.2 years (IQR 4.4, 6.0) Five metabolites were statistically significantly associated with change in EF (Table 1). In the fully adjusted model the same 5 metabolites remained the top associations but narrowly missed statistical significance. Changes in malate (FDR=0.015) and alpha-ketoglutarate (FDR=0.022) over time were also associated with corresponding changes in EF. Conclusions: Plasma metabolomic profiling in patients with HF reveals that organic acids, including several citric acid cycle intermediates, are predictive of future EF changes over 5 years follow-up. These metabolite levels may be a new tool to predict disease course, and further investigation is needed to illuminate the biologic mechanisms underlying this association.

Anesthesiology

Sahota R, **Maroun W**, **Reddy S**, and **Uduman J**. A RARE CASE OF PROLIFERATIVE ANCA-NEGATIVE PAUCI-IMMUNE CRESCENTIC GLOMERULONEPHRITIS. *Am J Kidney Dis* 2023; 81(4):S41-S41. [Full Text](#)

Cardiology/Cardiovascular Research

Castagna F, Onat D, Wong K, Harxhi A, Hayashi Y, Pinsino A, Mebazaa A, Arrigo M, LeJemtel TH, **Sabbah H**, Schmidt A, Yuzefpolskaya M, Demmer R, and Colombo PC. Enhanced Release of Endothelin-1 and Angiotensin-2 During Experimentally-Induced Peripheral Venous Congestion is Associated with Heart Failure-Related Clinical Events. *J Heart Lung Transplant* 2023; 42(4):S323-S324. [Full Text](#)

P.C. Colombo, Columbia University Medical Center, New York, NY, United States

Purpose: Growing evidence suggests that venous congestion (VC) is a contributor to the pathophysiology of heart failure (HF) progression by causing inflammation, vasoconstriction, oxidative stress and endothelial activation. We hypothesized that: 1) euvolemic HF with reduced ejection fraction (HFREF) pts with a recent history of HF hospitalization have more pronounced phenotypic response to VC compared to pts not hospitalized; 2) greater phenotypic response to VC is associated with subsequent HF-related events. Methods: Two matched groups of euvolemic NYHA Class II-III HFREF pts, with and without history of HF hospitalization within prior 6 months, were studied. We modeled acute VC by inflating a cuff around

multicenter feasibility study in Australia, Europe, and Asia. Patients, Clinicians, and Device Developers share a mutual interest to confirm device safety and performance as early as possible. Methods: Up to 15 patients will be enrolled using typical LVAD inclusion/exclusion criteria: patients with worsening heart failure despite optimal medical management. As in other LVAD trials, the primary endpoint will be survival. Secondary endpoints include freedom from adverse events (AEs), (e.g. stroke, bleeding, infection, and pump replacement), quality of life and neurocognitive measures. Given that this is a feasibility study, not powered to demonstrate clinical benefit, we also plan to collect data predictive of AEs, validating preclinical data where applicable. These will include von Willebrand Factor assays, arterial pulse pressure and aortic valve opening, which are factors implicated in bleeding and aortic insufficiency. Increased aorta stiffness post-LVAD, correlated with increased AEs, will be measured. The synchronous, pulsatile flow of the CorWave LVAD is hypothesized to improve patient exercise capacity and possibly native ventricular recovery. Thus, patients will undergo exercise testing and evaluation of ventricular size and ejection fraction while on pump support. Results: Potential outcomes include 1) Low AEs and favorable biomarker and functional test data, permitting judicious initiation of a pivotal trial, 2) Equivocal AEs and/or inconclusive biomarker and functional results, enabling Clinicians and Device Developers to collaborate to identify improvements prior to a pivotal trial, or 3) Increased AEs with negative biomarker and functional data, requiring device design and/or management revisions prior to recommencing clinical studies. Conclusion: Survival rates achieved with current LVADs create a challenging standard, but the high AE rates offer opportunities for new technologies to prevent stagnation in the field. New approaches to cost-effective early LVAD trial design are required to sustain innovation and safely transition into pivotal trials.

Cardiology/Cardiovascular Research

Kyriakopoulos CP, Taleb I, Wever-Pinzon O, Selzman C, Bonios M, Dranow E, Wever-Pinzon J, Yin M, Tseliou E, Stehlik J, Alharethi R, Kfoury A, Hanff T, Fang J, Koliopoulou A, Sideris K, Krauspe E, Nelson M, Elmer A, Singh R, Psothka M, Birks E, Slaughter M, Koenig S, Kyvernitakis A, Hoffman K, Guglin M, Kotter J, Campbell K, Silvestry S, Vidic A, Raval N, Mehra M, **Cowger J**, Kanwar M, Shah P, and Drakos SG. Multicenter Development and Validation of a Machine Learning Model to Predict Myocardial Recovery During LVAD Support: The UCAR Score. *J Heart Lung Transplant* 2023; 42(4):S106. [Full Text](#)

C.P. Kyriakopoulos, Utah Cardiac Recovery (UCAR) Program (University of Utah Health and School of Medicine, Intermountain Medical Center, George E. Wahlen Department of Veterans Affairs Medical Center), Salt Lake City, UT, United States

Purpose: Although significant cardiac reverse remodeling is a prerequisite for a left ventricular (LV) assist device (LVAD) patient to be considered for device weaning, multiple factors including patient goals, physician comfort, and center experience, weigh in on this complex decision. Existing predictive models defining recovery as device withdrawal, entail the above-mentioned confounders, and may under detect patients that could benefit from a targeted bridge to recovery strategy. We sought to derive and validate a predictive tool to identify patients prone to reverse remodel, independent of the complex decision to remove a durable, surgically deployed device. Methods: Heart failure patients (N=782) requiring LVAD were enrolled at one (n=537) and five US programs (n=245). Baseline characteristics were recorded. The primary outcome was responder incidence, defined as follow-up LV ejection fraction $\geq 40\%$ and LV end-diastolic diameter ≤ 6 cm within one year on LVAD support. Bootstrap imputation and lasso variable selection techniques were used to derive a predictive model which was then validated using our multicenter dataset. A predictive calculator was developed, and patients were classified into groups with varying potential for reverse remodeling. Results: Patients were predominantly white (84%), male (82%), aged 56 ± 1 years. Overall, 14.8% patients were identified as responders. Nine preoperative variables associated with reverse remodeling were included in the multivariate model achieving an optimism corrected C-statistic of 0.77 (95% CI: 0.71-0.82) (Figure). Conclusion: The UCAR calculator is a machine learning-based multicenter and validated risk tool, implementing routine clinical data, that effectively stratifies patients into groups with varying potential for reverse remodeling. This tool can be useful in selecting patients to implement diagnostic and therapeutic protocols that can promote reverse remodeling and myocardial recovery.

Cardiology/Cardiovascular Research

Nayak A, Hall S, Uriel N, Goldstein D, Cleveland J, **Cowger J**, Salerno C, Naka Y, Horstmanshof D, Somo S, Wang A, and Mehra MR. Clinical Predictors of 5-year Outcomes Following Heartmate 3 Left Ventricular Assist Device Implant: The Momentum 3 Trial. *J Heart Lung Transplant* 2023; 42(4):S88-S89. [Full Text](#)

A. Nayak, Harvard Medical School, Boston, MA, United States

Purpose: The MOMENTUM 3 pivotal trial reported a median survival that exceeds 5-years in patients supported with a fully magnetically levitated HeartMate 3 (HM3) left ventricular assist device (LVAD), even in transplant ineligible patients (*JAMA* 2022;328:1233-1242). Additionally, a HM 3 Risk Score with 6 pre-implant clinical characteristics was developed to predict 2-year outcome in those being considered for HM3 implantation (*JACC Heart Fail* 2022;online). However, it remains unknown how pre-implant variables in concert with implant related events during the index hospitalization influence 5-year outcomes, especially among those successfully discharged. **Methods:** We plan to utilize outcome data from the pivotal MOMENTUM 3 trial, conducted at 69 US centers, among 515 patients from the trial who were randomized to receive the HM3 (median age: 62 years, 20% female, 28% black, 62% destination therapy) in whom a survival of 58.4% was demonstrated at 5-years. The primary goal is to develop and validate clinical predictors for 5-year outcomes including survival, cause specific mortality and serious adverse events in patients successfully implanted with the HM3 pump and able to be discharged from the index hospitalization. In addition to pre-implant clinical characteristics, we shall evaluate surgical events, concomitant procedures, hemocompatibility and non-hemocompatibility related adverse events encountered peri-operatively, end organ function and discharge to a home setting as potential predictors for 5-year survival. **Secondarily,** we shall ascertain age and sex-based assessment of net survival time prediction at 5-years among this cohort, stratified by intended goal including bridge to transplant, bridge to candidacy or destination therapy. **Endpoints:** We expect that the detection of comprehensive clinical predictors (particularly events encountered during implant surgery and index hospitalization) for 5-year outcomes with HM3 LVAD support will guide efforts to enhance processes of medical and surgical care and improve quality of patient outcomes. **Importantly,** knowledge of patient-specific outcomes will enable clinicians to engage in informed patient centered counseling, estimate individualized long-term outcomes and plan appropriate management strategies in patients implanted with the HM3 LVAD.(NCT02224755 and NCT03982979)

Cardiology/Cardiovascular Research

Solomon R, Michaels A, and Cowger J. Cardiomyopathy Associated with Systemic Disease: The Case of a 31-Year-Old Female with Left Ventricular Thickening. *J Heart Lung Transplant* 2023; 42(4):S204. [Full Text](#)

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Introduction: Cardiologists should be aware of rare diseases that can impact cardiac function. Our case involves a woman with cardiomyopathy and left ventricular (LV) thickening which was mistakenly diagnosed. **Case Report:** Our patient presented at age 27 in 2018 with palpitations and dyspnea, eventually being diagnosed with multiple pathologies including non-ischemic cardiomyopathy. In 2022, she was referred to our Advanced Heart Failure Clinic with pertinent findings outlined in figure 1. Genetic testing revealed a LAMP2 mutation consistent with Danon disease. She is presently undergoing evaluation for cardiac transplant. Danon disease is a systemic disorder of glycogen storage due to a lysosome-associated membrane protein 2 (LAMP2) deficiency. It can manifest with LV thickening due to myocyte vacuolization (not true cell hypertrophy), systolic dysfunction and Wolf-Parkinson-White (WPW), with or without associated skeletal myopathy (elevated creatine kinase, aspartate aminotransferase), retinal pigmentation, neuropsychiatric, gastrointestinal or respiratory abnormalities. An X-linked dominant disorder, the cardiomyopathy in males tends to be more severe and earlier in onset than women, with intellectual disability being more frequent. Detection of a mutation in the LAMP2 gene confirms the diagnosis. While CRISPR technologies are under study for gene editing, approved disease-specific treatments for reversing or slowing Danon are lacking. Cardiac transplantation is the common management choice for those eligible, but pulmonary hypertension and neurocognitive deficiencies may

limit candidacy. Danon disease is an uncommon genetic disorder with varying phenotypic presentation. Cardiologists should consider it in young patients with a WPW EKG pattern and LV thickening with reduced systolic function, with or without neurocognitive or muscular dysfunction. Referral to an advanced heart failure center for genetic counseling and management is recommended.

Cardiology/Cardiovascular Research

Steinberg R, Nayak A, Wang J, Okoh A, Morris A, **Cowger J**, and Nohria A. Associations Between Pre-Implant Cancer and Left Ventricular Assist Device Outcomes: An InterMACS Registry Analysis. *J Heart Lung Transplant* 2023; 42(4):S136. [Full Text](#)

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Purpose: Few studies have examined the effect of pre-implant cancer history on clinical outcomes in patients with left ventricular assist devices (LVAD). We used the INTERMACS registry to compare rates of post-LVAD adverse outcomes in patients with and without a history of a solid tumor or hematologic malignancy. **Methods:** We included LVAD recipients in the INTERMACS registry from 2007-2017 who had their cancer history reported (N=18053, age: 56.4 years, 22% female, 24% Black). Cox proportional hazard models were used to examine the association between pre-implant cancer and outcomes of all-cause mortality, major bleeding events, major infection events, stroke/transient ischemic attack (TIA), renal dysfunction, pump thrombosis, and heart transplantation. Logistic regression modeling was used to examine the association between pre-implant cancer and right ventricular failure (RVF). Multivariable models were adjusted for clinically relevant covariates. **Results:** A total of 1124 (6.2%) patients had a history of cancer, with 894 (5.0%) patients having solid tumors and 259 (1.4%) patients having hematologic malignancies. History of solid tumors was associated with increased risk of mortality, bleeding events, pump thrombosis, and decreased likelihood of transplantation compared to non-cancer patients on multivariable analyses (Table). History of hematologic malignancies was associated with an increased risk of major infection, RVF, and renal dysfunction compared with non-cancer patients on multivariable analyses. There were no significant associations between either cancer type and stroke/TIA after adjustment for covariates. **Conclusion:** The risk for post-LVAD complications differs based on cancer type. As survival in cancer patients improves and LVADs are increasingly used in this population, more data that will help in the prediction and management of post-LVAD complications is critical.

Cardiology/Cardiovascular Research

Willner S, Gardell S, **She R**, Li J, **Zeld N**, **Williams LK**, **Sabbah H**, Kapoor N, and **Lanfeer D**. Circulating Metabolomic Profile Predicts Change In Ejection Fraction In Heart Failure Patients. *J Card Fail* 2023; 29(4):569. [Full Text](#)

Introduction: Heart failure (HF) with reduced ejection fraction remains a major public health concern, despite multiple effective pharmacotherapies, and disease progression can be highly variable. Accumulating data indicates that HF disease severity and progression are likely influenced by impaired structure and function of the myocardial energetic apparatus. Growing interest in circulating metabolites in HF has revealed several metabolite derangements as well as the association of certain metabolomic profiles with survival. Still unclear is whether specific metabolite levels can predict disease course, and once identified, what is the mechanism of this association. This study aimed to test whether key metabolites can predict changes in ejection fraction (EF) over time. If true, this could aid in understanding the course of disease and identify the precise metabolite targets for further mechanistic study. **Methods:** We conducted a prospective registry of patients with HF and reduced ejection fraction, enrolling a total of 1122 patients who had a clinical EF assessed at <50%. Baseline fasting plasma samples underwent targeted metabolomic profiling for organic acids, amino acids, and acyl carnitines (108 species in all). Roughly five years later registry participants were re-contacted to undergo repeat echocardiogram and metabolite profiling. The association of 1) baseline metabolite levels and 2) change in metabolite level, with the change in EF was tested using linear regression adjusted for baseline EF. We also tested an additional model with adjustment for age, sex, race, diabetes, and creatinine. False discovery rate (FDR) was used to adjust for multiple comparisons with FDR<0.05 being considered statistically significant. **Results:** A total of 268 patients underwent EF and metabolite reassessment. Of these patients 97 were female (36.2%), 140 were African American (52.5%), the mean age was 63.6 (SD 10.2), and baseline EF

was 36.5% (SD 10.8). The median follow-up time was 5.2 years (IQR 4.4, 6.0) Five metabolites were statistically significantly associated with change in EF (Table 1). In the fully adjusted model the same 5 metabolites remained the top associations but narrowly missed statistical significance. Changes in malate (FDR=0.015) and alpha-ketoglutarate (FDR=0.022) over time were also associated with corresponding changes in EF. Conclusions: Plasma metabolomic profiling in patients with HF reveals that organic acids, including several citric acid cycle intermediates, are predictive of future EF changes over 5 years follow-up. These metabolite levels may be a new tool to predict disease course, and further investigation is needed to illuminate the biologic mechanisms underlying this association.

Center for Health Policy and Health Services Research

Willner S, Gardell S, **She R**, Li J, **Zeld N**, **Williams LK**, **Sabbah H**, Kapoor N, and **Lanfeard D**. Circulating Metabolomic Profile Predicts Change In Ejection Fraction In Heart Failure Patients. *J Card Fail* 2023; 29(4):569. [Full Text](#)

Introduction: Heart failure (HF) with reduced ejection fraction remains a major public health concern, despite multiple effective pharmacotherapies, and disease progression can be highly variable. Accumulating data indicates that HF disease severity and progression are likely influenced by impaired structure and function of the myocardial energetic apparatus. Growing interest in circulating metabolites in HF has revealed several metabolite derangements as well as the association of certain metabolomic profiles with survival. Still unclear is whether specific metabolite levels can predict disease course, and once identified, what is the mechanism of this association. This study aimed to test whether key metabolites can predict changes in ejection fraction (EF) over time. If true, this could aid in understanding the course of disease and identify the precise metabolite targets for further mechanistic study. Methods: We conducted a prospective registry of patients with HF and reduced ejection fraction, enrolling a total of 1122 patients who had a clinical EF assessed at <50%. Baseline fasting plasma samples underwent targeted metabolomic profiling for organic acids, amino acids, and acyl carnitines (108 species in all). Roughly five years later registry participants were re-contacted to undergo repeat echocardiogram and metabolite profiling. The association of 1) baseline metabolite levels and 2) change in metabolite level, with the change in EF was tested using linear regression adjusted for baseline EF. We also tested an additional model with adjustment for age, sex, race, diabetes, and creatinine. False discovery rate (FDR) was used to adjust for multiple comparisons with FDR<0.05 being considered statistically significant. Results: A total of 268 patients underwent EF and metabolite reassessment. Of these patients 97 were female (36.2%), 140 were African American (52.5%), the mean age was 63.6 (SD 10.2), and baseline EF was 36.5% (SD 10.8). The median follow-up time was 5.2 years (IQR 4.4, 6.0) Five metabolites were statistically significantly associated with change in EF (Table 1). In the fully adjusted model the same 5 metabolites remained the top associations but narrowly missed statistical significance. Changes in malate (FDR=0.015) and alpha-ketoglutarate (FDR=0.022) over time were also associated with corresponding changes in EF. Conclusions: Plasma metabolomic profiling in patients with HF reveals that organic acids, including several citric acid cycle intermediates, are predictive of future EF changes over 5 years follow-up. These metabolite levels may be a new tool to predict disease course, and further investigation is needed to illuminate the biologic mechanisms underlying this association.

Hematology-Oncology

Jänne PA, Spira A, Riely GJ, **Gadgeel S**, Heist R, Ou SHI, Johnson ML, Sabari J, Velastegui K, Christensen JG, Yang W, Anderes K, Chao R, and Paweletz C. 8MO Adagrasib (MRTX849) in patients with advanced/metastatic KRAS G12C-mutated non-small cell lung cancer (NSCLC): Preliminary analysis of mutation allele frequency. *J Thorac Oncol* 2023; 18(4):S41-S42. [Full Text](#)

Background KRASG12C mutations occur in ~14% of NSCLC adenocarcinomas. Adagrasib (ada), a KRASG12C inhibitor, was selected for favorable properties, including long half-life (23 h), dose-dependent pharmacokinetics, and central nervous system penetration. In the KRYSTAL-1 registrational phase II Cohort A, ada showed clinical activity with manageable tolerability in patients (pts) with previously treated KRASG12C-mutated NSCLC. Methods Pts with previously treated KRASG12C-mutated NSCLC received ada 600 mg orally BID. Study objectives included objective response rate [ORR], progression-free survival [PFS], overall survival [OS], safety and exploratory correlative analyses. An exploratory analysis of clinical response for pts with detectable circulating tumor (ct) DNA at baseline,

cycle 2 day 1, and cycle 4 day 1 (C4D1), who comprise the mutation allele frequency clearance (MAFC)-evaluable population, was also performed; KRASG12C ctDNA was assessed by digital droplet polymerase chain reaction. Results At data cutoff, 15 Oct 2021, Cohort A included 116 pts (median follow-up 12.9 months): median age 64 years, 56% female, median 2 prior systemic therapies. ORR by blinded independent central review (BICR) was 42.9%, disease control rate 79.5%, median PFS 6.5 months (95% CI 4.7–8.4) and, with longer follow-up (cutoff 15 Jan 2022), median OS 12.6 months (95% CI 9.2–19.2). Any grade treatment-related adverse events (TRAEs) occurred in 97% of pts (most commonly [$>40\%$] diarrhea [63%], nausea [62%], vomiting [47%], and fatigue [41%]), and Grade 3–4 TRAEs in 43% (most commonly [$\geq 5\%$] serum lipase increase [6%] and anemia [5%]). Two grade 5 TRAEs occurred; 8 (7%) TRAEs led to discontinuation. In MAFC-evaluable pts ($n = 35$), ORR by BICR was 60% (21/35) and all responses correlated with MAFC $>90\%$ by C4D1. Conclusions Ada showed promising efficacy and manageable tolerability in previously treated pts with KRASG12C-mutated NSCLC. Additional analyses are needed to further evaluate whether clinical response with ada correlates with MAFC in ctDNA. A phase III trial evaluating ada monotherapy vs docetaxel in previously treated pts with KRASG12C-mutated NSCLC is ongoing (NCT04685135). Clinical trial identification NCT03785249.

Hematology-Oncology

Johnson ML, Ou SHI, Felip E, Baik C, Besse B, Mazieres J, Camidge DR, **Gadgeel S**, Dilon A, Elamin YY, Liu G, Reuss JE, Kehrig T, Pelish HE, Zhu V, and Lin JJ. 81TiP NVL-655, a selective anaplastic lymphoma kinase (ALK) inhibitor, in patients with advanced ALK-positive solid tumors: The phase I/II ALKOVE-1 study. *J Thorac Oncol* 2023; 18(4):S86-S87. [Full Text](#)

Background Aberrations of the ALK oncogene drive tumor cell proliferation, survival, and metastasis in multiple adult and pediatric cancers. ALK gene fusions are detected in ~5% of advanced non-small cell lung cancers (NSCLC); among these patients, the incidence of central nervous system (CNS) metastases at diagnosis is ~40%. Although 5 tyrosine kinase inhibitors (TKIs) are approved by the FDA and EMA for ALK-positive NSCLC, therapeutic limitations remain, such as acquired resistance due to secondary and compound ALK mutations and/or neurologic adverse events attributed to off-target inhibition of TRK. NVL-655 is a novel, brain-penetrant ALK-selective TKI that exhibits preclinical activity against diverse ALK fusions and mutations, including G1202R and G1202R compound mutations, while sparing inhibition of TRK. The ALKOVE-1 study is evaluating the safety and preliminary activity of NVL-655 in patients with solid tumors harboring oncogenic ALK alterations, including those with acquired ALK resistance mutations and CNS metastases. Trial design ALKOVE-1 consists of a phase I dose escalation followed by a phase II expansion in cohorts defined by tumor type and prior therapies. Phase I includes adult patients with any solid tumor type harboring an oncogenic ALK gene fusion or activating mutation (by local testing), including ALK fusion-positive NSCLC after ≥ 1 prior 2nd or 3rd generation ALK TKI. Prior platinum-based chemotherapy and/or immunotherapy, CNS disease without progressive neurological symptoms or increasing corticosteroid doses, and evaluable but non-measurable disease are allowed. Patients will receive NVL-655 by daily oral administration. Primary phase I objectives are to determine the NVL-655 recommended phase II dose and, if applicable, maximum tolerated dose. Additional objectives include evaluation of safety/ tolerability, preliminary activity, and characterization of the pharmacokinetic and pharmacodynamic profiles of NVL-655. Longitudinal analysis of circulating tumor DNA will be performed, including ALK mutation profiling and other relevant biomarkers. The phase I portion of the study is ongoing. Clinical trial identification NCT05384626 (May 20, 2022).

Internal Medicine

Johnson SC, Ali SA, Shah CD, Arman HE, Nabrzyski R, Elsemesmani HI, **Gandy R**, Wong D, Gibbawi MA, Omar HR, Siddegowda Bangalore B, Duncan M, and Guglin M. Invasive Hemodynamic Indices That Are Associated with Mortality at One Year in Patients with Pulmonary Hypertension Per Newly Proposed Criteria. *J Heart Lung Transplant* 2023; 42(4):S371-S372. [Full Text](#)

S.C. Johnson, Indiana University, Indianapolis, IN, United States

Purpose: Pulmonary Hypertension (PH) is classified by hemodynamics and etiology. The majority of prognostic factors reported for PH are categorized by etiology. We aimed to study universal prognostic factors in PH irrespective of etiology and solely based on hemodynamics. Additionally, we compared

outcomes of different hemodynamic groups. The 6th World Symposium on Pulmonary Hypertension proposed a mean pulmonary arterial pressure (mPAP) >20mmhg which has introduced a new group of patients. Methods: We retrospectively reviewed 649 consecutive PH patients. PH was defined as any patient with mean pulmonary arterial pressure (mPAP) > 20mmHg. All patients with PH were further categorized into 4 groups based on invasive hemodynamics (Table 1). We used one-way ANOVA to compare groups, Pearson chi-square for categorical analysis, and t-test analysis to compare different hemodynamic parameters within each group. Results: Out of 649 patients with PH, 137 patients were classified as PH1, 289 as PH2, 141 as PH3, and 76 as PH4. We found that mean right atrial pressure (mRAP), pulmonary artery systolic pressure (PASP), pulmonary artery diastolic pressure (PADP), pulmonary capillary wedge pressure (PCWP), mPAP ($p < 0.01$), and peripheral vascular resistance (PVR) ($p < 0.05$) were universally predictive of increased risk of one-year mortality across all the hemodynamic groups. In our cohort of patients, pulmonary artery pulsatility index (PAPI) was not found to be predictive of one-year mortality ($p = 0.52$). Lastly, we found that combined death and cardiovascular outcomes at one year were worse for PH3 compared to PH1 and PH4 ($p < 0.01$). Conclusion: Our study found that postcapillary pulmonary hypertension is the most prevalent type in our unselected sample of consecutive patients meeting the criteria for PH. Elevated mRAP, PASP, PADP, PCWP, mPAP, and PVR were associated with an increased risk of one-year mortality in the whole cohort. Combined PH had the highest one-year mortality.

Nephrology

Sahota R, Maroun W, Reddy S, and Uduman J. A RARE CASE OF PROLIFERATIVE ANCA-NEGATIVE PAUCI-IMMUNE CRESCENTIC GLOMERULONEPHRITIS. *Am J Kidney Dis* 2023; 81(4):S41-S41. [Full Text](#)

Public Health Sciences

Willner S, Gardell S, She R, Li J, Zeld N, Williams LK, Sabbah H, Kapoor N, and Lanfear D. Circulating Metabolomic Profile Predicts Change In Ejection Fraction In Heart Failure Patients. *J Card Fail* 2023; 29(4):569. [Full Text](#)

Introduction: Heart failure (HF) with reduced ejection fraction remains a major public health concern, despite multiple effective pharmacotherapies, and disease progression can be highly variable. Accumulating data indicates that HF disease severity and progression are likely influenced by impaired structure and function of the myocardial energetic apparatus. Growing interest in circulating metabolites in HF has revealed several metabolite derangements as well as the association of certain metabolomic profiles with survival. Still unclear is whether specific metabolite levels can predict disease course, and once identified, what is the mechanism of this association. This study aimed to test whether key metabolites can predict changes in ejection fraction (EF) over time. If true, this could aid in understanding the course of disease and identify the precise metabolite targets for further mechanistic study. Methods: We conducted a prospective registry of patients with HF and reduced ejection fraction, enrolling a total of 1122 patients who had a clinical EF assessed at <50%. Baseline fasting plasma samples underwent targeted metabolomic profiling for organic acids, amino acids, and acyl carnitines (108 species in all). Roughly five years later registry participants were re-contacted to undergo repeat echocardiogram and metabolite profiling. The association of 1) baseline metabolite levels and 2) change in metabolite level, with the change in EF was tested using linear regression adjusted for baseline EF. We also tested an additional model with adjustment for age, sex, race, diabetes, and creatinine. False discovery rate (FDR) was used to adjust for multiple comparisons with FDR<0.05 being considered statistically significant. Results: A total of 268 patients underwent EF and metabolite reassessment. Of these patients 97 were female (36.2%), 140 were African American (52.5%), the mean age was 63.6 (SD 10.2), and baseline EF was 36.5% (SD 10.8). The median follow-up time was 5.2 years (IQR 4.4, 6.0) Five metabolites were statistically significantly associated with change in EF (Table 1). In the fully adjusted model the same 5 metabolites remained the top associations but narrowly missed statistical significance. Changes in malate (FDR=0.015) and alpha-ketoglutarate (FDR=0.022) over time were also associated with corresponding changes in EF. Conclusions: Plasma metabolomic profiling in patients with HF reveals that organic acids, including several citric acid cycle intermediates, are predictive of future EF changes over 5 years follow-up. These metabolite levels may be a new tool to predict disease course, and further investigation is needed to illuminate the biologic mechanisms underlying this association.

Surgery

Chaudhry SP, Baldrige AS, Gonzalez M, Yaranov D, Barr Biglane J, **Tanaka D**, Fischer W, Larkin C, Ullah R, and Pham D. Clinician Approach To Subtherapeutic INR Management In Patients With A Heartmate 3 LVAD: A Regional Subgroup Analysis Of The Momentum 3 (CAP And IDE) Trials. *J Card Fail* 2023; 29(4):612-613. [Full Text](#)

Introduction: Patients with Heartmate 3 LVADs are recommended to be on therapeutic anticoagulation consisting of aspirin and warfarin (with a goal INR of 2-3). No specific recommendations exist for the management of subtherapeutic INRs, leading to a variation in management. This study was performed to evaluate clinician behavior in the management of subtherapeutic INRs. Methods: We performed a regional subgroup analysis of the MOMENTUM 3 (CAP and IDE) Trials including 6 centers in the Mid-America Region. All patients implanted with a HeartMate 3 device and discharged alive were included in the analysis. Patients with subtherapeutic INRs (INR < 2) occurring after the index admission underwent manual chart review to determine the management strategies taken by clinicians. Management strategies were separated into three groups: no action taken, isolated adjustment of coumadin, or bridging with IV (heparin, bivalirudin) or parenteral agents (enoxaparin). Results: Among 225 patients included in the analysis, 130 (58%) patients had a total of 235 subtherapeutic INR events. Management strategy was associated with INR ($p < 0.001$; Figure 1). The most common management strategy was a change in coumadin dose ($n=100$, 42.5%), which occurred at a median (interquartile range [IQR]) INR of 1.70 (1.50-1.80). This was followed by no change in management ($n=79$, 33.6%), which occurred at a median (IQR) INR of 1.83 (1.60-1.90). Bridging events occurred the least frequently ($n=56$, 23.8%) at a median (IQR) INR of 1.50 (1.30-1.64). Conclusion: There was a direct relationship between INR and the management strategies of subtherapeutic INRs. At INRs closest to 2, less invasive strategies such as coumadin adjustments or no change were preferred, while bridging strategies (including enoxaparin, heparin, and bivalirudin) were used at lower INRs. The effect of bridging strategies on clinical outcomes including mortality, hospital re-admissions, thromboembolic events, and bleeding are unknown and warrants further evaluation.

Surgery

Huddleston S, Hertz M, Loor G, Garcha P, Hartwig M, Snyder L, Siddique A, Strah H, Kukreja J, Song T, Jablonski R, Smith M, Walia R, Arjuna A, Lozonschi L, Patel K, Katlaps G, **Nemeh H**, Suarez E, Huang H, Langer N, Madsen J, Lee A, Dhillon G, MacArthur J, Keshavamurthy S, Nandavaram S, Daneshmand M, Neujahr D, Bush E, Joyce D, Ardehali A, Budev M, and McCurry K. Impact of National OCS Lung Procurement & Management Program on Post-Transplant Survival - Real World Data from the Thoracic Organ Perfusion (TOP) Post-Approval Registry. *J Heart Lung Transplant* 2023; 42(4):S390. [Full Text](#)

S. Huddleston, University of Minnesota, Minneapolis, MN, United States

Purpose: National OCS Lung Procurement (NOP) of donor lungs utilizes a national network of dedicated cardiothoracic surgical procurement and OCS perfusion experts to procure, perfuse and assess donor lungs from donors to recipients. Using the TOP Registry data, this report compared post-transplant outcomes for lung transplanted using NOP vs traditional center-driven procurement and management of OCS Lung perfusion (Direct). Methods: The TOP registry is a multi-center, all-inclusive observational registry that was established to collect perfusion parameters and post-transplant clinical outcomes for lung transplants performed with donor lungs perfused and assessed on the OCS Lung system. We evaluated the impact of OCS Lung NOP on post-transplant survival in the TOP Registry patient cohort to discern any clinical correlation. We stratified the TOP Registry data between December 2019 and June 2022 into two groups; NOP group and Direct group. Results: Data from 262 OCS Lung transplant recipients in the registry were available for analysis. Of these, 108 patients were in NOP group and 154 patients were in the Direct group. Significant differences were seen in total cross-clamp times NOP 638 (range 285-1,886 mins) vs. Direct 548 mins (range 274-971 mins) ($p=0.004$); and total OCS perfusion time NOP 471 mins (range 162-1624 mins) vs. Direct 384 mins (range 27-858 mins) ($p=0.004$). The 1-year survival, probability was 84.8% in the NOP group, and 81.4% in the Direct group (Log-rank $p=0.436$ - Figure 1) Conclusion: NOP enabled distant procurement of donor lungs while resulting in similar survival

outcomes compared to traditional direct method. This finding demonstrates that NOP is a valid method to enable lung transplant programs to expand their capability to utilize donor lungs from outside the historical standard acceptance radius. Importantly, the NOP could enable better manage transplant procedure logistics and clinical staffing.

Surgery

Loor G, Garcha P, Huddleston S, Hertz M, Hartwig M, Snyder L, Siddique A, Strah H, Kukreja J, Song T, Jablonski R, Smith M, Walia R, Arjuna A, Lozonschi L, Patel K, Katlaps G, **Nemeh H**, Suarez E, Huang H, Langer N, Madsen J, Lee A, Dhillon G, MacArthur J, Keshavamurthy S, Nandavaram S, Daneshmand M, Neujahr D, Bush E, Joyce D, Ardehali A, Budev M, and McCurry K. First Report of the Organ Care System (OCS) Thoracic Organ Perfusion (TOP) Post-Approval Registry. *J Heart Lung Transplant* 2023; 42(4):S20-S21. [Full Text](#)

G. Loor, Cardiothoracic Surgery, Baylor St. Luke's Medical Center, Houston, TX, United States

Purpose: The TOP Registry is a multi-center, all-inclusive observational registry that was established to collect perfusion parameters and post-transplant clinical outcomes for lung transplants performed with donor lungs perfused and assessed on the OCS Lung system in the commercial setting. **Methods:** Registry outcomes were categorized into three groups according to the prespecified analysis populations: Standard criteria donor (SCD), extended criteria donor (ECD), and Other which included retransplants, multi-organ transplants and single lung recipients. All data were prospectively collected and verified in the Registry database. **Results:** At time of submission, 318 patients were transplanted using the OCS Lung system. Complete data on 262 OCS recipients was available for analysis. Of these, 70 (26.7%) were SCD, 137 (52.3%) were ECD, and 55 (20.9%) were Other. Donor and recipient characteristics and risk factors were similar between the groups. Kaplan-Meier survival analysis through 1-year post-transplant showed 85.7% for SCD, 82% for ECD, and 80% for Other ($p=0.654$) Figure 1. Cox regression analysis demonstrated that recipients' LAS score at transplantation was a significant independent predictor for mortality ($p=0.012$) Figure 2. **Conclusion:** This initial report of the TOP Registry shows that the OCS Lung system has been used predominantly in ECD lungs but also in a variety of other scenarios including SCD, multiorgan, retransplants, and single lung transplants. Outcomes in all scenarios were comparable to contemporary lung transplantation in the US with survival determined primarily by the recipient's degree of illness rather than the characteristics of the donor.

Surgery

Loor G, Garcha P, Huddleston S, Hertz M, Hartwig M, Snyder L, Siddique A, Strah H, Kukreja J, Song T, Jablonski R, Smith M, Walia R, Arjuna A, Lozonschi L, Patel K, Katlaps G, **Nemeh H**, Suarez E, Huang H, Langer N, Madsen J, Lee A, Dhillon G, MacArthur J, Keshavamurthy S, Nandavaram S, Daneshmand M, Neujahr D, Bush E, Joyce D, Ardehali A, Budev M, and McCurry K. Impact of OCS Lung Warm Perfusion Times on Post-Transplant Survival - "Real-World" Experience from Thoracic Organ Perfusion (TOP) Registry. *J Heart Lung Transplant* 2023; 42(4):S390-S391. [Full Text](#)

G. Loor, Cardiothoracic Surgery, Baylor St. Luke's Medical Center, Houston, TX, United States

Purpose: The TOP registry is a multi-center, all-inclusive observational registry that was established to collect perfusion parameters and post-transplant clinical outcomes for lung transplants performed with donor lungs perfused and assessed on the OCS Lung system. The current report establishes the association between OCS Lung warm perfusion time and post-transplant survival in the initial TOP Registry cohort. **Methods:** We evaluated the impact of OCS Lung perfusion time on post-transplant survival in the TOP Registry patient cohort to discern any clinical correlation. We defined 3 clinically relevant time points to analyze. Group A: ≤ 6 hours of OCS perfusion, Group B: 6-12 hours of OCS perfusion, and Group C: >12 hours of OCS perfusion. **Results:** Data from 262 OCS lung transplant recipients in the registry were available for analysis. Of these, 70 were standard criteria lungs, 137 were extended criteria including DCD lungs, and 55 were characterized as "other" including single lung, retransplants and multi-organ transplants. There were 129 patients in Group A, 117 patients in Group B, and 12 patients in Group C. The 1-year survival, probability was 83.7% in Group A, 82% in Group B, and 87.5% in Group C Log-rank ($p= 0.793$ - Figure 1). **Conclusion:** OCS Lung system perfusion times were

associated with good post-transplant survival even when extended beyond 12 hours. This finding has two important clinical implications: (1) the OCS Lung can be utilized to transport and preserve donor lungs from outside the recipients' standard acceptance radius; and (2) the OCS Lung can be used to perfuse the donor lungs overnight to better manage transplant procedure logistics.

Surgery

Yaranov DM, Baldrige AS, Chaudhry SP, Gonzalez M, Barr Biglane J, **Tanaka D**, Fischer W, Larkin C, Ullah R, and Pham D. Anticoagulation Bridging In Patients With Heartmate3 Left Ventricular Assist Device: A Regional Analysis Of The Momentum 3 Trial. *J Card Fail* 2023; 29(4):609. [Full Text](#)

Introduction: Advances in left ventricular assist device (LVAD) technologies have led to a significant improvement in pump hemocompatibility. Due to concerns of thromboembolic complications in older generation LVADs, bridging was commonly performed in patients with subtherapeutic INRs. The effects of this strategy on new generation devices are unclear. We analyzed management strategies of subtherapeutic INRs and their effect on outcomes in a subset of patients enrolled in MOMENTUM 3 trial (CAP and IDE). Methods: All patients enrolled in the MOMENTUM 3 trial (CAP and IDE) across 6 centers were screened for inclusion. Patients were included if they underwent implantation of an HMIII device and had a subtherapeutic INR following discharge from their admission for LVAD implant. All episodes of subtherapeutic INR underwent manual chart review to evaluate management strategies taken by clinicians. Strategies were divided into two groups, bridging (with parenteral or intravenous agents) or non-bridging (consisting of adjustments or no change in coumadin dosing). The primary outcome was a composite of death, rehospitalization, CVA, and bleeding events. Results: Of the 225 patients included in the analysis there were total of 235 subtherapeutic INR events. Fifty-six (23.8%) of these INR's were treated with bridging (n= 30 with parenteral agents, n=26 with IV agents) and 179 patients that were not bridged (n=100 coumadin dose adjustment, n=79 no change in coumadin dose). There was no difference in the composite outcome of patients that were bridged compared to those that were not. Conclusion: Subtherapeutic INR is a common event in patients with HM3 LVAD. The management strategy of subtherapeutic INR varies. Management strategy had no effect on mortality, rehospitalization, CVA, or bleeding events.