Sladen Library
Great Research • Great Care • Start Here

HENRY FORD HEALTH

Henry Ford Health Publication List – October 2024

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health personnel. Searches were conducted in PubMed, Embase, Web of Science, CINAHL, and PsycINFO during the month, and then imported into EndNote for formatting. There are 263 unique citations listed this month, including 155 articles and 108 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.

Click the "Full Text" link to view the articles to which Sladen Library provides access. If the full-text of the article is not available, you may request it through ILLiad by clicking on "Request Article," or calling us at (313) 916-2550. If you would like to be added to the monthly email distribution list to automatically receive a PDF of this bibliography, or you have any questions or comments, please contact smoore31@hfhs.org. If your published work has been missed, please use this form to notify us for inclusion on next month's list. All articles and abstracts listed here are deposited into Scholarly Commons, the Henry Ford Health institutional repository.

Articles

Conference Abstracts

Articles

Allergy and Immunology

Eapen AA, Gupta MR, Lockey RF, Bardin PG, and **Baptist AP**. Gastroesophageal reflux disease, laryngopharyngeal reflux, and vocal cord dysfunction/Inducible laryngeal obstruction - overlapping conditions that impact asthma. *J Allergy Clin Immunol* 2024; Epub ahead of print. PMID: 39426423. Full Text

Division of Allergy and Clinical Immunology, Department of Internal Medicine, Henry Ford Health + Michigan State University, Detroit, MI.
Division Immunology, Allergy, and Retrovirology, Texas Children's Hospital and Baylor College of Medicine, Houston, Texas.
Division of Allergy and Immunology, Department of Internal Medicine, University of South Florida Morsani College of Medicine, Tampa, FL.
Monash Lung Sleep Allergy & Immunology AND Hudson Institute and Monash Hospital and University, Melbourne, Australia.
Division of Allergy and Clinical Immunology, Department of Internal Medicine, Henry Ford Health + Michigan State University, Detroit, MI. Electronic address: abaptis1@hfhs.org.

Asthma is a chronic lung condition that may be affected by numerous medical comorbidities. Such comorbidities can influence the presentation and even the severity of asthma. Alternatively, asthma may be misdiagnosed as a comorbidity when symptoms overlap. Three medical conditions that commonly affect asthma management are gastroesophageal reflux disease (GERD), laryngopharyngeal reflux (LPR), and vocal cord dysfunction/Inducible laryngeal obstruction (VCD/ILO). These conditions can be difficult to distinguish from one another, and from asthma itself. In the following review, the epidemiology, pathophysiology, symptomatology, and diagnostic considerations of each condition in both adult and pediatric populations are discussed. Treatment options, and how such options may influence asthma outcomes, are included. Finally, knowledge gaps are highlighted in each area, as a better understanding of the optimal diagnostic and therapeutic approaches will allow for improved individualized care of asthma patients.

Anesthesiology

Alghanem H, Liu NC, Gupta A, Liao C, Wool GD, Rubin DS, and Carll T. Ratios of calcium to citrate administration in blood transfusion for traumatic hemorrhage: A retrospective cohort study. *Transfusion* 2024; Epub ahead of print. PMID: 39351914. Full Text

Department of Anesthesiology, Pain Medicine, and Perioperative Medicine, Henry Ford Health System, Detroit, Michigan, USA.
Department of Anesthesia and Critical Care, University of Chicago, Chicago, Illinois, USA.
Department of Public Health Sciences, University of Chicago, Chicago, Illinois, USA.
Department of Pathology, University of Chicago, Chicago, Illinois, USA.

BACKGROUND: Massive transfusion with citrated blood products causes hypocalcemia, which is associated with mortality. Recognition of this problem has led to increased calcium administration; however, the optimal dosing is still unknown. STUDY DESIGN AND METHODS: This retrospective, single-center study included level 1 trauma patients in 2019 and 2020 who underwent an operation within 12 h of arrival and received a transfusion. Preoperative and intraoperative administrations were totaled to calculate the ratio of administered calcium to the number of blood transfusions for each patient. The citrate content of each blood component was estimated to calculate a second ratio, the ratio of administered calcium to administered citrate. Receiver Operating Characteristic (ROC) curves were performed on both ratios to determine the optimal cutoff values for predicting severe hypocalcemia (ionized calcium <0.9 mmol/L) and hypercalcemia (>1.35 mmol/L) at the end of the intraoperative period. RESULTS: A total of 506 trauma activations were included, receiving a mean of 17.4 citrated blood products and 16.3 mmol of calcium (equivalent to 2400 mg of calcium chloride). No ratio was statistically significant in differentiating severely hypocalcemic patients from the rest. A calcium to blood ratio of

0.903 mmol of administered calcium per citrated blood product differentiated hypercalcemic patients from the rest. DISCUSSION: Quantifying received calcium and citrated blood products was insufficient to predict severe hypocalcemia, suggesting other contributions to hypocalcemia. We demonstrated an upper-limit ratio for calcium administration in traumatic hemorrhage; however, further studies are required to determine what calcium dosing regimen results in the best outcomes.

Anesthesiology
Caruso TJ, Rama A, **Uribe-Marquez S**, and **Mitchell JD**. Pro-Con Debate: Virtual Reality Compared to Augmented Reality for Medical Simulation. *Anesth Analg* 2024; Epub ahead of print. PMID: 39424614. Full Text

From the Division of Pediatric Anesthesiology, Department of Anesthesiology, Perioperative, and Pain Medicine, Stanford University School of Medicine,Stanford, California.
Department of Anesthesiology, Pain Management, and Perioperative Medicine, Henry Ford Health, Detroit, Michigan.

Behavioral Health Services/Psychiatry/Neuropsychology
Chen K, Sun Y, Ni T, Zhu L, **Gui H**, and Guan F. Age effects challenge psychiatric research. *Science* 2024; 386(6721):502. PMID: 39480918. Full Text

Department of Forensic Psychiatry, Key Laboratory of National Health Commission for Forensic Sciences, School of Medicine and Forensics, Xi'an Jiaotong University, Xi'an, China.
Institute of Neuroscience, Bio-evidence Sciences Academy, Xi'an Jiaotong University Health Science Center, Xi'an, China.
Institute of Endocrine and Metabolic Diseases, Shandong University, Jinan, China.
Behavioral Health Services and Psychiatry Research, Henry Ford Health, Detroit, MI, USA.
Department of Psychiatry, Michigan State University, East Lansing, MI, USA.

Behavioral Health Services/Psychiatry/Neuropsychology
Cheng P, **Jennings MB**, **Kalmbach D**, Johnson DA, **Habash S**, Casement MD, and **Drake C**. Neighborhood social vulnerability as a mediator of racial disparities in insomnia severity. *Sleep Health* 2024; Epub ahead of print. PMID: 39477783. Full Text

Sleep Disorders and Research Center, Henry Ford Health, Detroit, Michigan, USA. Electronic address: pcheng1@hfhs.org.
Sleep Disorders and Research Center, Henry Ford Health, Detroit, Michigan, USA.
Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia, USA.
Department of Psychology, University of Oregon, Eugene, Oregon, USA.

STUDY OBJECTIVES: Recent data has indicated that Black Americans experience more severe insomnia compared to their White counterparts. Although previous studies have identified psychosocial mechanisms driving this disparity, little is known about the structural determinants of insomnia disparities. This study tested neighborhood social vulnerability as a mechanism driving Black-White disparities in insomnia severity in the United States. METHODS: Participants with a previous diagnosis of insomnia (N = 196) reported their race and insomnia severity (Insomnia Severity Index). As a measure of the neighborhood environment Social Vulnerability Index was calculated by geocoding home address at the time of participation to the respective census tract from the 2020 US Census. A mediation analysis tested the indirect effect of the Social Vulnerability Index between race and insomnia severity. RESULTS: Black participants reported worse insomnia severity compared to White participants. Black participants also had 3.3 times the odds of living in neighborhoods with higher social vulnerability compared to White participants, with a group median difference of 0.26 percentile points (scale 0 to 1). As hypothesized, results revealed a significant indirect effect of the Social Vulnerability Index, which accounted for 31.1% of the variance between race and insomnia severity. CONCLUSION: Living in a socially vulnerable neighborhood environment may be a mechanism driving racial disparities in insomnia severity. Interventions that consider structural determinants of health, including community-based and policy-level

interventions could have an enhanced impact on addressing insomnia and its public health consequences.

Behavioral Health Services/Psychiatry/Neuropsychology
Lau K, **Patel S**, Rogers K, Smith S, and Riba M. Cancer-Related Lymphedema and Psychological Distress. *Curr Psychiatry Rep* 2024; Epub ahead of print. PMID: 39377989. Full Text

Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, MI, USA.
Department of Psychiatry, University of Michigan, Ann Arbor, MI, USA. Spatel8@hfhs.org.
Department of Psychiatry and Behavioral Medicine, Henry Ford Health, Detroit, MI, USA. Spatel8@hfhs.org.
Department of Occupational Therapy and Lymphedema, University of Michigan, Ann Arbor, MI, USA.
University of Michigan Rogel Cancer Center, Ann Arbor, MI, USA.
Department of Psychiatry, University of Michigan, Ann Arbor, MI, USA.

PURPOSE OF REVIEW: Cancer-related lymphedema (CRL) places an already vulnerable patient population at risk for the development and worsening of psychological distress. The purpose of this review is to highlight factors contributing to distress in lymphedema secondary to breast, head and neck, genitourinary cancers, and melanoma and discuss pertinent treatment considerations. RECENT FINDINGS: Multiple factors contribute to distress in CRL, including changes in body image, sleep, sexuality, functional capacity, and social interaction. There is limited literature describing psychopharmacological considerations in CRL, though exercise, which may be used for the treatment of depression and anxiety, may also improve CRL. Psychiatrists, oncologists, physiatrists, palliative medicine physicians, and physical and occupational therapists should have an awareness and understanding of CRL. To effectively manage distress in these patients, it is crucial to be mindful of psychotropic side-effect profiles, emphasize non-pharmacologic modalities including psychotherapy and exercise, and ensure patients receive evidence-based treatments for CRL.

Behavioral Health Services/Psychiatry/Neuropsychology
Miller-Matero LR, **Hecht LM**, **Gavrilova L**, **Haage B**, **Autio K**, **Tobin ET**, and **Ahmedani BK**. Utilizing primary care to engage underserved patients in a psychological intervention for chronic pain. *Prim Health Care Res Dev* 2024; 25:e54. PMID: 39450755. Full Text

Henry Ford Health, Behavioral Health, Detroit, MI, USA.
Henry Ford Health, Center for Health Policy & Health Services Research, Detroit, MI, USA.
Michigan State University, East Lansing, MI, USA.
Henry Ford Health, Public Health Sciences, Detroit, MI, USA.
Henry Ford Health, Internal Medicine, Detroit, MI, USA.

BACKGROUND: Although psychological interventions can be used to improve chronic pain management, underserved individuals (i.e., racially minoritized and socioeconomically disadvantaged) may be less likely to engage in such services. The purpose of this study was to examine whether offering a psychological intervention for chronic pain in a primary care clinic could be a method in which to successfully engage underserved patients. METHODS: There were 220 patients with chronic pain in a primary care clinic located in a socioeconomically and racially diverse city who were approached to discuss enrolment in a pilot randomized controlled trial of a five-session psychological intervention for chronic pain. Patients were introduced to the study by their primary care provider using the warm handoff model. We compared whether there were sociodemographic differences between those who enrolled in the study and those who declined to enrol. RESULTS: There were no differences between those who enrolled and those who declined enrolment with regard to race, age, insurance type, and household income. However, females were more likely to enrol in the study compared to males. CONCLUSIONS: Recruiting patients to participate in a trial of a psychological intervention for chronic pain in a primary care clinic appeared to be effective for engaging Black patients, patients with lower income, and those with government insurance. Thus, offering a psychological intervention for chronic pain in a primary care clinic may encourage engagement among racially minoritized individuals and those with lower socioeconomic status.

Behavioral Health Services/Psychiatry/Neuropsychology

Miller-Matero LR, **Pappas C**, **Altairi S**, **Sehgal M**, Chrusciel T, Salas J, Secrest S, Wilson L, Carpenter RW, Sullivan MD, **Ahmedani BK**, Lustman PJ, and Scherrer JF. Alcohol, Tobacco, and Marijuana use Among Individuals Receiving Prescription Opioids for Pain Management. *Clin J Pain* 2024; Epub ahead of print. PMID: 39470110. Full Text

Behavioral Health, Henry Ford Health.
Center for Health Policy and Health Services Research, Henry Ford Health.
Department of Family and Community Medicine, Saint Louis University School of Medicine.
Advanced HEAlth Data (AHEAD) Research Institute, Saint Louis University School of Medicine.
Department of Health and Clinical Outcomes Research, Saint Louis University School of Medicine.
Department of Psychological Sciences, University of Missouri - St. Louis.
Department of Psychiatry and Behavioral Science, University of Washington School of Medicine.
Department of Psychiatry, Washington University School of Medicine.
Department of Psychiatry and Behavioral Neuroscience, Saint Louis University School of Medicine.

OBJECTIVE: Substance use among individuals receiving prescription opioids for pain may be associated with poorer functioning. The purpose was to examine whether use of substances (i.e., alcohol, marijuana, or tobacco) among individuals prescribed opioids for pain management was associated with pain, psychiatric disorders, and opioid misuse. METHODS: Patients with non-cancer pain and a new opioid prescription were recruited from two health systems. Participants (N= 827) completed measures regarding pain severity, pain interference, psychiatric symptoms, and substance use. RESULTS: Substance use was common with 58.0%, 26.2%, and 28.9% reporting alcohol, tobacco, and marijuana use, respectively. Use of tobacco or marijuana was associated with poorer functioning. Those with tobacco use had greater pain severity, interference, number of pain sites, and concern for opioid misuse, and were more likely to have probable depression, anxiety, and PTSD. Participants reporting marijuana use were more likely to have higher concern for opioid misuse scores and probable depression, anxiety, and PTSD. Use of alcohol was associated with lower pain severity and interference and fewer number of pain sites. DISCUSSION: Substance use is common among individuals receiving prescription opioids. Some types of substance use may be related to poorer opioid, pain, and psychiatric functioning. Clinicians prescribing opioids for pain management should assess for substance use, including tobacco, and be aware of the association with poorer functioning. Interventions could target pain, psychiatric symptoms, and substance use simultaneously to optimize outcomes for individuals with pain and substance use.

Behavioral Health Services/Psychiatry/Neuropsychology

Reffi AN, **Cheng P**, **Kalmbach DA**, **Moore DA**, **Mahr GC**, Seymour GM, **Solway M**, and **Drake CL**. Understanding nightmares after traumatic events in Detroit (UNiTED): prospective associations with interpersonal violence and posttraumatic stress disorder symptoms. *Eur J Psychotraumatol* 2024; 15(1):2409561. PMID: 39376120. Full Text

Sleep Disorders & Research Center, Henry Ford Health, Detroit, MI, USA.
Department of Psychiatry, Michigan State University College of Human Medicine, Grand Rapids, MI, USA.
Department of Surgery, Division of Acute Care Surgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Psychiatry and Behavioral Health, Division of Consultation Liaison Psychiatry, Henry Ford Hospital, Detroit, MI, USA.
Department of Psychology, University of Kentucky, Lexington, Kentucky, USA.
Department of Psychiatry, Henry Ford Hospital, Detroit, MI, USA.

ABSTRACTBackground: Research suggests trauma-related nightmares (TRNs) during the acute aftermath of trauma may contribute to posttraumatic stress disorder (PTSD). However, it is unknown who is most vulnerable to TRNs, which is critical to identify at-risk patients toward whom early nightmare-focused treatments can be targeted to prevent PTSD.Objective: We tested trauma type (interpersonal violence [e.g. assault] vs non-interpersonal trauma [e.g. motor vehicle collision]) as a risk factor for TRNs

in a predominantly low-income, Black, urban sample in Detroit, MI, USA.Method: We recruited patients from the intensive care unit following traumatic injury (N = 88; M(age) = 39.53 ± SD 14.31 years, 67.0% male, 67.0% Black, 47.7% annual income ≤ $20,000) and administered surveys at three post trauma timepoints: one week (T1), one month (T2; n = 61), and two months (T3; n = 59). Trauma type was assessed at T1 via electronic medical records. Participants reported the extent to which their dreams' content was similar to the trauma for which they were hospitalized across T1-T3. Participants then completed the PTSD Checklist for DSM-5 at T3.Results: TRNs were more prevalent over time among patients exposed to interpersonal violence (80%) vs non-interpersonal trauma (48.7%, p = .005). Patients hospitalized for interpersonal violence faced greater odds for TRNs across timepoints relative to non-interpersonal trauma patients (Odds Ratio = 4.95, p = .021). TRNs, in turn, prospectively predicted PTSD symptoms such that TRNs at T2 presaged more severe PTSD at T3 (p = .040, η(p)(2)= .31), above and beyond T1 PTSD status.Conclusions: This prospective study provides first evidence that interpersonal violence exposure is a robust risk factor for TRNs, which prospectively contribute to PTSD symptom development. Early intervention on TRNs after interpersonal violence exposure may decrease PTSD risk. Future studies are encouraged to use ambulatory methods to capture nightmares sooner after they occur. Interpersonal violence exposure is a risk factor for trauma-related nightmaresTrauma-related nightmares predict PTSD symptoms, above and beyond baseline PTSDTreating nightmares early after interpersonal violence may decrease PTSD risk.
eng

Cardiology/Cardiovascular Research

Abdelradi A, Mosleh W, Kattel S, **Al-Jebaje Z**, Tajlil A, Pokharel S, and Sharma UC. Galectin-3 Predicts Long-Term Risk of Cerebral Disability and Mortality in Out-of-Hospital Cardiac Arrest Survivors. *J Pers Med* 2024; 14(9). PMID: 39338248. Full Text

Division of Cardiology, Department of Medicine, Jacob's School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY 14068, USA.
Division of Cardiovascular Medicine, Department of Medicine, University of Minnesota, Minneapolis, MN 55455, USA.
Division of Cardiovascular Medicine, Department of Medicine, Henry Ford Health System, Detroit, MI 48202, USA.
Division of Thoracic Pathology and Oncology, Department of Pathology, Roswell Park Comprehensive Cancer Center, Buffalo, NY 14203, USA.

BACKGROUND: Out-of-hospital cardiac arrest (OHCA) is associated with high mortality and cerebral disability in survivors. Current models of risk prediction and survival are mainly based on resuscitation duration. We examined the prognostic value of circulating biomarkers in predicting mortality and severe cerebral disability for OHCA survivors, alongside traditional clinical risk indicators. METHODS: Biomarkers including BNP, troponin I, and galectin-3 were measured at hospital admission in resuscitated OHCA patients. Prognostic significance for mortality and cerebral disability involving circulating biomarkers, resuscitation duration, demographics, and laboratory and clinical characteristics was examined via univariate and multivariate Cox proportional hazards regression models. The incremental prognostic value of the index covariates was examined through model diagnostics, focusing on the Akaike information criterion (AIC) and Harrell's concordance statistic (c-statistic). RESULTS: In a combinatorial analysis of 144 OHCA survivors (median follow-up 5.7 years (IQR 2.9-6.6)), BNP, galectin-3, arterial pH, and resuscitation time were significant predictors of all-cause death and severe cerebral disability, whereas troponin I levels were not. Multivariate regression, adjusting for BNP, arterial pH, and resuscitation time, identified galectin-3 as an independent predictor of long-term mortality. Multiple linear regression models also confirmed galectin-3 as the strongest predictor of cerebral disability. The incorporation of galectin-3 into models for predicting mortality and cerebral disability enhanced fit and discrimination, demonstrating the incremental value of galectin-3 beyond traditional risk predictors. CONCLUSIONS: Galectin-3 is a significant, independent long-term risk predictor of cerebral disability and mortality in OHCA survivors. Incorporating galectin-3 into current risk stratification models may enhance early prognostication and guide targeted clinical interventions.

Cardiology/Cardiovascular Research

Al Jebaje Z, **Jabri A**, **Mishra T**, **Halboni A**, **Ayyad A**, **Alameh A**, **Ellauzi R**, **Alexandrino FB**, **Alaswad K**, and **Basir MB**. Use of mechanical circulatory support in high-risk percutaneous coronary interventions. *Prog Cardiovasc Dis* 2024; Epub ahead of print. PMID: 39442599. Full Text

Henry Ford Health System, Detroit, MI, USA. Electronic address: zaljeb1@hfhs.org.
Henry Ford Health System, Detroit, MI, USA.

As the field of percutaneous coronary intervention grows in volume, expertise, and available tools, interventional cardiologists are increasingly performing more complex and higher-risk coronary artery procedures. Mechanical circulatory support devices, previously used only in urgent situations, are now being utilized as supplementary tools to enhance outcomes in elective complex cases. This shift has sparked significant discussions about patient and device selection, as well as the potential risks involved. In this article, we explore the various devices and their distinct features. Additionally, we also introduce algorithms for device selection, placement and weaning to help guide physicians during their care for their high-risk PCI patients.

Cardiology/Cardiovascular Research

Alaswad K, and Jabri A. Another Frontier to Conquer in Coronary Chronic Total Occlusion: Aorto-Ostial Lesions. *JACC Cardiovasc Interv* 2024; 17(19):2256-2258. PMID: 39415384. Full Text

Division of Cardiology, Henry Ford Hospital, Detroit, Michigan, USA; Michigan State University, College of Human Medicine, East Lansing, Michigan, USA. Electronic address: kalaswa1@hfhs.org.
Department of Cardiovascular Medicine, William Beaumont University Hospital, Corewell Health East, Royal Oak, Michigan, USA.

Cardiology/Cardiovascular Research

Alexandrou M, Rempakos A, Mutlu D, Strepkos D, Carvalho PEP, Al Ogaili A, Bahbah A, Milkas A, Tsiafoutis I, **Alaswad K**, **Basir MB**, Davies R, Jaffer FA, Nicholson W, Azzalini L, Gorgulu S, Khatri JJ, Bangalore S, Rangan BV, Mastrodemos OC, Burke MN, Sandoval Y, and Brilakis ES. Artificial intelligence for predicting primary antegrade wiring success of chronic total occlusion crossing. *J Invasive Cardiol* 2024; Epub ahead of print. PMID: 39356730. Request Article

Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota, USA.
Athens Naval and Veterans Hospital, Athens, Greece.
Red Cross Hospital of Athens, Athens, Greece.
Henry Ford Cardiovascular Division, Detroit, Michigan, USA.
WellSpan York Hospital, York, Pennsylvania, USA.
Massachusetts General Hospital, Boston, Massachusetts, USA.
Emory University Hospital Midtown, Atlanta, Georgia, USA.
Division of Cardiology, Department of Medicine, University of Washington, Seattle, Washington, USA.
Biruni University Medical School, Istanbul, Turkey.
Cleveland Clinic, Cleveland, Ohio, USA.
Division of Cardiology, New York University, New York, USA.
Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota, USA. Email: esbrilakis@gmail.com.

Cardiology/Cardiovascular Research

Arnold SV, Hahn RT, Thourani VH, Makkar R, Makar M, Sharma RP, Haeffele C, Davidson CJ, Narang A, **O'Neill B**, **Lee J**, Yadav P, Zahr F, Chadderdon S, Eleid M, Pislaru S, Smith R, Szerlip M, Whisenant B, Sekaran N, Garcia S, Stewart-Dehner T, Grayburn PA, Sannino A, Snyder C, Zhang Y, Mack MJ, Leon MB, Lurz P, Kodali S, and Cohen DJ. Quality of Life After Transcatheter Tricuspid Valve Replacement: 1-Year Results From TRISCEND II Pivotal Trial. *J Am Coll Cardiol* 2024; Epub ahead of print. PMID: 39480380. Full Text

Saint Luke's Mid America Heart Institute/University of Missouri-Kansas City, Kansas City, Missouri, USA. Electronic address: sarnold@saint-lukes.org.
Columbia University Irving Medical Center, New York, New York, USA.
Piedmont Heart Institute, Atlanta, Georgia, USA.
Cedars-Sinai Medical Center, Los Angeles, California, USA.
Stanford University, Stanford, California, USA.
Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA.
Henry Ford Hospital, Detroit, Michigan, USA.
Oregon Health and Science University, Portland, Oregon, USA.
Mayo Clinic, Rochester, Minnesota, USA.
Baylor Scott & White The Heart Hospital-Plano, Plano, Texas, USA.
Intermountain Medical Center, Murray, Utah, USA.
Christ Hospital, Cincinnati, Ohio, USA.
Baylor Scott & White The Heart Hospital-Plano, Plano, Texas, USA; Baylor Scott and White Research Institute Cardiac Imaging Core Laboratory, Plano, Texas, USA.
Baylor Scott and White Research Institute Cardiac Imaging Core Laboratory, Plano, Texas, USA.
Cardiovascular Research Foundation, New York, New York, USA.
University Medical Center Mainz, Mainz, Germany.
Cardiovascular Research Foundation, New York, New York, USA; St Francis Hospital, Roslyn, New York, USA.

BACKGROUND: Severe tricuspid regurgitation (TR) often causes substantial impairment in patient-reported health status (ie, symptoms, physical and social function, and quality of life), which may improve with transcatheter tricuspid valve replacement (TTVR). OBJECTIVES: We performed an in-depth analysis of health status of patients enrolled in the TRISCEND (Edwards EVOQUE Transcatheter Tricuspid Valve Replacement: Pivotal Clinical Investigation of Safety and Clinical Efficacy using a Novel Device) II pivotal trial to help quantify the benefit of intervention to patients. METHODS: The TRISCEND II pivotal trial randomized 400 patients with symptomatic and severe or greater TR 2:1 to TTVR with the EVOQUE tricuspid valve replacement system plus optimal medical therapy (OMT) or OMT alone. Health status was assessed with the Kansas City Cardiomyopathy Questionnaire and the 36-Item Short Form Health Survey. Changes in health status over 1 year were compared between treatment groups using mixed-effects repeated-measures models. RESULTS: The analysis cohort included 392 patients, of whom 259 underwent attempted TTVR and 133 received OMT alone (mean age 79.2 ± 7.6 years, 75.5% women, 56.1% with massive or torrential TR). Patients had substantially impaired health status at baseline (mean Kansas City Cardiomyopathy Questionnaire Overall Summary Score [KCCQ-OS] 52.1 ± 22.8; mean 36-Item Short Form Health Survey physical component summary score 35.2 ± 8.4). TTVR+OMT patients reported significantly greater improvement in both disease-specific and generic health status at each follow-up time point. Mean between-group differences in the KCCQ-OS favored TTVR+OMT at each time point: 11.8 points (95% CI: 7.4-16.3 points) at 30 days, 20.8 points (95% CI: 16.1-25.5 points) at 6 months, and 17.8 points (95% CI: 13.0-22.5 points) at 1 year. In subgroup analyses, TTVR+OMT improved health status to a greater extent among patients with torrential or massive TR vs severe TR (treatment effect 23.3 vs 22.6 vs 11.3; interaction P = 0.049). At 1 year, 64.6% of TTVR+OMT patients were alive and well (KCCQ-OS ≥60 points and no decline of ≥10 points from baseline) compared with 31.0% with OMT alone. CONCLUSIONS: Compared with OMT alone, treatment of patients with symptomatic and severe or greater TR with TTVR+OMT resulted in substantial improvement in patients' symptoms, function, and quality of life. These benefits were evident 30 days after TTVR, continued to increase through 6 months, and remained durable through 1 year. (TRISCEND II Pivotal Trial [Edwards EVOQUE Transcatheter Tricuspid Valve Replacement: Pivotal Clinical Investigation of Safety and Clinical Efficacy using a Novel Device]; NCT04482062).

Cardiology/Cardiovascular Research

Ayyad A, **Fadel R**, **Kollman P**, **Parson A**, **Almajed MR**, **Shadid AM**, **Jabri A**, **Basir MB**, and **Alqarqaz M**. Surviving venoarterial extracorporeal membrane oxygenation (VA-ECMO): The roles of severity scores and post-operative lactate clearance. *Cardiovasc Revasc Med* 2024; Epub ahead of print. PMID: 39477754. Full Text

Henry Ford Hospital, Internal Medicine Department, Detroit, MI, USA. Electronic address: asemayyad96@gmail.com.
Henry Ford Hospital, Cardiology Department, Detroit, MI, USA.
Wayne State University, Detroit, MI, USA.
Henry Ford Hospital, Internal Medicine Department, Detroit, MI, USA.

BACKGROUND: This study investigated the association of the Survival After VA-ECMO (SAVE) score, Sequential Organ Failure Assessment (SOFA) score, and post-cannulation lactate levels with mortality among patients treated with veno-arterial extra-corporeal membrane oxygenation (VA-ECMO) for refractory cardiogenic shock (CS). METHODS: We performed a retrospective review of adult patients who underwent peripheral VA-ECMO cannulation from January 2018 to September 2022 at a quaternary care center. All-cause in-hospital mortality was assessed and compared to predicted mortality by SAVE and SOFA scores prior to cannulation, with adjusted odds ratio of risk factors for mortality identified by multivariate logistic regression analysis. Additionally, the prognostic value of 8-h post-cannulation serum lactate levels was analyzed by receiver operating characteristic (ROC) curve and Kaplan Meier analysis of 30-day survival. RESULTS: 244 patients were included in final analysis. All-cause in-hospital mortality was 70 %, and 54 % of patients died while on ECMO or within 24 h of decannulation. Pre-cannulation SAVE score (OR 0.93 per unit increase, 95 % CI 0.86-0.99, p = 0.008), SOFA score (OR 1.54 per unit increase, 95 % CI 1.32-1.75), and 8-h post-cannulation lactate levels (OR 1.20 per mmol/L increase, 95 % CI 1.04-1.36, p = 0.008) were independently associated with all-cause in-hospital mortality. 8-h post-cannulation lactate levels ≥5.3 mmol/L demonstrated high specificity for in-hospital mortality (90.0 %), while levels ≥7.8 mmol/L were demonstrated high specificity for VA-ECMO death (91.1 %). These thresholds were significantly associated with 30-day all-cause mortality (p < 0.001). CONCLUSION: Pre-cannulation SAVE and SOFA scores are useful prognostic tools in patients with CS. 8-h post-cannulation serum lactate levels are a pragmatic biomarker and can further assist in prognostication of patients on VA-ECMO, and the cutoffs of 5.3 mmol/L and 7.8 mmol/L have high specificity for all-cause mortality and VA-ECMO mortality, respectively. The development of accurate prognostic tools is critical in managing and optimizing care for patients with CS.

Cardiology/Cardiovascular Research

Basir MB, Bentley D, Truesdell AG, Kunkel K, Lemor A, Megaly M, **Alqarqaz M**, **Alaswad K**, **Khandewal A**, Jortberg E, Kalra S, Kaki A, Burkhoff D, Moses JW, Pinto DS, Stone GW, and **O'Neill WW**. Clinical Outcomes of Patients Experiencing Transient Loss of Pulse Pressure During High-Risk PCI with Impella. *J Card Fail* 2024; 30(10):1287-1299. PMID: 39389740. Full Text

Division of Cardiology, Henry Ford Hospital, Detroit, Michigan. Electronic address: Mbasir1@hfhs.org.
Abiomed Inc, Danvers, Massachusetts.
Virginia Heart / Inova Heart and Vascular Institute, Falls Church, Virginia.
Division of Cardiology, Piedmont Health, Atlanta, Georgia.
Division of Cardiology, University of Mississippi Medical Center, Jackson, Mississippi.
Division of Cardiology, Willis Knighton Heart Institute, Shreveport, Louisiana.
Division of Cardiology, Henry Ford Hospital, Detroit, Michigan.
Division of Cardiology, Toronto General Hospital, Toronto, Ontario, Canada.
Division of Cardiology, St John's Hospital, Detroit, Michigan.
Cardiovascular Research Foundation, New York, New York.
Cardiovascular Research Foundation, New York, New York; Division of Cardiology, St Francis Heart Center, Roslyn, New York.
Division of Cardiology, Beth Israel Deaconess Hospital, Boston, Massachusetts.
Division of Cardiology, Mount Sinai Hospital, New York, New York.

BACKGROUND: Patients experiencing loss of pulse pressure (LOPP) during high-risk percutaneous coronary intervention (HR-PCI) are transiently dependent on mechanical circulatory support devices. We sought to define the frequency and clinic outcomes of patients who experience LOPP during HR-PCI. METHODS AND RESULTS: Patients enrolled in the PROTECT III study and had automated Impella controller logs capturing real-time hemodynamics were included in this analysis. A LOPP event was defined as a mean pulse pressure on Impella of <20 mm Hg for ≥5 seconds during PCI. Clinical

characteristics and outcomes were then compared between those with and without LOPP. Logistic regression identified clinical and hemodynamic predictors of LOPP. We included 302 patients, of whom 148 patients (49%) experienced LOPP. Age, sex, and comorbidities were similar in patients with and without LOPP. Mean baseline systolic blood pressure (118.6 mm Hg vs 129.8 mm Hg; P < .001) and mean arterial pressure (86.9 mm Hg vs 91.6 mm Hg; P = .011) were lower in patients with LOPP, whereas heart rate (78 bpm vs 73 bpm; P = .012) was higher. Anatomical complexity was similar between groups. Patients with LOPP were more likely to experience major adverse cardiac and cerebrovascular events (23.5% vs 8.8%; P = .002), acute kidney injury (10.1% vs 2.6%; P = .030), and death (20.2% vs 7.9%; P = .008) within 90 days. A low baseline systolic blood pressure and cardiomyopathy were the strongest predictors of LOPP (P = .003 and P = .001, respectively). CONCLUSIONS: LOPP on Impella during HR-PCI was common and occurred more frequently in patients with cardiomyopathy and a low systolic blood pressure. LOPP was strongly associated with higher 90-day major adverse cardiac and cerebrovascular events, acute kidney injury, and mortality. Condensed Abstract We sought to define the frequency and clinic outcomes of patients who experience LOPP during high-risk percutaneous coronary intervention (HR-PCI). We included 302 patients, of whom 148 (49%) experienced LOPP. Patients with LOPP were more likely to experience major adverse cardiac and cerebrovascular events (23.5% vs 8.8%; P = .002), acute kidney injury (10.1% vs 2.6%; P = .030), and death (20.2% vs 7.9%; P = .008) within 90 days. A low baseline systolic blood pressure and cardiomyopathy were the strongest predictors of LOPP (P = .003 and P = .001, respectively).

Cardiology/Cardiovascular Research

Carnicelli AP, **Cowger J**, Tedford RJ, and Kanwar M. Authors' Response to Comment and Opinion. *J Heart Lung Transplant* 2024; Epub ahead of print. PMID: 39341422. Full Text

Division of Cardiology, Department of Medicine, Medical University of South Carolina, Charleston, SC, USA.
Cardiovascular Medicine, Henry Ford Hospital, Detroit, MI, USA.
Cardiovascular Institute at Allegheny Health Network, Pittsburgh, PA, USA.

Cardiology/Cardiovascular Research

Carvalho PEP, Strepkos D, Alexandrou M, Mutlu D, Ser OS, Choi JW, Gorgulu S, Jaffer FA, Chandwaney R, **Alaswad K**, **Basir MB**, Azzalini L, Ozdemir R, Uluganyan M, Khatri J, Young L, Poommipanit P, Aygul N, Davies R, Krestyaninov O, Khelimskii D, Goktekin O, Akyel A, Tuner H, Rafeh NA, Elguindy A, Rangan BV, Mastrodemos OC, Voudris K, Burke MN, Sandoval Y, and Brilakis ES. Intravascular Lithotripsy versus Rotational Atherectomy in Coronary Chronic Total Occlusions: Analysis from the PROGRESS-CTO registry. *Am J Cardiol* 2024; Epub ahead of print. PMID: 39454696. Full Text

Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota, USA.
Texas Health Presbyterian Hospital, Dallas, TX, USA.
Biruni University Medical School, Istanbul, Turkey.
Massachusetts General Hospital, Boston, MA, USA.
Oklahoma Heart Institute, Tulsa, OK, USA.
Henry Ford Cardiovascular Division, Detroit, MI, USA.
Division of Cardiology, Department of Medicine, University of Washington, Seattle, WA, USA.
Bezmiâlem Vakıf University, Istanbul, Turkey.
Cleveland Clinic, Cleveland, OH, USA.
University Hospitals, Case Western Reserve University, Cleveland, OH, USA.
Selcuk University, Konya, Turkey.
WellSpan Health, York, PA, USA.
Meshalkin Novosibirsk Research Institute, Novosibirsk, Russia.
Memorial Bahcelievler Hospital, Istanbul, Turkey.
North Oaks Health System, Hammond, Louisiana, USA.
Aswan Heart Centre, Magdi Yacoub Foundation, Aswan, Egypt.
Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota, USA. Electronic address: esbrilakis@gmail.com.

BACKGROUND: There is limited comparative data on the use of plaque modification devices during chronic total occlusion (CTO) percutaneous coronary intervention (PCI). METHODS: We compared intravascular lithotripsy (IVL) with rotational atherectomy (RA) for lesion preparation in patients who underwent CTO PCI across 50 US and non-US centers from 2019 to 2024. RESULTS: Among 15,690 patients who underwent CTO PCI during the study period, 436 (2.78%) underwent IVL and 381 (2.45%) RA. Patients treated with IVL had more comorbidities and more complex CTO lesions. Antegrade wiring was the most commonly used initial and successful crossing strategy for lesions treated with both IVL and RA, although the retrograde approach was more frequently employed in IVL cases. Procedure and fluoroscopy times, as well as air kerma radiation doses and contrast volumes, were higher in patients treated with RA compared with IVL. There were no significant differences between the groups in technical success (97.2% vs. 95.3%, p=0.20), procedural success (94.7% vs. 91.8%, p=0.14), and in-hospital major adverse cardiac events (MACE) (3.0 % vs. 4.2%, p=0.47). However, coronary perforations were more frequent in patients undergoing RA (9.5% vs. 3.2%, p<0.001). Multivariable logistic regression analysis revealed that IVL compared with RA was not independently associated with technical success, procedural success, or in-hospital MACE. CONCLUSIONS: In patients undergoing CTO PCI, IVL is associated with similar in-hospital MACE, technical success, and procedural success, but lower incidence of coronary perforation, compared with RA.

Cardiology/Cardiovascular Research

Coyne P, **Susick L**, **Schultz L**, **Santarossa S**, **Gough P**, **Rice S**, **Brewster N**, **Behrendt R**, and **Bilicki V**. Using Care Navigation to Improve Patient-Reported Outcomes Among Older Adult Patients: Preliminary Results From a Pilot Study. *J Patient Exp* 2024; 11:23743735241272152. PMID: 39484230. Full Text

Department of Public Health Sciences, Henry Ford Health, Detroit, MI, USA. RINGGOLD: 2971
Henry Ford Health + Michigan State University Health Sciences, East Lansing, MI, USA. RINGGOLD: 657020
College of Human Medicine, Michigan State University, East Lansing, MI, USA. RINGGOLD: 12268
Department of Care Experience, Henry Ford Health, Detroit, MI, USA.

Navigating health and social care in the United States can be difficult for people of all ages, but older adults often have multiple health problems, chronic illnesses, and disabilities that can increase the complexities of their care. To assist older adult patients and/or their caregivers with coordinating care, and providing information, advocacy, and resources, Henry Ford Health (HFH) implemented a Senior Care Navigation Program (SCNP). Older HFH patients or their caregivers were referred to the SCNP either by a provider or another member of their care team. A senior navigator (SN) then reached out to the patient/caregiver by telephone to discuss the SCNP and their support/care needs. The SN scheduled follow-up calls as needed. Patients/caregivers enrolled in Phase 1 of this pilot program were given the option to join the evaluation group. These patients were interviewed by an independent research interviewer at baseline, 3-, 6-, and 9-month post initial contact to complete 5 patient-reported outcomes measures. Our Phase 1 pilot has demonstrated significant improvements in the EQ5D (health-related quality of life) and two patient-reported outcomes measurement information system (PROMIS) measures (depression and anxiety) suggesting that the SCNP program at HFH is having a positive impact on older adult patients' health and well-being. In Phase 2, we will further evaluate the impact of the SCNP on healthcare utilization.

Cardiology/Cardiovascular Research

Deshmukh A, Yokokawa M, McBride D, Simpson J, **Chou A**, Ghannam M, Liang JJ, Saeed M, Cunnane R, Ghanbari H, Latchamsetty R, Crawford T, Jongnarangsin K, Pelosi F, Jr., Chugh A, Morady F, Bogun F, and Oral H. Dofetilide for the treatment of premature ventricular complexes and ventricular tachycardia in patients with structural heart disease. *J Cardiovasc Electrophysiol* 2024; Epub ahead of print. PMID: 39363447. Full Text

Division of Cardiovascular Medicine, Cardiac Arrhythmia Service, University of Michigan, Ann Arbor, Michigan, USA.

Henry Ford Heart and Vascular Institute, Henry Ford Hospital, Detroit, Michigan, USA.

BACKGROUND: Dofetilide is a class III antiarrhythmic agent approved for the treatment of atrial fibrillation and atrial flutter. Given the efficacy of other class III agents, it has been used off-label for the treatment of premature ventricular complexes (PVCs) and ventricular tachycardias (VTs). OBJECTIVE: The purpose of this study was to determine the efficacy and safety of dofetilide for ventricular arrythmias (VAs). METHODS: In this retrospective cohort study, 81 patients (59 men; age = 60 ± 14 years; LVEF = 0.34 ± 0.16) were admitted for dofetilide initiation to treat PVCs (29), VTs (42) or both (10). A ≥ 80% decrease in PVC burden was defined as a satisfactory response. An ICD was present in 72 patients (89%). Another antiarrhythmic was previously used in 50 patients (62%). Prior catheter ablation had been performed in 33 patients (41%). RESULTS: During intitiation, dofetilide was discontinued in 12 patients (15%) due to QT prolongation (8) and inefficacy to suppress VAs (4). Among the 32 patients with PVCs who successfully started dofetilide, the mean PVC burden decreased from 20 ± 10% to 8 ± 8% at a median follow-up of 2.6 months ($p < .001$). PVC burden was reduced by ≥80% in only 11/32 patients (34%). During 7 ± 1 years of follow-up, 41/69 patients (59%) continued to have VAs and received appropriate ICD therapies for monomorphic VTs (35) and polymorphic VT/VF (6) at a median of 8.0 (IQR 2.6-33.2) months. Dofetilide had to be discontinued in 50/69 patients (72%) due to inefficacy or intolerance. The composite outcome of VT/VF recurrence, heart transplantation, or death occurred in 6/12 patients (50%) without dofetilide and 49/69 patients (71%) with dofetilide. The event free survival was similar between patients treated with and without dofetilide (log-rank $p = .55$). CONCLUSIONS: Treatment with dofetilide was associated with a decrease in PVCs, however clinically significant suppression occurred in a minority of patients. Dofetilide failed to suppress the occurrence of VTs in a majority of patients.

Cardiology/Cardiovascular Research

Fang JX, **Giustino G**, **Villablanca PA**, **O'Neill BP**, **Alrayes H**, **Selektor Y**, **Lee JC**, **Engel Gonzalez P**, **O'Neill WW**, and **Frisoli TM**. The Challenge of Transcatheter Aortic Valve Replacement in Quadricuspid Aortic Valve With Pure Insufficiency. *JACC Cardiovasc Interv* 2024; Epub ahead of print. PMID: 39466210. Full Text

Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan, USA. Electronic address: fangjonathan@gmail.com.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan, USA.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan, USA. Electronic address: tfrisoli@gmail.com.

Cardiology/Cardiovascular Research

Généreux P, Schwartz A, Oldemeyer JB, Pibarot P, Cohen DJ, Blanke P, Lindman BR, Babaliaros V, Fearon WF, Daniels DV, Chhatriwalla AK, Kavinsky C, Gada H, Shah P, Szerlip M, Dahle T, Goel K, **O'Neill W**, Sheth T, Davidson CJ, Makkar RR, Prince H, Zhao Y, Hahn RT, Leipsic J, Redfors B, Pocock SJ, Mack M, and Leon MB. Transcatheter Aortic-Valve Replacement for Asymptomatic Severe Aortic Stenosis. *N Engl J Med* 2024; Epub ahead of print. PMID: 39466903. Full Text

From Gagnon Cardiovascular Institute, Morristown Medical Center, Morristown, NJ (P.G.); Columbia University Medical Center/New York Presbyterian Hospital (A.S., R.T.H., M.B.L.), the Cardiovascular Research Foundation (D.J.C., R.T.H., B.R., M.B.L.), and Weill Cornell Medicine (B.R.), New York, and St. Francis Hospital and Heart Center, Roslyn (D.J.C.) - all in New York; University of Colorado Health, Medical Center of the Rockies, Loveland (J.B.O.); Laval University, Quebec, QC (P.P.), St. Paul's Hospital, University of British Columbia, Vancouver (P.B., J.L.), and McMaster University, Hamilton, ON (T.S.) - all in Canada; Vanderbilt University Medical Center, Nashville (B.R.L., K.G.); Emory University, Atlanta (V.B.); the Division of Cardiovascular Medicine and Stanford Cardiovascular Institute, Stanford University, Stanford (W.F.F.), VA Palo Alto Health Care System, Palo Alto (W.F.F.), California Pacific Medical Center, San Francisco (D.V.D.), Cedars-Sinai Medical Center, Los Angeles (R.R.M.), and Edwards Lifesciences, Irvine (H.P., Y.Z.) - all in California; Saint Luke's Mid America Heart Institute, Kansas City, MO (A.K.C.); Beth Israel Deaconess Medical Center/Harvard Medical School (C.K.) and Brigham and Women's Hospital (P.S.) - both in Boston; Pinnacle Health Harrisburg, Harrisburg, PA

(H.G.); Baylor Scott and White The Heart Hospital Plano, Plano, TX (M.S., M.M.); CentraCare Heart and Vascular Center, St. Cloud, MN (T.D.); Henry Ford Hospital, Detroit (W.O.); Northwestern University, Chicago (C.J.D.); Gothenburg University/Sahlgrenska University Hospital, Gothenburg, Sweden (B.R.); and London School of Hygiene and Tropical Medicine, London (S.J.P.).

BACKGROUND: For patients with asymptomatic severe aortic stenosis and preserved left ventricular ejection fraction, current guidelines recommend routine clinical surveillance every 6 to 12 months. Data from randomized trials examining whether early intervention with transcatheter aortic-valve replacement (TAVR) will improve outcomes in these patients are lacking. METHODS: At 75 centers in the United States and Canada, we randomly assigned, in a 1:1 ratio, patients with asymptomatic severe aortic stenosis to undergo early TAVR with transfemoral placement of a balloon-expandable valve or clinical surveillance. The primary end point was a composite of death, stroke, or unplanned hospitalization for cardiovascular causes. Superiority testing was performed in the intention-to-treat population. RESULTS: A total of 901 patients underwent randomization; 455 patients were assigned to TAVR and 446 to clinical surveillance. The mean age of the patients was 75.8 years, the mean Society of Thoracic Surgeons Predicted Risk of Mortality score was 1.8% (on a scale from 0 to 100%, with higher scores indicating a greater risk of death within 30 days after surgery), and 83.6% of patients were at low surgical risk. A primary end-point event occurred in 122 patients (26.8%) in the TAVR group and in 202 patients (45.3%) in the clinical surveillance group (hazard ratio, 0.50; 95% confidence interval, 0.40 to 0.63; P<0.001). Death occurred in 8.4% of the patients assigned to TAVR and in 9.2% of the patients assigned to clinical surveillance, stroke occurred in 4.2% and 6.7%, respectively, and unplanned hospitalization for cardiovascular causes occurred in 20.9% and 41.7%. During a median follow-up of 3.8 years, 87.0% of patients in the clinical surveillance group underwent aortic-valve replacement. There were no apparent differences in procedure-related adverse events between patients in the TAVR group and those in the clinical surveillance group who underwent aortic-valve replacement. CONCLUSIONS: Among patients with asymptomatic severe aortic stenosis, a strategy of early TAVR was superior to clinical surveillance in reducing the incidence of death, stroke, or unplanned hospitalization for cardiovascular causes. (Funded by Edwards Lifesciences; EARLY TAVR ClinicalTrials.gov number, NCT03042104.).

Cardiology/Cardiovascular Research

Gorgis S, **Gupta K**, Lemor A, Bentley D, Moyer C, Mc RT, Khuddus M, Sharma R, Lim M, Nsair A, Wohns D, Mehra A, Lin L, Bharadwaj A, Tedford R, Kapur N, **Cowger J**, **O'Neill W**, and **Basir MB**. Impact of Right Ventricular Dysfunction on Outcomes in Acute Myocardial Infarction and Cardiogenic Shock: Insights from the National Cardiogenic Shock Initiative. *J Card Fail* 2024; 30(10):1275-1284. PMID: 39389738. Full Text

Henry Ford Hospital; Detroit, MI, USA. Electronic address: sgorgis1@hfhs.org.
Henry Ford Hospital; Detroit, MI, USA.
University of Mississippi; Oxford, MS, USA.
Johnson & Johnson, New Brunswick, NJ, USA.
TriStar Centennial Medical Center; Nashville, TN, USA.
The Cardiac and Vascular Institute; Gainesville, FL, USA.
Cardiac Solutions and Banner Health; Peoria, AZ, USA.
Poplar Bluff Regional Medical Center; Poplar Bluff, MO, USA.
Ronald Reagan UCLA Medical Center; Los Angeles, CA, USA.
Corewell Health, Frederik Meijer Heart and Vascular Institute; Grand Rapids, MI, USA.
Jersey Shore University Medical Center; Neptune City, NJ, USA.
BayCare Medical Group Cardiology; Clearwater, FL, USA.
Loma Linda University Health Care; Loma Linda, CA, USA.
Medical University of South Carolina, Charleston, SC, USA.
Tufts Medical Center; Boston, MA, USA.

BACKGROUND: Right ventricular dysfunction (RVD) complicates 30%-40% of cases in acute myocardial infarction (AMI) and cardiogenic shock (CS). There are sparse data on the effects of RVD on outcomes and the impact of providing early left ventricular (LV) mechanical circulatory support (MCS) on RV function and hemodynamics. METHODS AND RESULTS: Between July 2016 and December 2020, 80

sites participated in the study. All centers agreed to treat patients with AMI-CS using a standard protocol emphasizing invasive hemodynamic monitoring and rapid initiation of LV-MCS. RVD was defined as a right atrial (RA) pressure of >12 mm Hg and a pulmonary artery pulsatility index (PAPI) of <1 within 24 hours of the index procedure. The primary outcome was survival to discharge. In a subgroup analysis, data available from the Automated Impella Controller console was used to analyze diastolic suction alarms from LV placement signal and its relation to RVD. A total of 361 patients were included in the analysis, of whom 28% had RVD. The median age was 64 years (interquartile range 55-72 years), 22.7% were female and 75.7% were White. There was no difference in age, sex, or comorbidities between those with or without RVD. Patients with RVD had a higher probability of active CPR during LV-MCS implant (14.7% vs 6.3%), Society for Cardiovascular Angiography and Interventions stage E shock (39.2% vs 23.2%), and higher admission lactate levels (5.1 mg/dL vs 3.0 mg/dL). Survival to discharge was significantly lower among those with RVD (61.8% vs 73.4%, odds ratio 0.89, 95% confidence interval 0.36-0.95, P = .031). This association remained significant in the multivariate analysis. There was no significant difference in hemodynamic variables within 24 hours of LV-MCS support among those with or without RVD. At 24 hours, patients with a CPO of >0.6 W and a PAPi of >1 had a trend toward better survival to discharge compared with those with a CPO of ≤0.6 W and a PAPi of ≤1 (77.1% vs 54.6%, P = .092). Patients with RVD were significantly more likely to have diastolic suction alarms within 24 hours of LV-MCS initiation. CONCLUSIONS: RVD in AMI-CS is common and associated with worse survival to discharge. Early LV-MCS decreases filling pressures rapidly within the first 24 hours and decreases the rate of RVD. Achieving a CPO of >0.6 W and a PAPi of >1 within 24 hours is associated with high survival. Diastolic suction alarms may have usefulness as an early marker of RVD.

Cardiology/Cardiovascular Research

Hahn RT, Makkar R, Thourani VH, Makar M, Sharma RP, Haeffele C, Davidson CJ, Narang A, **O'Neill B**, **Lee J**, Yadav P, Zahr F, Chadderdon S, Eleid M, Pislaru S, Smith R, Szerlip M, Whisenant B, Sekaran NK, Garcia S, Stewart-Dehner T, Thiele H, Kipperman R, Koulogiannis K, Lim DS, Fowler D, Kapadia S, Harb SC, Grayburn PA, Sannino A, Mack MJ, Leon MB, Lurz P, and Kodali SK. Transcatheter Valve Replacement in Severe Tricuspid Regurgitation. *N Engl J Med* 2024; Epub ahead of print. PMID: 39475399. Full Text

From Columbia University Irving Medical Center, New York (R.T.H., M.B.L., S.K.K.); Cedars-Sinai Medical Center, Los Angeles (R.M., M.M.), and Stanford University, Stanford (R.P.S., C.H.) - both in California; Piedmont Heart Institute, Marcus Heart Valve Center, Atlanta (V.H.T., P.Y.); Northwestern University Feinberg School of Medicine, Chicago (C.J.D., A.N.); Henry Ford Hospital, Detroit (B.O., J.L.); Oregon Health and Science University, Portland (F.Z., S.C.); Mayo Clinic, Rochester, MN (M.E., S.P.); Baylor Scott and White Heart Hospital Plano (R.S., M.S., P.A.G., M.J.M.) and Baylor Scott and White Research Institute Cardiac Imaging Core Laboratory (P.A.G., A.S.) - both in Plano, TX; Intermountain Medical Center, Murray, UT (B.W., N.K.S.); Christ Hospital, Cincinnati (S.G., T.S.-D.), and the Cleveland Clinic Foundation, Cleveland (S.K., S.C.H.); Heart Center Leipzig at Leipzig University, Leipzig (H.T.), and University Medical Center Mainz, Mainz (P.L.) - both in Germany; Morristown Medical Center, Morristown, NJ (R.K., K.K.); and the University of Virginia, Charlottesville (D.S.L., D.F.).

BACKGROUND: Severe tricuspid regurgitation is associated with disabling symptoms and an increased risk of death. Data regarding outcomes after percutaneous transcatheter tricuspid-valve replacement are needed. METHODS: In this international, multicenter trial, we randomly assigned 400 patients with severe symptomatic tricuspid regurgitation in a 2:1 ratio to undergo either transcatheter tricuspid-valve replacement and medical therapy (valve-replacement group) or medical therapy alone (control group). The hierarchical composite primary outcome was death from any cause, implantation of a right ventricular assist device or heart transplantation, postindex tricuspid-valve intervention, hospitalization for heart failure, an improvement of at least 10 points in the score on the Kansas City Cardiomyopathy Questionnaire overall summary (KCCQ-OS), an improvement of at least one New York Heart Association (NYHA) functional class, and an improvement of at least 30 m on the 6-minute walk distance. A win ratio was calculated for the primary outcome by comparing all possible patient pairs, starting with the first event in the hierarchy. RESULTS: A total of 267 patients were assigned to the valve-replacement group and 133 to the control group. At 1 year, the win ratio favoring valve replacement was 2.02 (95% confidence interval [CI], 1.56 to 2.62; P<0.001). In comparisons of patient pairs, those in the valve-replacement group

had more wins than the control group with respect to death from any cause (14.8% vs. 12.5%), postindex tricuspid-valve intervention (3.2% vs. 0.6%), and improvement in the KCCQ-OS score (23.1% vs. 6.0%), NYHA class (10.2% vs. 0.8%), and 6-minute walk distance (1.1% vs. 0.9%). The valve-replacement group had fewer wins than the control group with respect to the annualized rate of hospitalization for heart failure (9.7% vs. 10.0%). Severe bleeding occurred in 15.4% of the valve-replacement group and in 5.3% of the control group (P = 0.003); new permanent pacemakers were implanted in 17.4% and 2.3%, respectively (P<0.001). CONCLUSIONS: For patients with severe tricuspid regurgitation, transcatheter tricuspid-valve replacement was superior to medical therapy alone for the primary composite outcome, driven primarily by improvements in symptoms and quality of life. (Funded by Edwards Lifesciences; TRISCEND II ClinicalTrials.gov number, NCT04482062.).

Cardiology/Cardiovascular Research

Hirata GM, Rempakos A, Walker Boyd A, Alexandrou M, Mutlu D, Choi JW, Poommipanit P, Khatri JJ, Young L, Davies R, Gorgulu S, Jaffer FA, Chandwaney R, Jefferson B, Elbarouni B, Azzalini L, Kearney KE, **Alaswad K**, **Basir MB**, Krestyaninov O, Khelimskii D, Aygul N, Abi-Rafeh N, ElGuindy A, Goktekin O, Rangan BV, Mastrodemos OC, Al-Ogaili A, Sandoval Y, Burke MN, Brilakis ES, and Frizzell JD. Chronic total occlusion percutaneous coronary intervention of anomalous coronary arteries: insights from the PROGRESS CTO registry. *Catheter Cardiovasc Interv* 2024; Epub ahead of print. PMID: 39363798. Full Text

The Christ Hospital Heart and Vascular Institute and Lindner Center for Research and Education, Cincinnati, OH, USA.
Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota, USA.
Texas Health Presbyterian Hospital, Dallas, Texas, USA.
University Hospitals, Case Western Reserve University, Cleveland, Ohio, USA.
Cleveland Clinic, Cleveland, Ohio, USA.
WellSpan York Hospital, York, Pennsylvania, USA.
Biruni University Medical School, Istanbul, Turkey.
Massachusetts General Hospital, Boston, Massachusetts, USA.
Oklahoma Heart Institute, Tulsa, Oklahoma, USA.
Tristar Centennial Medical Center, Nashville, Tennessee, USA.
Section of Cardiology, St. Boniface Hospital, University of Manitoba, Winnipeg, Manitoba, Canada.
Division of Cardiology, Department of Medicine, University of Washington, Seattle, Washington, USA.
Division of Cardiology, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Invasive Cardiology, Meshalkin National Medical Research Center, Ministry of Health of the Russian Federation, Novosibirsk, Russian Federation.
Department of Cardiology, Selcuk University, Konya, Turkey.
Cardiology, North Oaks Health System, Hammond, Louisiana.
Department of Cardiology, Aswan Heart Center, Magdi Yacoub Foundation, Cairo, Egypt.
Department of Cardiology, Memorial Bahcelievler Hospital, Istanbul, Turkey.

BACKGROUND: There is limited information about the frequency and outcomes of chronic total occlusion (CTO) percutaneous coronary intervention (PCI) in anomalous coronary arteries (ACA). METHODS: We examined the clinical and angiographic characteristics and procedural outcomes of CTO PCI in ACA among 14,173 patients who underwent 14,470 CTO PCIs at 46 US and non-US centers between 2012 and 2023. RESULTS: Of 14,470 CTO PCIs, 36 (0.24%) were CTO PCIs in an ACA. ACA patients had similar baseline characteristics as those without an ACA. The type of ACA in which the CTO lesion was found were as follows: anomalous origin of the right coronary artery (ARCA) (17, 48.5%), anomalous origin of left circumflex coronary artery (9, 25.7%), left anterior descending artery and left circumflex artery with separate origins (4, 11.4%), anomalous origin of the left anterior descending artery (2, 5.7%), dual left anterior descending artery (2, 5.7%) and woven coronary artery 1 (2.8%). The Japan CTO score was similar between both groups (2.17 ± 1.32 vs 2.38 ± 1.26, p = 0.30). The target CTO in ACA patients was more likely to have moderate/severe tortuosity (44% vs 28%, p = 0.035), required more often use of retrograde approach (27% vs 12%, p = 0.028), and was associated with longer procedure (142.5 min vs 112.00 min [74.0, 164.0], p = 0.028) and fluoroscopy (56 min [40, 79 ml] vs 42 min [25, 67], p = 0.014) time

and higher contrast volume (260 ml [190, 450] vs 200 ml [150, 300], p = 0.004) but had similar procedural (91.4% vs 85.6%, p = 0.46) and technical (91.4% vs 87.0%, p = 0.59) success. No major adverse cardiac events (MACE) were seen in ACA patients (0% [0] vs 1.9% [281] in non-ACA patients, p = 1.00). Two coronary perforations were reported in ACA CTO PCI (p = 0.7 vs. non-ACA CTO PCI). CONCLUSIONS: CTO PCI of ACA comprise 0.24% of all CTO PCIs performed in the PROGRESS CTO registry and was associated with higher procedural complexity but similar technical and procedural success rates and similar MACE compared with non-ACA CTO PCI.

Cardiology/Cardiovascular Research

Imran HM, Has P, Kassis N, Shippey E, Elkaryoni A, Gordon PC, Sharaf BL, Soukas PA, Hyder ON, Sellke F, Ehsan A, Sodha N, Mentias A, Elgendy IY, Alkhouli M, Abbott JD, **Aronow HD**, and Saad M. Characteristics, Trends, and Outcomes of Intravascular Lithotripsy-Assisted Transfemoral Transcatheter Aortic Valve Replacement in United States. *JACC Cardiovasc Interv* 2024; 17(20):2367-2376. PMID: 39477639. Full Text

Lifespan Cardiovascular Institute, Providence, Rhode Island, USA; Department of Medicine, Division of Cardiology, Warren Alpert Medical School of Brown University, Providence, Rhode Island, USA.
Department of Medicine, Division of Cardiology, Warren Alpert Medical School of Brown University, Providence, Rhode Island, USA.
Vizient Center for Advanced Analytics, Chicago, Illinois, USA.
Lifespan Cardiovascular Institute, Providence, Rhode Island, USA; Division of Cardiothoracic Surgery, Warren Alpert Medical School of Brown University, Providence, Rhode Island, USA.
Heart, Vascular and Thoracic Institute, Cleveland Clinic Foundation, Cleveland, Ohio, USA.
Division of Cardiovascular Medicine, Gill Heart Institute, University of Kentucky, Lexington, Kentucky, USA.
Department of Cardiology, Mayo Clinic School of Medicine, Rochester, Minnesota, USA.
Henry Ford Health and Michigan State University, Detroit, Michigan, USA.
Lifespan Cardiovascular Institute, Providence, Rhode Island, USA; Department of Medicine, Division of Cardiology, Warren Alpert Medical School of Brown University, Providence, Rhode Island, USA.
Electronic address: marwan_saad@brown.edu.

BACKGROUND: Transfemoral (TF) access is the preferred approach for transcatheter aortic valve replacement (TAVR). Limited data exist regarding the outcomes of intravascular lithotripsy (IVL)-assisted TF TAVR in patients with peripheral artery disease. OBJECTIVES: This study sought to examine contemporary characteristics, trends, and outcomes of IVL TAVR in the United States. METHODS: The Vizient Clinical Database was queried for patients who underwent percutaneous TAVR between October 1, 2020, and November 30, 2023. Outcomes with IVL TAVR vs non-IVL TAVR were examined after propensity score matching. The primary outcome was a composite of in-hospital death, stroke, vascular complications, surgical vascular intervention, and major bleeding. RESULTS: Over the study period, 129,655 patients (mean age of 78.4 years, 42.2% women, 87.1% White) underwent percutaneous TAVR at 361 hospitals, 1,242 (0.96%) of whom underwent IVL TAVR. There was an uptrend in IVL TAVR, but the frequency remained low. IVL TAVR patients had a higher median Elixhauser comorbidity score (5 [Q1-Q3: 4-7] vs 4 [Q1-Q3: 3-6]) compared to non-IVL TAVR. TAVR was completed via the TF approach in 1,238 (99.7%) IVL TAVR patients. In a 3:1 propensity score matching analysis, IVL TAVR was associated with a higher rate of the primary composite outcome (21.9% vs 13.7%; P < 0.001) driven by higher rates of vascular complications, surgical vascular intervention, and major bleeding. In-hospital death and stroke were similar in both groups. CONCLUSIONS: In the United States, IVL is increasingly adopted to facilitate TF TAVR. IVL TAVR patients exhibited a higher burden of comorbidities and experienced more complications compared to non-IVL TAVR patients. Further studies are needed to identify appropriate anatomical and clinical use criteria for IVL TAVR and to compare its outcomes vs alternative non-TF TAVR.

Cardiology/Cardiovascular Research

Jung RG, Stotts C, Gupta A, Prosperi-Porta G, Dhaliwal S, Motazedian P, Abdel-Razek O, Di Santo P, Parlow S, Belley-Cote E, Tran A, van Diepen S, Harel-Sterling L, Goyal V, Lepage-Ratte MF, Mathew R, Jentzer JC, Price S, Naidu SS, **Basir MB**, Kapur NK, Thiele H, Ramirez FD, Wells G, Rochwerg B, Fernando SM, and Hibbert B. Prognostic Factors Associated with Mortality in Cardiogenic Shock - A Systematic Review and Meta-Analysis. *NEJM Evid* 2024; 3(11):EVIDoa2300323. PMID: 39437131. Full Text

Division of Cardiology, University of Ottawa Heart Institute.
Vascular Biology and Experimental Medicine Laboratory, University of Ottawa Heart Institute.
Department of Cellular and Molecular Medicine, Faculty of Medicine, University of Ottawa.
Division of Internal Medicine, The Ottawa Hospital.
Faculty of Medicine, University of Ottawa.
School of Epidemiology and Public Health, University of Ottawa.
Division of Cardiology, Department of Medicine, McMaster University, Hamilton, ON, Canada.
Division of Critical Care Medicine, Department of Medicine, University of Ottawa.
Department Critical Care Medicine and Division of Cardiology, Department of Medicine, University of Alberta, Edmonton.
Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN.
Cardiology and Critical Care Departments, Royal Brompton and Harefield Hospitals, London.
Westchester Medical Center and New York Medical College, Valhalla, NY.
Division of Cardiology, Henry Ford Hospital, Detroit.
The Cardiovascular Center, Tufts Medical Center, Boston.
Department of Internal Medicine/Cardiology, Heart Center Leipzig at the University of Leipzig and Leipzig Heart Institute, Germany.
Department of Health Research Methods, Evidence, and Impact and Department of Medicine, McMaster University, Hamilton, ON, Canada.
Department of Critical Care, Lakeridge Health Corporation, Oshawa, ON, Canada.

BACKGROUND: Cardiogenic shock remains highly associated with early mortality, with mortality often exceeding 50%. We sought to determine the association between prognostic factors and in-hospital and 30-day mortality in cardiogenic shock. METHODS: We performed a systematic review and meta-analysis of prognostic factors in cardiogenic shock, searching MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials for records up to June 5, 2023. English-language studies that investigated prognostic factors and in-hospital and/or 30-day mortality in cardiogenic shock were included. Studies were excluded if they evaluated the pediatric population, were postmortem studies, or included fewer than 100 patients. The primary aim was to identify modifiable and non-modifiable prognostic factors associated with in-hospital and 30-day mortality in cardiogenic shock. RESULTS: We identified 160 studies, including 2,459,703 patients with a median in-hospital mortality of 41.4% (interquartile range, 33.6% to 49.2%). The majority were retrospective cohort studies. Patient factors potentially associated with an increase in early mortality included an age greater than or equal to 75 years of age, peripheral arterial disease, chronic kidney disease, and female sex. Procedural and presentation factors potentially associated with increased mortality included out-of-hospital cardiac arrest, left main culprit artery, left ventricular ejection fraction less than 30%, dialysis, and need for mechanical circulatory support. Revascularization in the form of coronary artery bypass graft and percutaneous coronary intervention were potentially associated with reduced in-hospital mortality. CONCLUSIONS: This analysis quantifies the association between patient, presentation, and treatment-related factors and early mortality in cardiogenic shock. Increased certainty in the association of these prognostic factors with cardiogenic shock outcomes can aid in clinical risk assessment, development of risk tools, and analysis of clinical trials.

Cardiology/Cardiovascular Research

Krittanawong C, Ang SP, Tangsrivimol JA, **Qadeer YK**, Wang Z, Virk HUH, Khalid U, Sharma SK, and Dardik A. Carotid artery stenting versus carotid endarterectomy for symptomatic or asymptomatic extracranial carotid stenosis: A national cohort study. *J Stroke Cerebrovasc Dis* 2024; 33(12):108094. PMID: 39424210. Full Text

Cardiology Division, NYU Langone Health and NYU School of Medicine, New York, NY, United States. Electronic address: chayakrit.krittanawong@va.gov.
Division of Internal Medicine, Rutgers Health Community Medical Center, NJ, United States.
Department of Neurosurgery, and Neuroscience, Weill Cornell Medicine, NewYork-Presbyterian Hospital, New York, NY, United States; Division of Neurosurgery, Department of Surgery, Chulabhorn Hospital, Chulabhorn Royal Academy, Bangkok 10210, Thailand.
Division of Cardiology, Department of Medicine, Henry Ford Hospital, Detroit, MI, United States. Electronic address: yusuf.qadeer@bcm.edu.
Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Mayo Clinic, Rochester, MN, United States; Division of Health Care Policy and Research, Department of Health Sciences Research, Mayo Clinic, Rochester, MN, United States. Electronic address: wang.zhen@mayo.edu.
Harrington Heart & Vascular Institute, Case Western Reserve University, University Hospitals Cleveland Medical Center, Cleveland, OH, United States.
Michael E. DeBakey VA Medical Center, Houston, Texas; Section of Cardiology, Baylor College of Medicine, Houston, TX, United States. Electronic address: mukhalid@bcm.edu.
Cardiac Catheterization Laboratory of the Cardiovascular Institute, Mount Sinai Hospital, New York, NY, United States. Electronic address: samin.sharma@mountsinai.org.
Vascular Biology and Therapeutics Program, Yale School of Medicine, New Haven, CT, United States; Division of Vascular and Endovascular Surgery, Department of Surgery, Yale School of Medicine, New Haven, CT, United States; Department of Surgery, VA Connecticut Healthcare Systems, West Haven, CT, United States; Yale School of Medicine, 10 Amistad Street, Room 437, PO Box 208089, New Haven, CT, United States. Electronic address: alan.dardik@yale.edu.

INTRODUCTION: Stroke is now the 5th leading cause of death in the United States, and carotid artery stenosis is the cause of about 20% to 25% of strokes. We hypothesized that CAS may be an alternative to CEA in both symptomatic and asymptomatic patients with carotid artery stenosis. METHODS: We evaluated the clinical characteristics, adverse events and mortality of patients with carotid artery stenosis comparing CEA vs. CAS using data from a national population-based cohort study from January 1, 2016, to December 30, 2020. RESULTS: We evaluated 374,875 patients with carotid stenosis, of whom 344,020 had asymptomatic carotid stenosis and 30,855 had symptomatic carotid stenosis. CAS was associated with higher mortality in both symptomatic and asymptomatic carotid stenosis, compared to CEA, with the trend slightly decreasing for both interventions from the years 2018-2020. CEA was associated with lower adverse events in both symptomatic and asymptomatic carotid stenosis, compared to CAS. CONCLUSIONS: Our current data suggest a benefit of CEA over CAS for both symptomatic and asymptomatic carotid stenosis with lower complications, lower mortality and a higher rate of discharge. However, this is not a head-to-head comparison as it becomes selection bias for this procedure; therefore, further prospective head-to-head comparison between 2 groups in the same patient population is needed.

Cardiology/Cardiovascular Research

Krittanawong C, **Qadeer YK**, Ang SP, Wang Z, Alam M, Sharma S, and Jneid H. Characteristics of Patients with Spontaneous Coronary Artery Dissection Presenting with Sudden Cardiac Arrest in the United States and the Potential Role of Implantable Cardioverter Defibrillator Therapy. *Rev Cardiovasc Med* 2024; 25(9):318. PMID: 39355574. Full Text

Cardiology Division, NYU Langone Health and NYU School of Medicine, New York, NY 10016, USA.
Division of Cardiology, Department of Medicine, Henry Ford Hospital, Detroit, MI 48202, USA.
Division of Internal Medicine, Rutgers Health Community Medical Center, Newark, NJ 08903, USA.
Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Mayo Clinic, Rochester, MN 55903, USA.
Division of Health Care Policy and Research, Department of Health Sciences Research, Mayo Clinic, Rochester, MN 55903, USA.
The Texas Heart Institute, Baylor College of Medicine, Houston, TX 77030, USA.
Cardiac Catheterization Laboratory of the Cardiovascular Institute, Mount Sinai Hospital, New York, NY 10018, USA.

John Sealy Distinguished Centennial Chair in Cardiology, Chief, Division of Cardiology, University of Texas Medical Branch, Houston, TX 77058-3609, USA.

BACKGROUND: Spontaneous coronary artery dissection (SCAD) is a disease entity that often occurs in young, healthy women and can cause life-threatening ventricular arrhythmias and sudden cardiac arrest. However, the characteristics and outcomes of SCAD with cardiac arrest are not well characterized. METHODS: This study investigated the baseline characteristics of SCAD patients with cardiac arrest using the National Inpatient Sample (NIS) database between 2016 and 2020. In addition, we also sought to determine the potential impact that implantable cardioverter defibrillator (ICD) therapy had on morbidity and mortality in SCAD patients presenting with cardiac arrest. RESULTS: Our findings showed that the SCAD with cardiac arrest population had significantly higher comorbidities, including cardiac arrhythmias, congestive heart failure, pulmonary circulation disorders, liver diseases, solid tumors, coagulopathy, fluid disorders, chronic kidney disease (CKD), anemia secondary to deficiency, psychosis, neurological disorders, carotid artery disease, atrial fibrillation, ventricular arrhythmias (ventricular tachycardia (VT), ventricular fibrillation (VF)), and acute myocardial infarction (AMI), compared to the SCAD without cardiac arrest population. Likewise, for SCAD patients who did not have an ICD in place, we found increasing age, fluid and electrolyte disorders, uncomplicated diabetes, neurological disorders, peripheral vascular disease, pulmonary circulatory disorders, cardiac arrhythmias, and congestive heart failure to be associated with greater mortality. CONCLUSIONS: SCAD patients with certain comorbidities (e.g., pulmonary diseases, liver diseases, cancers, coagulopathy, and CKD) who presented with AMI or congestive heart failure should be monitored closely for ventricular arrhythmias as they have a higher chance of progressing to cardiac arrest. ICD therapy can be considered for these patients, but data on the success of this treatment option are limited, and more research needs to be performed to determine whether the benefits of this outweigh the risks.

Cardiology/Cardiovascular Research

Littleton SDR, **Lanfear DE**, Dorsch MP, **Liu B**, and Luzum JA. Equal Treatment, Unequal Outcomes? Debunking the Racial Disparity in Renin Angiotensin Aldosterone System Inhibitor Associated Reduction in Heart Failure Hospitalizations. *J Card Fail* 2024; Epub ahead of print. PMID: 39442611. Full Text

University of Michigan College of Pharmacy, Ann Arbor, MI, USA.
Henry Ford Health System, Detroit, MI, USA.
University of Michigan College of Pharmacy, Ann Arbor, MI, USA. Electronic address: jluzum@med.umich.edu.

BACKGROUND: Renin angiotensin aldosterone system inhibitors (RAASi) are a mainstay treatment in patients with heart failure with reduced ejection fraction (HFrEF) in part to prevent hospitalizations. However, whether RAAS inhibitors reduce the risk of hospitalization in Black patients is not entirely clear because enrollment of Black patients in previous clinical trials was low, and a previous meta-analysis showed a significant racial disparity: reduction in hospitalizations with an RAAS inhibitor in White patients but not Black patients. Previous studies relied on the use of self-identified race instead of genomic ancestry. Therefore, this study aimed to investigate the role of self-identified race and genomic ancestry in the racial disparity in RAAS inhibitor associated reductions in HFrEF hospitalizations. METHODS: The primary outcome was time to first heart failure hospitalization. A (de-identified) heart failure patient registry and data from the GUIDE-IT multi-center randomized control trial were analyzed with Cox proportional hazards models un/adjusted for clinical risk factors, death as a competing risk, and time-varying RAAS inhibitor exposure. The proportion of Yoruba African ancestry was quantified.. Analysis of self - identified race were performed in both the registry and GUIDE-IT. Analysis of genomic ancestry was only performed in the registry since this information was not available in GUIDE-IT. A fixed effect meta-analysis combined results of both the registry and GUIDE-IT for race. RESULTS: The registry had 1010 total HFrEF patients (Black = 509 and White = 501) with 852 having ancestry quantification (>80% Yoruba African Ancestry = 381 and <5% Yoruba African Ancestry = 471). GUIDE-IT had 810 HFrEF patients (Black = 322 and White = 488). There was no significant difference in the association of RAAS inhibitor exposure with heart failure hospitalization by race (meta-analysis p-value for race*RAAS inhibitor exposure interaction = 0.49; Black patients HR [95% CI] for RAAS inhibitor exposure = 0.89 [0.64-1.23)] P = 0.47; White patients = 1.20 (0.83-1.75) P = 0.34). Results were similar when analyzed by ancestry (p-

value for ancestry*RAAS inhibitor exposure interaction = 0.57; >80% Yoruba African Ancestry = 0.93 [0.51-1.69] P = 0.80; <5% Yoruba African Ancestry = 1.29 [0.57-2.92] P = 0.54). CONCLUSIONS: In contrast to a previous meta-analysis, this more contemporary analysis of 2 HFrEF patient datasets demonstrates the absence of a racial disparity in RAAS inhibitor associated reductions in heart failure hospitalizations. The difference in this racial disparity over time may be due to improvements in background heart failure therapies, racial differences in healthcare usage, and the use of more advanced statistical approaches.

Cardiology/Cardiovascular Research
Mansour AI, Seth M, Thompson MP, Casey M, **Keteyian SJ**, Smith FA, Gurm HS, and Sukul D. Use of a Liaison-Mediated Referral Strategy and Participation in Cardiac Rehabilitation After Percutaneous Coronary Intervention. *Circ Cardiovasc Qual Outcomes* 2024; 17(10):e010874. PMID: 39364590. Full Text

Johns Hopkins Hospital, Baltimore, MD (A.I.M.).
Department of Internal Medicine, Division of Cardiovascular Medicine (M.S., M.C., H.S.G., D.S.), University of Michigan, Ann Arbor.
Institute of Healthcare Policy and Innovation (M.T., H.S.G., D.S.), University of Michigan, Ann Arbor.
Section of Health Services Research and Quality, Department of Cardiac Surgery, Michigan Medicine, Ann Arbor (M.T.).
Michigan Value Collaborative, Ann Arbor (M.T.).
Division of Cardiovascular Medicine, Henry Ford Medical Group, Detroit, MI (S.J.K.).
Intensive Cardiac Rehabilitation Program, Trinity Health Ann Arbor and Trinity Health Livingston, MI (F.A.S.).

BACKGROUND: Cardiac rehabilitation (CR) improves outcomes following percutaneous coronary intervention (PCI) but remains underutilized. A liaison-mediated referral (LMR), where a health care professional explains CR's benefits, addresses barriers to participation, and places a referral before discharge, may promote CR use. Our objective was to assess the impact of an LMR on CR participation after PCI. METHODS: This was a retrospective study of patients who underwent PCI across 48 hospitals in Michigan between January 2021 and April 2022 and referred to CR before discharge. Clinical registry data were linked to administrative claims to identify the primary outcome, CR participation, defined as ≥1 CR session within 90 days of discharge. Bayesian hierarchical logistic regression was used to compare CR participation between patients with and without an LMR. For the secondary outcome, frailty proportional hazard modeling compared days elapsed between discharge and first CR session between liaison cohorts. RESULTS: Among 9023 patients referred to CR after PCI, 4323 (47.9%) underwent an LMR (mean age, 69.3 [SD=11] years; 68.3% male) and 3390 (36.7%) attended ≥1 CR session within 90 days of discharge. The LMR cohort had a higher unadjusted CR participation rate (43.1% [95% CI, 41.5%-44.6%] versus 32.4% [95% CI, 31.1%-33.8%]; P<0.001), a higher adjusted odds ratio of attending ≥1 CR session (adjusted odds ratio, 1.21; 95% credible interval, 1.07-1.38), and a shorter delay in attending the first CR session compared with the non-LMR cohort (28 [interquartile range, 19-42] versus 33 [interquartile range, 21-47] days; P<0.001). CONCLUSIONS: An LMR was associated with higher odds of CR participation and may mitigate delays in CR enrollment. This referral strategy may improve CR participation and patient outcomes after PCI.

Cardiology/Cardiovascular Research
Noten AME, Szili-Torok T, Ernst S, Burkhardt D, Cavaco D, Chen X, Cheung JW, de Chillou C, Crystal E, Cooper DH, Gasparini M, Geczy T, Goehl K, Hügl B, Jin Q, Kampus P, Kazemian P, Khan M, Kongstad O, Magga J, Peress D, Raatikainen P, Romanov A, Rossvoll O, **Singh G**, Vatasescu R, Wijchers S, Yamashiro K, Yap SC, and Weiss JP. Best practices in robotic magnetic navigation-guided catheter ablation of cardiac arrhythmias, a position paper of the Society for Cardiac Robotic Navigation. *Front Cardiovasc Med* 2024; 11:1431396. PMID: 39399515. Full Text

Department of Clinical Electrophysiology, Thorax Center, Erasmus Medical Center, Rotterdam, Netherlands.
Department of Internal Medicine, Cardiology Center, University of Szeged, Szeged, Hungary.

Royal Brompton and Harefield NHS Foundation Trust, National Heart and Lung Institute, Imperial College London, London, United Kingdom.
Texas Cardiac Arrhythmia Institute, St. David's Medical Center, Austin, TX, United States.
Heart Rhythm Center, Hospital da Luz, Lisbon, Portugal.
Department of Cardiology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark.
Division of Cardiology, Weill Cornell Medicine, NewYork Presbyterian Hospital, New York, NY, United States.
Department of Cardiology, CHU de Nancy, University Hospital Nancy, Nancy, France.
Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada.
Cardiovascular Division, Washington University School of Medicine, St. Louis, MO, United States.
Department of Cardiology, Humanitas University Hospital, Rozzano, Italy.
Department of Internal Medicine, Division of Cardiology, Medical University of Graz, Graz, Austria.
Department of Electrophysiology, Klinikum Nürnberg Süd, Nuremberg, Germany.
Department of Cardiology and Rhythmology, Marienhaus Klinikum St. Elisabeth, Neuwied, Germany.
Department of Cardiology, Shanghai Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China.
Department of Cardiology, North Estonian Medical Centre, Tallinn, Estonia.
Deborah Heart and Lung Center, Browns Mills, NJ, United States.
Department of Cardiology, Onze Lieve Vrouwe Gasthuis, Amsterdam, Netherlands.
Department of Cardiology, Lund University, Lund, Sweden.
Department of Cardiology, Oulu University Hospital, Oulu, Finland.
Pima Heart Physicians, PC, Tucson, AZ, United States.
Heart and Lung Center, Helsinki University Central Hospital, Helsinki, Finland.
E. Meshalkin National Medical Research Center of the Ministry of Health of the Russian Federation, Novosibirsk, Russia.
Department of Cardiology, St'Olavs University Hospital, Trondheim, Norway.
Division of Cardiology, Henry Ford Health System, Detroit, MI, United States.
Cardiology Department, Clinical Emergency Hospital, Bucharest, Romania.
Heart Rhythm Center, Takatsuki General Hospital, Osaka, Japan.
Department of Cardiology, Banner University Medical Center, The University of Arizona College of Medicine-Phoenix, Phoenix, AZ, United States.

PREAMBLE: Robotic magnetic navigation (RMN)-guided catheter ablation (CA) technology has been used for the treatment of cardiac arrhythmias for almost 20 years. Various studies reported that RMN allows for high catheter stability, improved lesion formation and a superior safety profile. So far, no guidelines or recommendations on RMN-guided CA have been published. PURPOSE: The aim of this consensus paper was to summarize knowledge and provide recommendations on management of arrhythmias using RMN-guided CA as treatment of atrial fibrillation (AF) and ventricular arrhythmias (VA). METHODOLOGY: An expert writing group, performed a detailed review of available literature, and drawing on their own experience, drafted and voted on recommendations and summarized current knowledge and practice in the field. Recommendations on RMN-guided CA are presented in a guideline format with three levels of recommendations to serve as a reference for best practices in RMN procedures. Each recommendation is accompanied by supportive text and references. The various sections cover the practical spectrum from system and patient set-up, EP laboratory staffing, combination of RMN with fluoroscopy and mapping systems, use of automation features and ablation settings and targets, for different cardiac arrhythmias. CONCLUSION: This manuscript, presenting the combined experience of expert robotic users and knowledge from the available literature, offers a unique resource for providers interested in the use of RMN in the treatment of cardiac arrhythmias.

Cardiology/Cardiovascular Research

Rinfret S, Henry GA, Khatri JJ, Mashayekhi K, **Alaswad K**, Azzalini L, Ybarra LF, Vijayaraghavan R, Frizzell JD, Avran A, McEntegart MB, Lombardi WL, Grantham JA, and Brilakis E. Knuckle Guidewires to Create Dissections in Chronic Total Occlusion Percutaneous Coronary Intervention: Position Statement. *JACC Cardiovasc Interv* 2024; 17(20):2411-2424. PMID: 39477645. Full Text

Georgia Heart Institute, Northeast Georgia Health System, Gainesville, Georgia, USA. Electronic address: stephane.rinfret@nghs.com.
Georgia Heart Institute, Northeast Georgia Health System, Gainesville, Georgia, USA.
Heart, Vascular, and Thoracic Institute, Cleveland Clinic Foundation, Cleveland, Ohio, USA.
Division of Cardiology and Angiology II, University Heart Center Freiburg - Bad Krozingen, Bad Krozingen, Germany; Division of Internal Medicine and Cardiology, Heart Center Lahr, Lahr, Germany.
Henry Ford Hospital, Detroit, Michigan, USA.
Division of Cardiology, Department of Medicine, University of Washington, Seattle, Washington, USA.
London Health Sciences Centre, Division of Cardiology, Department of Medicine, Western University, London, Ontario, Canada.
Heart Health Institute, Scarborough, Ontario, Canada; University of Toronto, Toronto, Ontario, Canada.
The Christ Hospital Heart and Vascular Institute, Cincinnati, Ohio, USA.
Hôpital Valenciennes, Valenciennes, France.
NewYork-Presbyterian Hospital, Columbia University, New York, New York, USA.
Saint Luke's Mid America Heart Institute, Kansas City, Missouri, USA.
Minneapolis Heart Institute, Minneapolis, Minnesota, USA.

Dissection and re-entry techniques are essential to achieve safe and effective chronic total occlusion recanalization. Several studies have demonstrated similar outcomes following extraplaque stenting compared with intraplaque stenting. Dissection techniques most often involve the use of knuckled wires to progress within and beyond the chronic total occlusion segment. In this expert consensus document, the authors compare the properties of different polymer-jacketed wires for their use in dissection techniques. The authors also describe 2 principal knuckle wire behaviors, the rolling and the traveling knuckles. Finally, several adjunctive techniques for safer dissection are described.

Cardiology/Cardiovascular Research

Rommel KP, Bonnet G, Bellumkonda L, Lansky AJ, Zhao D, Thompson JB, Zhang Y, Redfors B, Lurz PC, Granada JF, Bharadwaj AS, **Basir MB**, **O'Neill WW**, and Burkhoff D. Right Ventricular Dysfunction in Patients Undergoing High-Risk PCI with Impella. *J Card Fail* 2024; 30(10):1244-1254. PMID: 39389734.
Full Text

Department of Cardiology, Heart Center at University of Leipzig and Leipzig Heart Institute, Leipzig, Germany, University Medical Center Mainz, Mainz, Germany; Clinical Trials Center, Cardiovascular Research Foundation, New York, New York, USA. Electronic address: Karl_Ph_Rommel@web.de.
Clinical Trials Center, Cardiovascular Research Foundation, New York, New York, USA; University of Bordeaux, Hôpital Cardiologique Haut-Lévêque, University Hospital, Bordeaux, France.
Division of Cardiology, Yale School of Medicine, New Haven, Connecticut, USA.
Division of Cardiology, Yale School of Medicine, New Haven, Connecticut, USA; Barts Heart Centre, London and Queen Mary University of London, London, United Kingdom.
Clinical Trials Center, Cardiovascular Research Foundation, New York, New York, USA.
Clinical Trials Center, Cardiovascular Research Foundation, New York, New York, USA; Department of Population Health Sciences, Weill Cornell Medicine, New York, New York, USA; Department of Molecular and Clinical Medicine, Gothenburg University, Gothenburg, Sweden; Department of Cardiology, Sahlgrenska University Hospital, Gothenburg, Sweden.
Department of Cardiology, Cardiology I, University Medical Center Mainz, Mainz, Germany; German Centre for Cardiovascular Research (DZHK), Partnersite RheinMain, Mainz, Germany.
Loma Linda University Heart Institute, Loma Linda, CA, USA.
Center for Structural Heart Disease, Division of Cardiology, Henry Ford Health System, Detroit, Michigan, USA.

BACKGROUND: Right ventricular dysfunction (RVD) is an important prognostic factor in several cardiac conditions, including acute and chronic heart failure. The impact of baseline RVD on clinical outcomes of patients undergoing high-risk percutaneous coronary intervention (HRPCI) supported by Impella is unknown. METHODS: Patients from the single-arm, multicenter PROTECT III study of Impella-supported HRPCI were stratified based on the presence or absence of RVD. RVD was quantitatively assessed by an echocardiography core laboratory and was defined as fractional area change < 35%, tricuspid annular

plane systolic excursion < 17 mm or pulsed-wave Doppler S-wave of the lateral tricuspid annulus < 9.5 cm/s. Procedural outcomes, 90-day major adverse cardiac and cerebrovascular events (MACCE: the composite of all-cause mortality, myocardial infarction, stroke/TIA, and repeat revascularization), and 1-year mortality were assessed. RESULTS: Of the 239 patients who underwent RV function assessment, 124 were found to have RVD. Lower left ventricular ejection fraction, higher blood urea nitrogen levels, and more severe RV dilation were independently associated with RVD. The incidence of hypotensive episodes during PCI, the proportion of patients requiring prolonged Impella support, the completeness of revascularization, and the rate of in-hospital mortality did not differ significantly between patients with vs without RVD. However, 90-day MACCE rates were higher in those with RVD, and RVD was a robust predictor of 1-year mortality in multivariable Cox-regression analyses. CONCLUSION: In patients undergoing HRPCI with Impella, RVD was associated with more advanced biventricular failure. The use of Impella support during HRPCI facilitated effective revascularization, even in those with concomitant RVD. Nevertheless, RVD was associated with unfavorable long-term prognoses.

Cardiology/Cardiovascular Research

Rymer J, Pichan C, Page C, Alhanti B, Bhatt DL, Kochar A, Angiolillo DJ, Diaz M, Wimmer NJ, Waksman R, Ang L, Bach R, Jenkins R, El-Sabae H, Brothers L, Ohman EM, Jones WS, Washam JB, Wang TY, Narcisse D, and **Basir MB**. The Use of Cangrelor in Cardiogenic Shock: Insights from the CAMEO Registry. *J Card Fail* 2024; 30(10):1233-1240. PMID: 39389732. Full Text

Duke University, Durham, NC; Duke Clinical Research Institute, Durham, NC. Electronic address: jennifer.rymer@duke.edu.
Duke University, Durham, NC.
Duke Clinical Research Institute, Durham, NC.
Mount Sinai Fuster Heart Hospital, Icahn School of Medicine at Mount Sinai, New York, NY.
University of Florida, Jacksonville, FL.
Palmetto General Hospital, Hialeah, FL.
ChristianaCare, Newark, DE.
Washington MedStar, Washington, D.C.
University of California San Diego, San Diego, CA.
Washington University in St. Louis, St. Louis, MO.
Kootenai Health, Coeur d'Alene, ID.
Chiesi, Cary, NC.
Duke University, Durham, NC; Duke Clinical Research Institute, Durham, NC.
Henry Ford Health, Detroit, MI.

INTRODUCTION: Little is known about the use of cangrelor in patients with myocardial infarction (MI) presenting with cardiogenic shock (CS). METHODS: CAMEO (Cangrelor in Acute MI: Effectiveness and Outcomes) is a multicenter observational registry evaluating platelet inhibition in patients with MI. We examined the duration of cangrelor infusion and the amount of time to transition from cangrelor to an oral P2Y(12) inhibitor in patients with CS. We also assessed major adverse cardiovascular events (MACEs) and bleeding risks, stratified by dosage duration, time to transition and oral P2Y(12) inhibitor potency. RESULTS: Among 2352 cangrelor-treated patients with MI, 249 patients were in CS. Among the patients with CS, 16 (6.4%) received the "bridge" infusion dose, 202 (81.1%) the PCI cangrelor infusion dose, and 30 (12.0%) had a combination of both infusion doses. Patients with CS had a median age of 66 years; 32% were women; 21% were Black patients; 35% had diabetes; 19% received thrombectomy; and 59% received mechanical circulatory support (MCS) (35% intra-aortic balloon pump, 27% Impella). The median duration of infusion was 3.9 (2-21.5 hours) in patients with CS and was 2 (1.6-3.1 hours) for all cangrelor-treated patients. The median duration of transition from cangrelor to oral P2Y(12) inhibitor administration was 0.1 (-0.5-21.0 hours) for patients with CS. In multivariable modeling, chronic lung disease and the use of MCS and was associated with longer cangrelor infusions (defined as > 3.9 hours). Among cangrelor-treated patients with CS, 24.1% of these patients had a bleeding event, and 41.8% had a MACE event. After adjustment, a longer cangrelor infusion duration was associated with increased risk of bleeding (P < 0.05). CONCLUSIONS: The median duration of cangrelor infusion was longer for patients presenting with CS. Use of MCS was associated with longer cangrelor infusion durations in

patients with CS. Further work is needed to understand the pharmacodynamics of antiplatelet agents in patients with CS.

Cardiology/Cardiovascular Research
Secemsky EA, **Aronow HD**, Kwolek CJ, Meissner M, Muck PE, Parikh SA, Winokur RS, George JC, Salazar G, Murphy EH, Costantino MM, Zhou W, Li J, Lookstein R, and Desai KR. Intravascular Ultrasound Use in Peripheral Arterial and Deep Venous Interventions: Multidisciplinary Expert Opinion From SCAI/AVF/AVLS/SIR/SVM/SVS. *J Soc Cardiovasc Angiogr Interv* 2024; 3(1):101205. PMID: 39131984. Full Text

Richard A. and Susan F. Smith Center for Outcomes Research in Cardiology and Division of Cardiovascular Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts.
Harvard Medical School, Boston, Massachusetts.
Department of Medicine, Michigan State University, East Lansing, Michigan.
Heart & Vascular Services, Henry Ford Health, Detroit, Michigan.
Newton-Wellesley Hospital, Wellesley, Massachusetts.
Department of Surgery, University of Washington School of Medicine, Seattle, Washington.
Department of Vascular Surgery, Good Samaritan Hospital, Cincinnati, Ohio.
Center for Interventional Cardiovascular Care, Division of Cardiology, Columbia University Irving Medical Center, New York, New York.
Weill Cornell Vein Treatment Center and Division of Interventional Radiology, Department of Radiology, Weill Cornell Medicine, New York, New York.
Division of Interventional Cardiology and Endovascular Medicine, Pennsylvania Hospital, Philadelphia, Pennsylvania.
Department of Radiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.
Venous and Lymphatic Center, Division of Vascular Surgery, Sanger Heart and Vascular, Atrium Health, Charlotte, North Carolina.
Advanced Vascular Centers, Portland, Oregon.
Division of Vascular Surgery, University of Arizona and Banner University Medical Center, Tucson, Arizona.
Harrington Heart and Vascular Institute, University Hospitals, Cleveland, Ohio.
Icahn School of Medicine at Mount Sinai, New York, New York.
Department of Radiology, Northwestern University Feinberg School of Medicine, Chicago, Illinois.

Percutaneous revascularization is the primary strategy for treating lower extremity venous and arterial disease. Angiography is limited by its ability to accurately size vessels, precisely determine the degree of stenosis and length of lesions, characterize lesion morphology, or correctly diagnose postintervention complications. These limitations are overcome with use of intravascular ultrasound (IVUS). IVUS has demonstrated the ability to improve outcomes following percutaneous coronary intervention, and there is increasing evidence to support its benefits in the setting of peripheral vascular intervention. At this stage in its evolution, there remains a need to standardize the use and approach to peripheral vascular IVUS imaging. This manuscript represents considerations and consensus perspectives that emerged from a roundtable discussion including 15 physicians with expertise in interventional cardiology, interventional radiology, and vascular surgery, representing 6 cardiovascular specialty societies, held on February 3, 2023. The roundtable's aims were to assess the current state of lower extremity revascularization, identify knowledge gaps and need for evidence, and determine how IVUS can improve care and outcomes for patients with peripheral arterial and deep venous pathology.

Cardiology/Cardiovascular Research
Selvaraj S, Patel S, Sauer AJ, McGarrah RW, Jones P, Kwee LC, Windsor SL, Ilkayeva O, Muehlbauer MJ, Newgard CB, Borlaug BA, Kitzman DW, Shah SJ, Margulies KB, Husain M, Inzucchi SE, McGuire DK, **Lanfear DE**, Javaheri A, Umpierrez G, Mentz RJ, Sharma K, Kosiborod MN, and Shah SH. Metabolic Effects of the SGLT2 Inhibitor Dapagliflozin in Heart Failure Across the Spectrum of Ejection Fraction. *Circ Heart Fail* 2024; e011980. Epub ahead of print. PMID: 39421941. Full Text

Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, NC (S.S., R.W.M., R.J.M., S.H.S.).
Duke Molecular Physiology Institute, Duke University, Durham, NC (S.S., R.W.M., L.C.K., O.I., M.J.M., C.B.N., S.H.S.).
Saint Luke's Mid America Heart Institute, Kansas City, MO (S.P., A.J.S., P.J., S.L.W., M.N.K.).
University of Missouri-Kansas City (A.J.S., M.N.K.).
Division of Endocrinology, Metabolism, and Nutrition, Department of Medicine, Duke University School of Medicine, Durham, NC (O.I.).
Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN (B.A.B.).
Department of Internal Medicine, Sections on Cardiovascular Medicine and Geriatrics, Wake Forest School of Medicine, Winston-Salem, NC (D.W.K.).
Division of Cardiology, Department of Medicine, Bluhm Cardiovascular Institute, Northwestern University Feinberg School of Medicine, Chicago, IL (S.J.S.).
Division of Cardiology, Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia (K.B.M.).
Ted Rogers Centre for Heart Research, University of Toronto, ON, Canada (M.H.).
Yale University School of Medicine, New Haven, CT (S.E.I.).
University of Texas Southwestern Medical Center and Parkland Health and Hospital System, Dallas (D.K.M.).
Center for Individual and Genomic Medicine Research and Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, MI (D.E.L.).
Washington University School of Medicine, St. Louis, MO (A.J.).
Division of Endocrinology, Emory University School of Medicine, Atlanta, GA (G.U.).
Division of Cardiology, Johns Hopkins University School of Medicine, Baltimore, MD (K.S.).

BACKGROUND: Mechanisms of benefit with SGLT2is (sodium-glucose cotransporter-2 inhibitors) in heart failure (HF) remain incompletely characterized. Dapagliflozin alters ketone and fatty acid metabolism in HF with reduced ejection fraction though similar effects have not been observed in HF with preserved ejection fraction. We explore whether metabolic effects of SGLT2is vary across the left ventricular ejection fraction spectrum and their relationship with cardiometabolic end points in 2 randomized trials of dapagliflozin in HF. METHODS: Metabolomic profiling of 61 metabolites was performed in 527 participants from DEFINE-HF (Dapagliflozin Effects on Biomarkers, Symptoms and Functional Status in Patients With HF With Reduced Ejection Fraction) and PRESERVED-HF (Dapagliflozin in PRESERVED Ejection Fraction HF; 12-week, placebo-controlled trials of dapagliflozin in HF with reduced ejection fraction and HF with preserved ejection fraction, respectively). Linear regression was used to assess changes in principal components analysis-defined metabolite factors with treatment from baseline to 12 weeks, as well as the relationship between changes in metabolite clusters and HF-related end points. RESULTS: The mean age was 66±11 years, 43% were female, and 33% were self-identified as Black. Two principal components analysis-derived metabolite factors (which were comprised of ketone and short-/medium-chain acylcarnitines) increased with dapagliflozin compared with placebo. Ketosis (defined as 3-hydroxybutyrate >500 μM) was achieved in 4.5% with dapagliflozin versus 1.2% with placebo (P=0.03). There were no appreciable treatment effects on amino acids, including branched-chain amino acids. Increases in several acylcarnitines were consistent across LVEF (P(interaction)>0.10), whereas the ketogenic effect diminished at higher LVEF (P(interaction)=0.01 for 3-hydroxybutyrate). Increases in metabolites reflecting mitochondrial dysfunction (particularly long-chain acylcarnitines) and aromatic amino acids and decreases in branched-chain amino acids were associated with worse HF-related outcomes in the overall cohort, with consistency across treatment and LVEF. CONCLUSIONS: SGLT2is demonstrate common (fatty acid) and distinct (ketogenic) metabolic signatures across the LVEF spectrum. Changes in key pathways related to fatty acid and amino acid metabolism are associated with HF-related end points and may serve as therapeutic targets across HF subtypes. REGISTRATION: URL: https://www.clinicaltrials.gov; Unique Identifiers: NCT03030235 and NCT02653482.

Cardiology/Cardiovascular Research

Shah P, **Cowger JA**, Mehra MR, Lu Q, and Uriel N. Reply: Enhancing Dynamic Risk Prediction in LVAD Patients: Methodological Considerations. *JACC: Heart Failure* 2024; 12(11):1953. Not assigned. Full Text

P. Shah, George Washington University, 3300 Gallows Road, Falls Church, VA, United States

Cardiology/Cardiovascular Research
VanAken G, Rubick D, Wieczorek D, Chatterjee S, Moles VM, Agarwal PP, Haft JW, Cascino TM, Visovatti S, and **Aggarwal V**. Exercise Training in Patients with Chronic Thromboembolic Pulmonary Hypertension and Pulmonary Arterial Hypertension: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Heart Fail Clin* 2024. PMID: Not assigned. Full Text

G. VanAken, 1500 East Medical Center Drive TC 311Q, Ann Arbor, MI, United States

Cardiology/Cardiovascular Research
VanAken G, Wieczorek D, Rubick D, **Jabri A**, **Franco-Palacios D**, **Grafton G**, **Kelly B**, **Osinbowale O**, **Ahsan ST**, **Awdish R**, **Aronow HD**, Shore S, and **Aggarwal V**. Cardiopulmonary exercise testing following acute pulmonary embolism: Systematic review and pooled analysis of global studies. *Pulm Circ* 2024; 14(4):e12451. PMID: 39391222. Full Text

Department of Internal Medicine University of Michigan Ann Arbor Michigan USA.
University of Michigan Medical School Ann Arbor Michigan USA.
Central Michigan University College of Medicine Mount Pleasant Michigan USA.
Division of Cardiology Henry Ford Health Detroit Michigan USA.
Division of Pulmonary and Critical Care Medicine Henry Ford Health Detroit Michigan USA.
Department of Osteopathic Medical Specialties Michigan State University College of Osteopathic Medicine East Lansing Michigan USA.
Michigan State University College of Human Medicine East Lansing Michigan USA.
Division of Cardiology (Frankel Cardiovascular Center), Department of Internal Medicine University of Michigan Ann Arbor Michigan USA.

Recent reports have revealed a substantial morbidity burden associated with "post-PE syndrome" (PPES). Cardiopulmonary exercise testing (CPET) has shown promise in better characterizing these patients. In this systematic review and pooled analysis, we aim to use CPET data from PE survivors to understand PPES better. A literature search was conducted in PubMed, EMBASE, and Cochrane for studies reporting CPET results in post-PE patients without known pulmonary hypertension published before August 1, 2023. Studies were independently reviewed by two authors. CPET findings were subcategorized into (1) exercise capacity (percent predicted pVO(2) and pVO(2)) and (2) ventilatory efficiency (VE/VCO(2) slope and V(D)/V(T)). We identified 14 studies (n = 804), 9 prospective observational studies, 4 prospective case-control studies, and 1 randomized trial. Pooled analysis demonstrated a weighted mean percent predicted pVO(2) of 76.09 ± 20.21% (n = 184), with no difference between patients tested <6 months (n = 76, 81.69±26.06%) compared to ≥6 months post-acute PE (n = 88, 82.55 ± 21.47%; p = 0.817). No difference was seen in pVO(2) in those tested <6 months (n = 76, 1.67 ± 0.51 L/min) compared to ≥6 months post-acute PE occurrence (n = 144, 1.75 ± 0.57 L/min; p = 0.306). The weighted mean VE/VCO(2) slope was 32.72 ± 6.02 (n = 244), with a significant difference noted between those tested <6 months (n = 91, 36.52 ± 6.64) compared to ≥6 months post-acute PE (n = 191, 31.99 ± 5.7; p < 0.001). In conclusion, this study, which was limited by small sample sizes and few multicenter studies, found no significant difference in exercise capacity between individuals tested <6 months versus ≥6 months after acute PE. However, ventilatory efficiency was significantly improved in patients undergoing CPET ≥ 6 months compared to those <6 months from the index PE.

Center for Health Policy and Health Services Research
Angerhofer Richards J, Cruz M, Stewart C, Lee AK, Ryan TC, **Ahmedani BK**, and Simon GE. Effectiveness of Integrating Suicide Care in Primary Care : Secondary Analysis of a Stepped-Wedge, Cluster Randomized Implementation Trial. *Ann Intern Med* 2024; Epub ahead of print. PMID: 39348695. Full Text

Kaiser Permanente Washington Heath Research Institute and Department of Health Systems and Population Health, University of Washington, Seattle, Washington (J.A.R.).

Kaiser Permanente Washington Heath Research Institute and Department of Biostatistics, School of Public Health, University of Washington, Seattle, Washington (M.C.).
Kaiser Permanente Washington Heath Research Institute, Seattle, Washington (C.S.).
Kaiser Permanente Washington Heath Research Institute and Kaiser Permanente Washington Department of Mental Health and Wellness, Seattle, Washington (A.K.L., G.E.S.).
Department of Health Systems and Population Health, University of Washington, Seattle, Washington (T.C.R.).
Center for Health Policy and Health Services Research (CHSR), Henry Ford Health System, Detroit, Michigan. (B.K.A.).

BACKGROUND: Primary care encounters are common among patients at risk for suicide. OBJECTIVE: To evaluate the effectiveness of implementing population-based suicide care (SC) in primary care for suicide attempt prevention. DESIGN: Secondary analysis of a stepped-wedge, cluster randomized implementation trial. (ClinicalTrials.gov: NCT02675777). SETTING: 19 primary care practices within a large health care system in Washington State, randomly assigned launch dates. PATIENTS: Adult patients (aged ≥18 years) with primary care visits from January 2015 to July 2018. INTERVENTION: Practice facilitators, electronic medical record (EMR) clinical decision support, and performance monitoring supported implementation of depression screening, suicide risk assessment, and safety planning. MEASUREMENTS: Clinical practice and patient measures relied on EMR and insurance claims data to compare usual care (UC) and SC periods. Primary outcomes included documented safety planning after population-based screening and suicide risk assessment and suicide attempts or deaths (with self-harm intent) within 90 days of a visit. Mixed-effects logistic models regressed binary outcome indicators on UC versus SC, adjusted for randomization stratification and calendar time, accounting for repeated outcomes from the same site. Monthly outcome rates (percentage per 10 000 patients) were estimated by applying marginal standardization. RESULTS: During UC, 255 789 patients made 953 402 primary care visits and 228 255 patients made 615 511 visits during the SC period. The rate of safety planning was higher in the SC group than in the UC group (38.3 vs. 32.8 per 10 000 patients; rate difference, 5.5 [95% CI, 2.3 to 8.7]). Suicide attempts within 90 days were lower in the SC group than in the UC group (4.5 vs. 6.0 per 10 000 patients; rate difference, -1.5 [CI, -2.6 to -0.4]). LIMITATION: Suicide care was implemented in combination with care for depression and substance use. CONCLUSION: Implementation of population-based SC concurrent with a substance use program resulted in a 25% reduction in the suicide attempt rate in the 90 days after primary care visits. PRIMARY FUNDING SOURCE: National Institute of Mental Health.

Center for Health Policy and Health Services Research
Braciszewski JM, Llamocca EN, **Lockhart E**, **Vanderziel AM**, **Boulay ML**, and **Ahmedani BK**. Assessing the Acceptability of Technology-Based Safety Planning in Primary Care. *J Gen Intern Med* 2024; Epub ahead of print. PMID: 39438377. Full Text

Center for Health Policy & Health Services Research, Henry Ford Health, One Ford Place, Suite 5E, Detroit, MI, 48202, USA. jbracis1@hfhs.org.
Department of Psychiatry, Henry Ford Health, Detroit, MI, One Ford Place, Suite 1F, Detroit, MI, 48202, USA. jbracis1@hfhs.org.
Nationwide Children's Hospital, Center for Suicide Prevention and Research, Big Lots Behavioral Health Pavilion, 444 Butterfly Gardens Drive, Suite 2B, Columbus, OH, 43215, USA.
Center for Health Policy & Health Services Research, Henry Ford Health, One Ford Place, Suite 5E, Detroit, MI, 48202, USA.
Department of Psychiatry, Henry Ford Health, Detroit, MI, One Ford Place, Suite 1F, Detroit, MI, 48202, USA.

Center for Health Policy and Health Services Research
Grosvenor LP, Croen LA, Lynch FL, Marafino BJ, **Maye M**, Penfold RB, Simon GE, and Ames JL. Autism Diagnosis Among US Children and Adults, 2011-2022. *JAMA Netw Open* 2024; 7(10):e2442218. PMID: 39476234. Full Text

Division of Research, Kaiser Permanente Northern California, Pleasanton, California.

Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, California.
Center for Health Research, Kaiser Permanente, Portland, Oregon.
Center for Health Services Research, Henry Ford Health System, Detroit, Michigan.
Pediatrics, College of Human Medicine, Michigan State University, East Lansing.
Kaiser Permanente Washington Health Research Institute, Seattle, Washington.

IMPORTANCE: An improved understanding of autism spectrum disorder (ASD) prevalence over time and across the lifespan can inform health care service delivery for the growing population of autistic children and adults. OBJECTIVE: To describe trends in the prevalence of ASD diagnoses using electronic records data from a large network of health systems in the US. DESIGN, SETTING, AND PARTICIPANTS: This cross-sectional study examined annual diagnosis rates in health records of patients in US health systems from January 1, 2011, to December 31, 2022. Eligible individuals were included in the study sample for a given calendar year if they were enrolled in a participating health system for at least 10 months out of the year. Data were extracted from 12 sites participating in the Mental Health Research Network, a consortium of research centers embedded within large, diverse health care systems. MAIN OUTCOME AND MEASURES: Diagnoses of ASD were ascertained using International Classification of Diseases, Ninth Revision (ICD-9) and International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) revision codes. Annual diagnosis rates were calculated as the number of unique members diagnosed, divided by the total members enrolled. RESULTS: A total of 12 264 003 members were enrolled in 2022 (2 359 359 children aged 0 to 17 years [19.2%]; 6 400 222 female [52.2%]; 93 002 American Indian or Alaska Native [0.8%], 1 711 950 Asian [14.0%], 952 287 Black or African American [7.8%], 2 971 355 Hispanic [24.2%], 166 144 Native Hawaiian or Pacific Islander [1.4%], and 6 462 298 White [52.7%]). The ASD diagnosis rate was greatest among 5-to-8-year-olds throughout the study period and increased by 175% among the full sample, from 2.3 per 1000 in 2011 to 6.3 per 1000 in 2022. The greatest relative increase in diagnosis rate from 2011 to 2022 occurred among 26-to-34-year-olds (450%) and increases were greater for female vs male individuals among children (305% [estimated annual percentage change (EAPC), 13.62 percentage points; 95% CI, 12.49-14.75 percentage points] vs 185% [EAPC, 9.63 percentage points; 95% CI, 8.54-10.72 percentage points], respectively) and adults (315% [EAPC, 13.73 percentage points; 95% CI, 12.61-14.86 percentage points] vs 215% [EAPC, 10.33 percentage points; 95% CI, 9.24-11.43 percentage points]). Relative increases were greater in racial and ethnic minority groups compared with White individuals among children, but not adults. CONCLUSIONS AND RELEVANCE: In this cross-sectional study of children and adults in the US, ASD diagnosis rates increased substantially between 2011 and 2022, particularly among young adults, female children and adults, and children from some racial or ethnic minority groups. Diagnosis prevalence trends generated using health system data can inform the allocation of resources to meet the service needs of this growing, medically complex population.

Center for Health Policy and Health Services Research
Miller-Matero LR, **Hecht LM**, **Gavrilova L**, **Haage B**, **Autio K**, **Tobin ET**, and **Ahmedani BK**. Utilizing primary care to engage underserved patients in a psychological intervention for chronic pain. *Prim Health Care Res Dev* 2024; 25:e54. PMID: 39450755. Full Text

Henry Ford Health, Behavioral Health, Detroit, MI, USA.
Henry Ford Health, Center for Health Policy & Health Services Research, Detroit, MI, USA.
Michigan State University, East Lansing, MI, USA.
Henry Ford Health, Public Health Sciences, Detroit, MI, USA.
Henry Ford Health, Internal Medicine, Detroit, MI, USA.

BACKGROUND: Although psychological interventions can be used to improve chronic pain management, underserved individuals (i.e., racially minoritized and socioeconomically disadvantaged) may be less likely to engage in such services. The purpose of this study was to examine whether offering a psychological intervention for chronic pain in a primary care clinic could be a method in which to successfully engage underserved patients. METHODS: There were 220 patients with chronic pain in a primary care clinic located in a socioeconomically and racially diverse city who were approached to discuss enrolment in a pilot randomized controlled trial of a five-session psychological intervention for chronic pain. Patients were introduced to the study by their primary care provider using the warm handoff

model. We compared whether there were sociodemographic differences between those who enrolled in the study and those who declined to enrol. RESULTS: There were no differences between those who enrolled and those who declined enrolment with regard to race, age, insurance type, and household income. However, females were more likely to enrol in the study compared to males. CONCLUSIONS: Recruiting patients to participate in a trial of a psychological intervention for chronic pain in a primary care clinic appeared to be effective for engaging Black patients, patients with lower income, and those with government insurance. Thus, offering a psychological intervention for chronic pain in a primary care clinic may encourage engagement among racially minoritized individuals and those with lower socioeconomic status.

Center for Health Policy and Health Services Research
Miller-Matero LR, **Pappas C**, **Altairi S**, **Sehgal M**, Chrusciel T, Salas J, Secrest S, Wilson L, Carpenter RW, Sullivan MD, **Ahmedani BK**, Lustman PJ, and Scherrer JF. Alcohol, Tobacco, and Marijuana use Among Individuals Receiving Prescription Opioids for Pain Management. *Clin J Pain* 2024; Epub ahead of print. PMID: 39470110. Full Text

Behavioral Health, Henry Ford Health.
Center for Health Policy and Health Services Research, Henry Ford Health.
Department of Family and Community Medicine, Saint Louis University School of Medicine.
Advanced HEAlth Data (AHEAD) Research Institute, Saint Louis University School of Medicine.
Department of Health and Clinical Outcomes Research, Saint Louis University School of Medicine.
Department of Psychological Sciences, University of Missouri - St. Louis.
Department of Psychiatry and Behavioral Science, University of Washington School of Medicine.
Department of Psychiatry, Washington University School of Medicine.
Department of Psychiatry and Behavioral Neuroscience, Saint Louis University School of Medicine.

OBJECTIVE: Substance use among individuals receiving prescription opioids for pain may be associated with poorer functioning. The purpose was to examine whether use of substances (i.e., alcohol, marijuana, or tobacco) among individuals prescribed opioids for pain management was associated with pain, psychiatric disorders, and opioid misuse. METHODS: Patients with non-cancer pain and a new opioid prescription were recruited from two health systems. Participants (N= 827) completed measures regarding pain severity, pain interference, psychiatric symptoms, and substance use. RESULTS: Substance use was common with 58.0%, 26.2%, and 28.9% reporting alcohol, tobacco, and marijuana use, respectively. Use of tobacco or marijuana was associated with poorer functioning. Those with tobacco use had greater pain severity, interference, number of pain sites, and concern for opioid misuse, and were more likely to have probable depression, anxiety, and PTSD. Participants reporting marijuana use were more likely to have higher concern for opioid misuse scores and probable depression, anxiety, and PTSD. Use of alcohol was associated with lower pain severity and interference and fewer number of pain sites. DISCUSSION: Substance use is common among individuals receiving prescription opioids. Some types of substance use may be related to poorer opioid, pain, and psychiatric functioning. Clinicians prescribing opioids for pain management should assess for substance use, including tobacco, and be aware of the association with poorer functioning. Interventions could target pain, psychiatric symptoms, and substance use simultaneously to optimize outcomes for individuals with pain and substance use.

Center for Health Policy and Health Services Research
Oberprieler NG, **Pladevall-Vila M**, Johannes C, Layton JB, Golozar A, Lavallee M, Liu F, Kubin M, and Vizcaya D. FOUNTAIN: a modular research platform for integrated real-world evidence generation. *BMC Med Res Methodol* 2024; 24(1):224. PMID: 39354358. Full Text

Bayer AS, Oslo, Norway. niki.oberprieler@bayer.com.
RTI Health Solutions, Barcelona, Spain.
The Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA.
RTI Health Solutions, Waltham, MA, USA.
RTI Health Solutions, Research Triangle Park, NC, USA.
Odysseus, Inc., New York, NY, USA.

Bayer AG, Wuppertal, Germany.
Bayer Pharmaceuticals, Sant Joan Despi, Spain.

BACKGROUND: Real-world evidence (RWE) plays a key role in regulatory and healthcare decision-making, but the potentially fragmentated nature of generated evidence may limit its utility for clinical decision-making. Heterogeneity and a lack of reproducibility in RWE resulting from inconsistent application of methodologies across data sources should be minimized through harmonization. METHODS: This paper's aim is to describe and reflect upon a multidisciplinary research platform (FOUNTAIN; FinerenOne mUlti-database NeTwork for evidence generAtIoN) with coordinated studies using diverse RWE generation approaches and explore the platform's strengths and limitations. With guidance from an executive advisory committee of multidisciplinary experts and patient representatives, the goal of the FOUNTAIN platform is to harmonize RWE generation across a portfolio of research projects, including research partner collaborations and a common data model (CDM)-based program. FOUNTAIN's overarching objectives as a research platform are to establish long-term collaborations among pharmacoepidemiology research partners and experts and to integrate diverse approaches for RWE generation, including global protocol execution by research partners in local data sources and common protocol execution in multiple data sources through federated data networks, while ensuring harmonization of medical definitions, methodology, and reproducible artifacts across all studies. Specifically, the aim of the multiple studies run within the frame of FOUNTAIN is to provide insight into the real-world utilization, effectiveness, and safety of finerenone across its life-cycle. RESULTS: Currently, the FOUNTAIN platform includes 9 research partner collaborations and 8 CDM-mapped data sources from 7 countries (United States, United Kingdom, China, Japan, The Netherlands, Spain, and Denmark). These databases and research partners were selected after a feasibility fit-for-purpose evaluation. Six multicountry, multidatabase, cohort studies are ongoing to describe patient populations, current standard of care, comorbidity profiles, healthcare resource use, and treatment effectiveness and safety in different patient populations with chronic kidney disease and type 2 diabetes. Strengths and potential limitations of FOUNTAIN are described in the context of valid RWE generation. CONCLUSION: The establishment of the FOUNTAIN platform has allowed harmonized execution of multiple studies, promoting consistency both within individual studies that employ multiple data sources and across all studies run within the platform's framework. FOUNTAIN presents a proposal to efficiently improve the consistency and generalizability of RWE on finerenone.

Center for Health Policy and Health Services Research

Ruth O, Tomajko S, Dabaja E, Munsel E, Rice K, Cwynar C, **Maye M**, and Malas N. Current Evidence Regarding the Evaluation and Management of Neonatal Delirium. *Curr Psychiatry Rep* 2024; Epub ahead of print. PMID: 39446295. Full Text

Department of Pediatrics, Division of Neonatal-Perinatal Medicine, University of Michigan Mott Children's Hospital, Ann Arbor, MI, USA. oruth@med.umich.edu.
Department of Pediatrics, Division of Neonatal-Perinatal Medicine, University of Michigan Mott Children's Hospital, Ann Arbor, MI, USA.
Department of Pediatrics, Division of Neonatology, Cleveland Clinic, Cleveland, OH, USA.
Department of Pharmacy, Michigan Medicine, University of Michigan, Ann Arbor, MI, USA.
Department of Psychiatry, Division of Child and Adolescent Psychiatry, University of Michigan Mott Children's Hospital, Ann Arbor, MI, USA.
Department of Women, Children, & Family Nursing; Primary Care Pediatric Nurse Practitioner Program, Rush University, Chicago, IL, USA.
Henry Ford Health and Michigan State University Health Sciences, East Lansing, MI, USA.
Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, MI, USA.
Department of Pediatrics, College of Human Medicine, Michigan State University, East Lansing, MI, USA.
Department of Pediatrics, University of Michigan Medical School, Ann Arbor, MI, USA.

PURPOSE OF REVIEW: Newborns and infants in the neonatal intensive care unit (NICU) may be at uniquely high risk of developing delirium. Because there is a dearth of NICU-focused literature, providers must rely on evidence derived from older children and infants in other care settings to guide management. The literature was rigorously reviewed to highlight evidence specific to newborns and

infants and is summarized here. RECENT FINDINGS: Delirium likely occurs in newborns and infants at similar or higher rates than what is seen in other care settings. Recent literature calls particular attention to the lack of assessment tools validated in a NICU setting. Evidence for the evaluation and management of delirium in the NICU is lacking. More study specific to the NICU is needed to build consensus toward best practice.

Center for Individualized and Genomic Medicine Research
Littleton SDR, **Lanfear DE**, Dorsch MP, **Liu B**, and Luzum JA. Equal Treatment, Unequal Outcomes? Debunking the Racial Disparity in Renin Angiotensin Aldosterone System Inhibitor Associated Reduction in Heart Failure Hospitalizations. *J Card Fail* 2024; Epub ahead of print. PMID: 39442611. Full Text

University of Michigan College of Pharmacy, Ann Arbor, MI, USA.
Henry Ford Health System, Detroit, MI, USA.
University of Michigan College of Pharmacy, Ann Arbor, MI, USA. Electronic address: jluzum@med.umich.edu.

BACKGROUND: Renin angiotensin aldosterone system inhibitors (RAASi) are a mainstay treatment in patients with heart failure with reduced ejection fraction (HFrEF) in part to prevent hospitalizations. However, whether RAAS inhibitors reduce the risk of hospitalization in Black patients is not entirely clear because enrollment of Black patients in previous clinical trials was low, and a previous meta-analysis showed a significant racial disparity: reduction in hospitalizations with an RAAS inhibitor in White patients but not Black patients. Previous studies relied on the use of self-identified race instead of genomic ancestry. Therefore, this study aimed to investigate the role of self-identified race and genomic ancestry in the racial disparity in RAAS inhibitor associated reductions in HFrEF hospitalizations. METHODS: The primary outcome was time to first heart failure hospitalization. A (de-identified) heart failure patient registry and data from the GUIDE-IT multi-center randomized control trial were analyzed with Cox proportional hazards models un/adjusted for clinical risk factors, death as a competing risk, and time-varying RAAS inhibitor exposure. The proportion of Yoruba African ancestry was quantified.. Analysis of self - identified race were performed in both the registry and GUIDE-IT. Analysis of genomic ancestry was only performed in the registry since this information was not available in GUIDE-IT. A fixed effect meta-analysis combined results of both the registry and GUIDE-IT for race. RESULTS: The registry had 1010 total HFrEF patients (Black = 509 and White = 501) with 852 having ancestry quantification (>80% Yoruba African Ancestry = 381 and <5% Yoruba African Ancestry = 471). GUIDE-IT had 810 HFrEF patients (Black = 322 and White = 488). There was no significant difference in the association of RAAS inhibitor exposure with heart failure hospitalization by race (meta-analysis p-value for race*RAAS inhibitor exposure interaction = 0.49; Black patients HR [95% CI] for RAAS inhibitor exposure = 0.89 [0.64-1.23)] P = 0.47; White patients = 1.20 (0.83-1.75) P = 0.34). Results were similar when analyzed by ancestry (p-value for ancestry*RAAS inhibitor exposure interaction = 0.57; >80% Yoruba African Ancestry = 0.93 [0.51-1.69] P = 0.80; <5% Yoruba African Ancestry = 1.29 [0.57-2.92] P = 0.54). CONCLUSIONS: In contrast to a previous meta-analysis, this more contemporary analysis of 2 HFrEF patient datasets demonstrates the absence of a racial disparity in RAAS inhibitor associated reductions in heart failure hospitalizations. The difference in this racial disparity over time may be due to improvements in background heart failure therapies, racial differences in healthcare usage, and the use of more advanced statistical approaches.

Center for Individualized and Genomic Medicine Research
Selvaraj S, Patel S, Sauer AJ, McGarrah RW, Jones P, Kwee LC, Windsor SL, Ilkayeva O, Muehlbauer MJ, Newgard CB, Borlaug BA, Kitzman DW, Shah SJ, Margulies KB, Husain M, Inzucchi SE, McGuire DK, **Lanfear DE**, Javaheri A, Umpierrez G, Mentz RJ, Sharma K, Kosiborod MN, and Shah SH. Metabolic Effects of the SGLT2 Inhibitor Dapagliflozin in Heart Failure Across the Spectrum of Ejection Fraction. *Circ Heart Fail* 2024; e011980. Epub ahead of print. PMID: 39421941. Full Text

Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, NC (S.S., R.W.M., R.J.M., S.H.S.).
Duke Molecular Physiology Institute, Duke University, Durham, NC (S.S., R.W.M., L.C.K., O.I., M.J.M., C.B.N., S.H.S.).

Saint Luke's Mid America Heart Institute, Kansas City, MO (S.P., A.J.S., P.J., S.L.W., M.N.K.).
University of Missouri-Kansas City (A.J.S., M.N.K.).
Division of Endocrinology, Metabolism, and Nutrition, Department of Medicine, Duke University School of Medicine, Durham, NC (O.I.).
Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN (B.A.B.).
Department of Internal Medicine, Sections on Cardiovascular Medicine and Geriatrics, Wake Forest School of Medicine, Winston-Salem, NC (D.W.K.).
Division of Cardiology, Department of Medicine, Bluhm Cardiovascular Institute, Northwestern University Feinberg School of Medicine, Chicago, IL (S.J.S.).
Division of Cardiology, Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia (K.B.M.).
Ted Rogers Centre for Heart Research, University of Toronto, ON, Canada (M.H.).
Yale University School of Medicine, New Haven, CT (S.E.I.).
University of Texas Southwestern Medical Center and Parkland Health and Hospital System, Dallas (D.K.M.).
Center for Individual and Genomic Medicine Research and Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, MI (D.E.L.).
Washington University School of Medicine, St. Louis, MO (A.J.).
Division of Endocrinology, Emory University School of Medicine, Atlanta, GA (G.U.).
Division of Cardiology, Johns Hopkins University School of Medicine, Baltimore, MD (K.S.).

BACKGROUND: Mechanisms of benefit with SGLT2is (sodium-glucose cotransporter-2 inhibitors) in heart failure (HF) remain incompletely characterized. Dapagliflozin alters ketone and fatty acid metabolism in HF with reduced ejection fraction though similar effects have not been observed in HF with preserved ejection fraction. We explore whether metabolic effects of SGLT2is vary across the left ventricular ejection fraction spectrum and their relationship with cardiometabolic end points in 2 randomized trials of dapagliflozin in HF. METHODS: Metabolomic profiling of 61 metabolites was performed in 527 participants from DEFINE-HF (Dapagliflozin Effects on Biomarkers, Symptoms and Functional Status in Patients With HF With Reduced Ejection Fraction) and PRESERVED-HF (Dapagliflozin in PRESERVED Ejection Fraction HF; 12-week, placebo-controlled trials of dapagliflozin in HF with reduced ejection fraction and HF with preserved ejection fraction, respectively). Linear regression was used to assess changes in principal components analysis-defined metabolite factors with treatment from baseline to 12 weeks, as well as the relationship between changes in metabolite clusters and HF-related end points. RESULTS: The mean age was 66±11 years, 43% were female, and 33% were self-identified as Black. Two principal components analysis-derived metabolite factors (which were comprised of ketone and short-/medium-chain acylcarnitines) increased with dapagliflozin compared with placebo. Ketosis (defined as 3-hydroxybutyrate >500 μM) was achieved in 4.5% with dapagliflozin versus 1.2% with placebo (P=0.03). There were no appreciable treatment effects on amino acids, including branched-chain amino acids. Increases in several acylcarnitines were consistent across LVEF (P(interaction)>0.10), whereas the ketogenic effect diminished at higher LVEF (P(interaction)=0.01 for 3-hydroxybutyrate). Increases in metabolites reflecting mitochondrial dysfunction (particularly long-chain acylcarnitines) and aromatic amino acids and decreases in branched-chain amino acids were associated with worse HF-related outcomes in the overall cohort, with consistency across treatment and LVEF. CONCLUSIONS: SGLT2is demonstrate common (fatty acid) and distinct (ketogenic) metabolic signatures across the LVEF spectrum. Changes in key pathways related to fatty acid and amino acid metabolism are associated with HF-related end points and may serve as therapeutic targets across HF subtypes. REGISTRATION: URL: https://www.clinicaltrials.gov; Unique Identifiers: NCT03030235 and NCT02653482.

Clinical Quality and Safety

Terhune J, Pylman S, and **Clarey J**. Rethinking Shared Decision-Making: Delivery of Care Options in a Telehealth World. *Telemed J E Health* 2024; Epub ahead of print. PMID: 39453462. Full Text

Michigan State University College of Human Medicine, East Lansing, Michigan, USA.
Henry Ford Health, Detroit, Michigan, USA.

Telehealth modalities have given patients options for delivery of care, and in some cases increased access to care. However, great effort needs to be made by providers and clinic staff to ensure patients are given choice in their delivery of care methods and technological support to work toward equity in care. We propose applying the BEACH model for shared decision-making to help providers support patients in choosing the best care delivery method, while also encouraging providers to seek further education on telehealth competencies. Lastly, we stress the importance of the clinical staff in ensuring patient autonomy, education, and support when choosing telehealth modalities of care.

Dermatology
Baldwin H, **Gold LS**, Harper JC, Alexis AF, Callender VD, Kircik L, Guenin E, and Eichenfield LF. Triple-Combination Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel for Acne in Adult and Pediatric Participants. *J Drugs Dermatol* 2024; 23(6):394-402. PMID: 38834226. Request Article

BACKGROUND: Topical clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel (CAB) is the first fixed-dose triple-combination approved for the treatment of acne. This post hoc analysis investigated the efficacy and safety of CAB in pediatric (<18 years) and adult (greater than or equal to 18 years) participants. METHODS: In two multicenter, double-blind, phase 3 studies (NCT04214639 and NCT04214652), participants greater than or equal to 9 years of age with moderate-to-severe acne were randomized (2:1) to 12 weeks of once-daily treatment with CAB or vehicle gel. Pooled data were analyzed for pediatric and adult subpopulations. Assessments included treatment success (greater than or equal to 2-grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 [clear] or 1 [almost clear], inflammatory/noninflammatory lesion counts, Acne-Specific Quality of Life (Acne-QoL) questionnaire, treatment-emergent adverse events (TEAEs), and cutaneous safety/tolerability. RESULTS: At week 12, treatment success rates for both pediatric and adult participants were significantly greater with CAB (52.7%; 45.9%) than with vehicle (24.0%; 23.5%; P<0.01, both). CAB-treated participants in both subgroups experienced greater reductions from baseline versus vehicle in inflammatory (pediatric: 78.6% vs 50.4%; adult: 76.6% vs 62.8%; P<0.001, both) and noninflammatory lesions (pediatric: 73.8% vs 41.1%; adult: 70.7% vs 52.2%; P<0.001, both). Acne-QoL improvements from baseline to week 12 were significantly greater with CAB than with a vehicle. Most TEAEs were of mild-to-moderate severity; no age-related trends for safety/tolerability were observed. Conclusions: CAB gel demonstrated comparable efficacy, quality of life improvements, and safety in pediatric and adult participants with moderate-to-severe acne. As the first fixed-dose, triple-combination topical formulation, CAB represents an important new treatment option for patients with acne. J Drugs Dermatol. 2024;23(6):394-402.   doi:10.36849/JDD.8357.

Dermatology
Ezzedine K, Soliman AM, Camp HS, Ladd MK, Pokrzywinski R, Coyne KS, Sen R, Schlosser BJ, Bae JM, and **Hamzavi I**. Psychometric Properties and Meaningful Change Thresholds of the Vitiligo Area Scoring Index. *JAMA Dermatol* 2024; Epub ahead of print. PMID: 39475960. Full Text

Department of Dermatology, Hôpital Henri Mondor, Assistance Publique-Hôpitaux de Paris, Créteil, France.
Équipe d'Accueil 7379 EpidermE (Epidemiology in Dermatology and Therapeutics Evaluation), Université Paris-Est Créteil, Créteil, France.
AbbVie Inc, North Chicago, Illinois.
Evidera, Wilmington, North Carolina.
Department of Dermatology, St Vincent's Hospital, College of Medicine, The Catholic University of Korea, Suwon, Korea.
Department of Dermatology, Multicultural Dermatology Center, Henry Ford Health, Detroit, Michigan.

IMPORTANCE: Defining meaningful improvement using the Total Vitiligo Area Scoring Index (T-VASI) and the Facial VASI (F-VASI) aids interpretation of findings from clinical trials evaluating vitiligo treatments; however, clear and clinically meaningful thresholds have not yet been established. OBJECTIVE: To assess concept validity and measurement performance of the T-VASI and F-VASI in patients with nonsegmental vitiligo and to identify meaningful change thresholds. DESIGN, SETTINGS,

AND PARTICIPANTS: This mixed-methods study consisted of a secondary analysis of a phase 2 multicenter double-blind dose-ranging randomized clinical trial and embedded qualitative interviews conducted at 35 sites in Canada, France, Japan, and the US. The secondary analysis included the trial's adult patients with nonsegmental vitiligo (T-VASI ≥5 and F-VASI ≥0.5 at baseline). Psychometric performance of the T-VASI and F-VASI and thresholds for meaningful change were evaluated using clinician- and patient-reported information. The trial's embedded interviews were used to qualitatively assess content validity and patient perceptions of meaningful repigmentation. Data analyses were performed from March to July 2023. INTERVENTION: Participants were randomized to 6-, 11-, or 22-mg/day upadacitinib or placebo for 24 weeks. MAIN OUTCOMES AND MEASURES: Psychometric performance of the T-VASI and F-VASI and thresholds for meaningful changed plus content validity and patient perceptions of meaningful repigmentation. Measurement instruments included the T-VASI, F-VASI, Vitiligo Noticeability Scale, Total-Patient Global Vitiligo Assessment, Face-Patient Global Vitiligo Assessment, Total-Physician Global Vitiligo Assessment (PhGVA-T), Face-Physician Global Vitiligo Assessment (PhGVA-F), Patient's Global Impression of Change-Vitiligo, Physician's Global Impression of Change-Vitiligo (PhGIC-V), Vitiligo Quality-of-Life Instrument, Dermatology Life Quality Index, the Hospital Anxiety and Depression Scale, and transcribed verbatim interviews with patients. RESULTS: The psychometric analysis included 164 participants (mean [SD] age, 46 years; 103 [63%] females) and the qualitative analysis included 14 participants (mean [SD] age, 48.8 [12.2] years; 9 females [64%] and 5 males [36%]). Intraclass correlation coefficients were 0.98 for T-VASI and 0.99 for F-VASI in patients with clinically stable vitiligo between baseline and week 4, supporting test-retest reliability. At baseline and week 24, correlations were moderate to strong between T-VASI and PhGVA-T (r = 0.63-0.65) and between F-VASI and PhGVA-F (r = 0.65-0.71). Average baseline and week-24 VASI scores decreased with repigmentation (ie, increasing PhGVA scores). Least-square mean VASI scores increased with greater repigmentation as measured by the PhGIC-V. Least-square mean VASI scores also differed between patients with improved PhGIC-V and those with no change or worsened V-PhGIC scores. Using a multiple anchor approach, improvements of 30% in T-VASI and 50% in F-VASI scores reflected meaningful repigmentation between baseline and week 24. CONCLUSION AND RELEVANCE: This mixed-methods study found that the T-VASI and F-VASI are reliable, valid, able to differentiate between clinically distinct groups, and responsive in patients with nonsegmental vitiligo. The thresholds for meaningful change were lower than those historically used in clinical trials, suggesting that T-VASI 50 and F-VASI 75 are conservative estimates and reflect improvements that would be meaningful in patients with nonsegmental vitiligo. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT04927975.

Dermatology

Feldman SR, Han G, Callender VD, Kircik LH, Bhatia N, Tyring SK, Zeichner JA, and **Gold LS**. Benefit of Topical Combination Therapy for Acne: Analyzing Effect Size Using Number Needed to Treat. *J Drugs Dermatol* 2024; 23(2):42-49. PMID: 38306147. Request Article

BACKGROUND: Topical acne trials often are confounded by high vehicle response rates and differing outcome measures, making it difficult to compare treatments. Number needed to treat (NNT) can be a simple, clinically meaningful way to indirectly compare treatment options without head-to-head data. NNT is the number of patients who need to be treated with an intervention to observe one additional patient successfully achieving a desired outcome versus vehicle/placebo. While treatment attributes such as adverse events may not be captured, lower NNT is a good indicator of a more effective treatment. METHODS: Following a search of combination topical treatments for acne vulgaris, all treatments that reported pivotal trial efficacy data consistent with the 2018 FDA definition of success were included in NNT analyses. Results: Of 13 treatments, 7 reported 12-week treatment success rates in 11 phase 3 trials, with similar baseline demographics/disease severity. Treatment success ranged from 26.8% with tretinoin 0.1%/benzoyl peroxide (BPO) 3% cream to 50% with triple-combination clindamycin phosphate 1.2%/adapalene 0.15%/BPO 3.1% gel. NNTs for the triple-combination gel were 4 and 5 (from 2 pivotal trials). Adapalene 0.3%/BPO 2.5% gel had an NNT of 5. Tretinoin/BPO had the largest range between trials, with NNTs of 4 and 9. The other 4 treatments had NNTs ranging from 6 to 8. CONCLUSION: A comparison of combination topical acne treatment trial data, using the same treatment outcome and similar patient populations, resulted in triple-combination clindamycin phosphate/adapalene/BPO gel and adapalene/BPO gel having the most favorable NNTs.J Drugs Dermatol. 2024;23(2):42-49. doi:10.36849/JDD.7927.

Dermatology

Fu C, **Wang J**, Ma T, **Yin C**, **Zhou L**, Clausen BE, **Mi QS**, and **Jiang A**. GSK-3β in Dendritic Cells Exerts Opposite Functions in Regulating Cross-Priming and Memory CD8 T Cell Responses Independent of β-Catenin. *Vaccines (Basel)* 2024; 12(9). PMID: 39340067. Full Text

Center for Cutaneous Biology and Immunology, Department of Dermatology, Henry Ford Health, Detroit, MI 48202, USA.
Immunology Program, Henry Ford Cancer Institute, Henry Ford Health, Detroit, MI 48202, USA.
Department of Medicine, College of Human Medicine, Michigan State University, East Lansing, MI 48824, USA.
Department of Computer Science and Engineering, School of Engineering and Computer Science, Oakland University, Rochester, MI 48309, USA.
Department of Internal Medicine, Henry Ford Health, Detroit, MI 48202, USA.
Institute for Molecular Medicine, Paul Klein Center for Immune Intervention, University Medical Center of the Johannes Gutenberg-University Mainz, Langenbeckstrasse 1, 55131 Mainz, Germany.

GSK-3β plays a critical role in regulating the Wnt/β-catenin signaling pathway, and manipulating GSK-3β in dendritic cells (DCs) has been shown to improve the antitumor efficacy of DC vaccines. Since the inhibition of GSK-3β leads to the activation of β-catenin, we hypothesize that blocking GSK-3β in DCs negatively regulates DC-mediated CD8 T cell immunity and antitumor immunity. Using CD11c-GSK-3β(-/-) conditional knockout mice in which GSK-3β is genetically deleted in CD11c-expressing DCs, we surprisingly found that the deletion of GSK-3β in DCs resulted in increased antitumor immunity, which contradicted our initial expectation of reduced antitumor immunity due to the presumed upregulation of β-catenin in DCs. Indeed, we found by both Western blot and flow cytometry that the deletion of GSK-3β in DCs did not lead to augmented expression of β-catenin protein, suggesting that GSK-3β exerts its function independent of β-catenin. Supporting this notion, our single-cell RNA sequencing (scRNA-seq) analysis revealed that GSK-3β-deficient DCs exhibited distinct gene expression patterns with minimally overlapping differentially expressed genes (DEGs) compared to DCs with activated β-catenin. This suggests that the deletion of GSK-3β in DCs is unlikely to lead to upregulation of β-catenin at the transcriptional level. Consistent with enhanced antitumor immunity, we also found that CD11c-GSK-3β(-/-) mice exhibited significantly augmented cross-priming of antigen-specific CD8 T cells following DC-targeted vaccines. We further found that the deletion of GSK-3β in DCs completely abrogated memory CD8 T cell responses, suggesting that GSK-3β in DCs also plays a negative role in regulating the differentiation and/or maintenance of memory CD8 T cells. scRNA-seq analysis further revealed that although the deletion of GSK-3β in DCs positively regulated transcriptional programs for effector differentiation and function of primed antigen-specific CD8 T cells in CD11c-GSK-3β(-/-) mice during the priming phase, it resulted in significantly reduced antigen-specific memory CD8 T cells, consistent with diminished memory responses. Taken together, our data demonstrate that GSK-3β in DCs has opposite functions in regulating cross-priming and memory CD8 T cell responses, and GSK-3β exerts its functions independent of its regulation of β-catenin. These novel insights suggest that targeting GSK-3β in cancer immunotherapies must consider its dual role in CD8 T cell responses.

Dermatology

Kingston P, Kircik L, Bhatia N, Del Rosso J, Desai SR, Harper JC, **Gold LS**, Hougeir F, and Armstrong AW. Consensus Statements on the Use of Novel Formulations of Isotretinoin: A Modified Delphi Process. *J Drugs Dermatol* 2024; 23(6):429-432. PMID: 38834212. Request Article

Oral isotretinoin remains a mainstay of treatment for severe, recalcitrant nodular acne. Novel formulations of isotretinoin have been developed over the past decade, including lidose isotretinoin and micronized isotretinoin. It is important to understand the differences between isotretinoin formulations to help guide clinical decision-making and selection of isotretinoin therapy. This study aims to provide evidence-based consensus statements regarding the use of novel formulations of isotretinoin for the treatment of moderate-to-severe acne. The Expert Consensus Group consisted of dermatologists with expertise in the treatment of acne. Voting members met in person to conduct a modified Delphi process; a maximum of 2 rounds of voting were conducted for each consensus statement. A total of 5 statements were generated regarding the use of novel formulations of isotretinoin, addressing the efficacy, tolerability, and side

effects of novel isotretinoin formulations. All 5 statements achieved agreement with high consensus. The Expert Consensus Group agrees that individualized selection of isotretinoin therapy is important to maximize efficacy and minimize side effects. Compared to generic isotretinoin, micronized isotretinoin may require lower doses to achieve sufficient plasma concentrations. With the increased bioavailability of micronized formulation, there is no need to calculate cumulative dose; instead, the general recommendation with micronized isotretinoin is to treat for at least 5 months, or longer if needed to achieve clearance. Micronized isotretinoin can be taken in the fed or fasted state and has an acceptable safety profile. J Drugs Dermatol. 2024;23(6):429-432.   doi:10.36849/JDD.7971.

Dermatology
Mokhtari M, **Bardhi R**, and **Hamzavi I**. A Canvas of Contemporary Insights into Clinical Vitiligo. *Dermatol Clin* 2024. PMID: Not assigned. Full Text

I. Hamzavi, Henry W. Lim Division of Photomedicine and Photobiology, Department of Dermatology, Multicultural Dermatology Center, Henry Ford Health, 2799 West Grand Boulevard, Detroit, MI, United States

Dermatology
Robinson CG, Gelabert-Mora A, Abuabara K, Taylor SC, and **Lim HW**. The importance of pathway programs in increasing diversity in dermatology: Efforts made by the American Academy of Dermatology. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 39365215. Full Text

Department of Dermatology, Henry Ford Health, Detroit, Michigan.
Department of Dermatology, University of California- San Francisco, San Francisco, California.
Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania.
Department of Dermatology, Henry Ford Health, Detroit, Michigan. Electronic address: hlim1@hfhs.org.

Our country's population continues to diversify, highlighting the need for an equally diverse physician workforce to care for patients. Unfortunately, the percentage of underrepresented minority residents in dermatology has remained relatively unchanged over the past several years. To address this disparity, the American Academy of Dermatology created the Pathways Programs to focus on early exposure to dermatology, skill-building workshops, research, and mentorship. The overarching goal is to increase the number of underrepresented minority dermatologists, which will result in improved patient care and mitigation of healthcare disparities.

Dermatology
Rose L, Khuhro A, Minta A, Novice M, **Novice T**, Lustberg MB, Ruddy KJ, Rake EC, Loprinzi CL, and Dulmage B. Eyebrow and Eyelash Loss in Patients With Cancer. *J Drugs Dermatol* 2024; 23(5):327-331. PMID: 38709698. Request Article

Though it is widely acknowledged that cancer treatments cause hair loss on the scalp, there are limited data on how they affect eyebrow and eyelash hairs. Patients with eyebrow and eyelash loss, or madarosis, seek various treatment options ranging from camouflage techniques with makeup, permanent tattoos, and prescription medications. Though not yet studied in patients with cancer-induced madarosis, techniques such as scalp cooling, cryotherapy, and topical vasoconstrictors are promising preventative options. More robust research is needed to improve both the quality and quantity of available treatment and preventative options. There is a clear need for dermatologists to play a role in supportive oncodermatology for patients who experience eyebrow and eyelash loss secondary to chemotherapy, endocrine therapies, and radiation therapy. J Drugs Dermatol. 2024;23(5):327-331. doi:10.36849/JDD.8003.

Dermatology
Santillan MR, **Kohli I**, and **Ozog D**. Optical Coherence Tomography for Mohs Margin Assessment of Basal Cell Carcinoma. *Dermatol Surg* 2024. PMID: Not assigned. Full Text

M.R. Santillan, Department of Dermatology, Henry Ford Hospital, Detroit, MI, United States
I. Kohli, Department of Dermatology, Henry Ford Hospital, Detroit, MI, United States
D. Ozog, Department of Dermatology, Henry Ford Hospital, Detroit, MI, United States

Dermatology

Shahinfar S, Shalabi MMK, **Nadir U**, Malick H, Lauck KC, Mehrmal S, Kelley B, and Tolkachjov SN. Trichilemmal carcinoma: surgical outcomes with wide local excision versus Mohs micrographic surgery. *Arch Dermatol Res* 2024; 316(10):696. PMID: 39417887. Full Text

Texas A&M University School of Medicine, Bryan, TX, USA.
Department of Dermatology, Baylor Scott & White Medical Center, Temple, TX, USA.
Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, USA. unadir1@hfhs.org.
Division of Dermatology, Baylor University Medical Center, Dallas, TX, USA.
Epiphany Dermatology, Dallas, TX, USA.
Bighorn Mohs Surgery and Dermatology Center, Scripps Clinic, La Jolla, CA, USA.
Department of Dermatology, University of Texas at Southwestern, Dallas, TX, USA.

Dermatology

Silverberg JI, Bunick CG, Hong HC, Mendes-Bastos P, **Stein Gold L**, Costanzo A, Ibrahim N, Sancho C, Wu X, Han Y, Levy G, Altman K, Calimlim B, and Eyerich K. Efficacy and Safety of Upadacitinib vs Dupilumab in Adults and Adolescents with Moderate-to-Severe Atopic Dermatitis: Week 16 results of an Open-label, Randomized, Efficacy Assessor-Blinded Head-to-Head Phase 3b/4 Study (Level Up). *Br J Dermatol* 2024; Epub ahead of print. PMID: 39438067. Full Text

Department of Dermatology, George Washington University School of Medicine and Health Sciences, Washington, DC, USA.
Department of Dermatology and Program in Translational Biomedicine, Yale University, New Haven, CT, USA.
Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada.
Probity Medical Research, Surrey, BC, Canada.
Dermatology Center, Hospital CUF Descobertas, Lisboa, Portugal.
Dermatology Clinical Research, Henry Ford Health System, West Bloomfield, MI, USA.
Dermatology Unit, Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Italy.
Humanitas Clinical and Research Center, IRCCS, Rozzano, Italy.
AbbVie, Inc, North Chicago, IL, USA.
Department of Dermatology and Venerology, Medical Center, University of Freiburg, Germany.

BACKGROUND: Atopic dermatitis (AD) is a chronic skin disease characterized by intense itch and eczematous skin lesions. Some patients continue to experience flares and substantial clinical burden despite ongoing systemic treatment. OBJECTIVES: This study assessed the efficacy and safety of once-daily upadacitinib (UPA), initiated at 15 mg and dose-escalated to 30 mg based on clinical response, compared with dupilumab (DUPI) per its label. Week 16 primary analysis results are presented. METHODS: Level Up is a phase 3b/4 global, randomized, open-label, efficacy assessor blinded study evaluating UPA vs DUPI in adolescents and adults with moderate-to-severe AD who had inadequate response to systemic therapy or when use was inadvisable. Patients were randomized to UPA or DUPI for 16 weeks of treatment (Period 1). Patients on UPA started on 15 mg and were dose-escalated to 30 mg if they did not achieve an Eczema Area and Severity Index reduction of at least 50% (EASI 50) or a ≥4-point Worst Pruritus Numerical Rating Scale (WP-NRS) improvement on/after Week 4, or EASI 75 on/after Week 8. The primary endpoint was simultaneous achievement of EASI 90 and WP-NRS 0/1 at Week 16. Ranked secondary endpoints included skin and itch responses at varying response levels and timepoints. Safety measures were assessed throughout the study. RESULTS: Superior efficacy in achieving simultaneous EASI 90 and WP-NRS 0/1 response at Week 16 was demonstrated with UPA vs DUPI (19.9% vs 8.9%, respectively; p<0.0001). UPA showed superiority vs DUPI for all ranked secondary endpoints, with post-hoc analyses exhibiting higher itch response rates as early as Day 2. No new safety signals were identified during this period. CONCLUSION: Treatment of moderate-to-severe AD with UPA, initiated at 15 mg and dose escalated based on clinical response, demonstrated superiority vs DUPI per

its label for the primary endpoint of simultaneous achievement of near complete skin clearance (EASI 90) and little to no itch (WP-NRS 0/1) at Week 16, with all ranked secondary endpoints demonstrating superiority at varying skin and itch response levels and timepoints. There were no new safety signals identified compared to the previously reported safety profiles of UPA and DUPI.

Dermatology
Singh IK, **Espinosa ML**, **Lim HW**, and **Mohammad TF**. A review of therapies for hyperpigmentation modulating the synthesis of eumelanin to pheomelanin. *Arch Dermatol Res* 2024; 316(9):668. PMID: 39382722. Full Text

Michigan State University College of Osteopathic Medicine, East Lansing, MI, USA.
Division of Photobiology and Photomedicine, Department of Dermatology, Henry Ford Health, 3031 W Grand Blvd, Suite 800 Dermatology, Detroit, MI, 48202, USA.
Division of Photobiology and Photomedicine, Department of Dermatology, Henry Ford Health, 3031 W Grand Blvd, Suite 800 Dermatology, Detroit, MI, 48202, USA. tmohamm2@hfhs.org.

There are significant psychosocial burdens in patients with hyperpigmentation, which emphasizes the importance of treatment. Current gold standard for treatment is hydroquinone; however, alternatives have been developed given the concern for side effects of hydroquinone. Melanogenesis is responsible for the production of eumelanin and pheomelanin; there are many factors that will determine whether eumelanin or pheomelanin will be produced. Eumelanin is known for its photoprotective qualities, while pheomelanin is implicated in photocarcinogenesis and photoaging. Multiple treatment modalities for hyperpigmentation that shift eumelanin to pheomelanin synthesis exist. Cysteamine, glutathione, kojic acid, and methyl sulfonyl methane are four agents used to treat hyperpigmentation by shifting the production of eumelanin to pheomelanin. It is critical to discuss photoprotection with patients to help reduce the potential impact of increased pheomelanin production and to expand research in this area.

Dermatology
Sodha D, Lio P, and **Gold LS**. The ABCs of JAKis: A Clinician's Guide to Safety and Monitoring of the Systemic JAK Inhibitors. *J Drugs Dermatol* 2024; 23(10):856. PMID: 39361691. Request Article

Janus kinase inhibitors (JAKis) have recently emerged in the arsenal of tools to treat dermatological conditions. However, there are some concerns regarding these treatments due to their boxed warning. Here we discuss the safe and effective use of JAKs for the treatment of a wide variety of dermatologic conditions. We will also discuss monitoring guidelines. J Drugs Dermatol. 2024;23(10):852-856. doi:10.36849/JDD.8073.

Dermatology
Vellaichamy G, Poulik J, **Palanisamy N**, **Kis O**, **Fang X**, **Al-Obaidy KI**, **Shwayder TA**, and **Friedman BJ**. Spitz-Type Proliferative Nodules Arising Within a Large Congenital Melanocytic Nevus Harboring a Novel LMNA-RAF1 Fusion. *J Cutan Pathol* 2024; Epub ahead of print. PMID: 39462150. Full Text

Department of Dermatology, Henry Ford Health, Detroit, Michigan, USA.
Detroit Medical Center, Children's Hospital of Michigan, Detroit, Michigan, USA.
Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, Michigan, USA.
Department of Pathology & Laboratory Medicine, Henry Ford Health, Detroit, Michigan, USA.

Diagnostic Radiology
Gonzalez HC, **Myers DT**, and **Venkat D**. Successful Implementation of a Multidisciplinary Weight Loss Program Including GLP1 Receptor Agonists for Liver Transplant Candidates With High Body Mass Index. *Transplantation* 2024; 108(11):2233-2237. PMID: 39466197. Full Text

Department of Gastroenterology and Hepatology, Henry Ford Health, Detroit, MI.
Department of Medicine, Wayne State University School of Medicine, Detroit, MI.
Department of Radiology, Henry Ford Health, Detroit, MI.
Department of Radiology, Wayne State University School of Medicine, Detroit, MI.

BACKGROUND: Body mass index (BMI) >40 is considered a relative contraindication to liver transplant. However, there is little research regarding best practices for weight loss in this population. We hypothesized that providing multidisciplinary support, including the use of glucagon-like protein 1 receptor agonists would facilitate patients' achievement of weight loss necessary for transplant eligibility. METHODS: Patients 18 y or older were referred to the Henry Ford Health Liver Metabolic Clinic from August 2019 to September 2023, with either BMI >40 or >35 with abdominal adiposity that would complicate surgery. Patients were provided individualized support from hepatologists, dieticians, and counselors, as well as prescribed antiobesity medication and monitored closely for weight loss progress. RESULTS: Among 19 patients referred to the Liver Metabolic Clinic, median baseline BMI was 42 (range, 34.6-48.8) with median goal weight loss of 14.1 kg (range, 4.1-31.4). Sixteen patients (84%) had metabolic dysfunction-associated steatohepatitis and 3 patients had alcohol-associated liver disease. Seven had comorbid hepatocellular carcinoma. Median Model for End-stage Liver Disease score was 14 (range, 7-22). Fifteen patients were treated with a glucagon-like peptide 1 receptor agonist (6 patients received liraglutide, 8 received semaglutide, and 1 received tirzepatide) and 4 received phentermine. Median weight loss was 11.7 kg for all 19 patients (range, 0-33). Eight patients received a transplant and 4 more patients were waitlisted. Time from baseline to waitlisting was ~5.5 mo (median 166 d; range, 68-840). Three patients remained on treatment, whereas 4 were deceased due to progressive liver disease or infection. CONCLUSIONS: Providing high BMI patients with individualized dietary and medical support can facilitate weight loss necessary to achieve liver transplant eligibility.

Diagnostic Radiology

Kadiyala D, **Sly M**, **Montecalvo J**, and **Vummidi D**. Benign Metastasizing Leiomyoma in a Patient With No Known History of Uterine Leiomyomas. *Cureus* 2024; 16(8):e68314. PMID: 39350828. Full Text

Department of Radiology, Wayne State University School of Medicine, Detroit, USA.
Department of Radiology, Henry Ford Health System, Detroit, USA.
Department of Pathology, Henry Ford Health System, Detroit, USA.

Benign metastasizing leiomyoma (BML) is a rare medical condition characterized by metastasis of fibroid tissue from uterine leiomyomas to other areas of the body, most commonly the lungs. While BML is mostly prevalent in women with a prior history of uterine leiomyomas who underwent surgical intervention, this case report explores the case of a 50-year-old female who was diagnosed with pulmonary benign metastasizing leiomyoma (PBML) with no prior history of confirmed leiomyomas. After initially presenting with worsening cough and congestion, chest radiograph and computed tomography revealed multiple bilateral pulmonary nodules, initially raising concerns for malignancy. Further, a workup with bronchoscopy with fine needle aspiration and pulmonary lesion biopsy revealed the presence of smooth muscle tissue suggestive of PBML. Subsequent uterine ultrasonography revealed a 3-cm intramural uterine fibroid, supporting the diagnosis. This case highlights the diagnostic challenge posed by PBML due to its asymptomatic manifestation and radiological similarity with other serious conditions such as malignancy and sarcoidosis. The case further highlights the importance of recognizing typical radiological features of PBML and the necessity of histological examination for accurate diagnosis. Finally, the critical role of a multidisciplinary approach in managing such rare conditions and the need for individualized treatment are also explored.

Diagnostic Radiology

Refai N, **Myers DT**, and **Williams T**. Rapunzel syndrome. *Abdom Radiol (NY)* 2024; Epub ahead of print. PMID: 39480608. Full Text

Grid.239864.2, Henry Ford Health System, Detroit, MI, USA.
Grid.239864.2, Henry Ford Health System, Detroit, MI, USA. danielm@rad.hfh.edu.

Diagnostic Radiology

Steiner JR, Morrison CK, **Vaya M**, Bevins N, **Christophel J**, and **Vanderhoek M**. A new method to evaluate fluoroscopic system collimator performance. *J Appl Clin Med Phys* 2024; e14536. Epub ahead of print. PMID: 39382833. Full Text

Department of Radiology, University of Chicago, Chicago, Illinois, USA.
Department of Diagnostic Radiology and Nuclear Medicine, RUSH University Medical Center, Chicago, Illinois, USA.
Department of Radiology, Henry Ford Health, Detroit, Michigan, USA.
Department of Radiology, Maine Medical Center, Portland, Maine, USA.

INTRODUCTION: Fluoroscopy uses collimators to limit the radiation field size. Collimators are often evaluated annually during equipment performance evaluations to maintain compliance with regulatory and/or accreditation bodies. A method to evaluate and quantify fluoroscopy collimator performance was developed. METHODS: A radiation field and displayed image measurement device consisting of radiopaque rulers and radiochromic film strips was placed on the x-ray source assembly exit window to evaluate fluoroscopy collimator performance. This method was used to evaluate collimator performance on 79 fluoroscopic imaging systems including fixed C-arms, mobile C-arms, mini C-arms, and radiographic fluoroscopic systems. RESULTS: The excess length (EL), excess width (EW), and sum EL + EW of the radiation field relative to the displayed image were measured and compared to the limits specified in 21CFR1020.32. Four systems exceeded these limits. Placing the radiation measurement device at the x-ray source assembly exit window relative to the image receptor cover increased the film exposure rate by a factor up to 14.6. The time required to set up and complete the fluoroscopy collimator performance measurements using this method ranged from 5 to 10 min. CONCLUSIONS: This method provides an easily implemented quantitative measure of fluoroscopy system collimator performance that satisfies regulatory and accreditation body requirements.

Emergency Medicine

Hill RW, **Manteuffel JJ**, and White BA. Apneic uptake of atmospheric O(2) by deeply hypothermic nestlings of the white-footed mouse (Peromyscus leucopus): circulation and lungs. *J Comp Physiol B* 2024; Epub ahead of print. PMID: 39375204. Full Text

Department of Integrative Biology, Michigan State University, East Lansing, MI, 48824, USA. hillr@msu.edu.
Emergency Medicine, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI, 48202, USA.
Center for Youth Development and Intervention, Department of Psychology, The University of Alabama, Tuscaloosa, AL, 35487, USA.

Nestling white-footed mice (Peromyscus leucopus) are born in the earliest days of spring in cold climates. If the nestlings are by accident exposed to ambient temperatures near freezing (0-7 °C) at early ages (2-10 days old), they may experience body temperatures (T(b)s) equally low. During such hypothermia, although their heart keeps beating, they become apneic (cease inhaling and exhaling). However, they have an exceptional ability (e.g., compared to Mus musculus) to tolerate these conditions for at least several hours, after which they revive if rewarmed by parents. This paper addresses the physiology of the apneic period. We show that apneic, hypothermic nestlings undergo physiologically important exchanges of gases with the atmosphere. These gas exchanges do not occur across the skin. Instead they occur via the trachea and lungs even though the animals are apneic. Most significantly, when hypothermic neonates are in apnea in ordinary air, they take up O(2) steadily from the atmosphere throughout the apneic period, and the evidence available indicates that this O(2) uptake is essential for the nestlings' survival. At T(b)s of 2-7 °C, the nestlings' rate of O(2) consumption varies quasi-exponentially with T(b) and averages 0.04 mL O(2) g(- 1) h(- 1), closely similar to the rate expressed by adult mammalian hibernators in hibernation at similar T(b)s. Morphometric analysis indicates that, at all focal ages, O(2) transport along the full length of the trachea can take place by diffusion at rates adequate to meet the measured rates of metabolic O(2) consumption.

Emergency Medicine

Hinojosa CA, van Rooij SJH, Fani N, Ellis RA, Harnett NG, Lebois LAM, Ely TD, Jovanovic T, Murty VP, House SL, Beaudoin FL, An X, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Hudak LA, Pascual JL, Seamon MJ, Harris E, Pearson C, Peak DA, Merchant RC, Domeier RM, Rathlev NK, O'Neil

BJ, Sergot P, Bruce SE, Pizzagalli DA, Sheridan JF, Harte SE, Koenen KC, Kessler RC, McLean SA, Ressler KJ, and Stevens JS. Reward neurocircuitry predicts longitudinal changes in alcohol use following trauma exposure. *Biol Psychiatry Cogn Neurosci Neuroimaging* 2024; Epub ahead of print. PMID: 39389310. Full Text

Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA, USA. Electronic address: cecilia.a.hinojosa@emory.edu.
Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA, USA.
McLean Hospital, Belmont, MA, USA; Department of Psychiatry, Harvard Medical School, Boston, MA, USA.
Department of Psychiatry, Harvard Medical School, Boston, MA, USA; Division of Depression and Anxiety, McLean Hospital, Belmont, MA, USA.
Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, MI, USA.
Department of Psychology, Temple University, Philadelphia, PA, USA.
Department of Emergency Medicine, Washington University School of Medicine, St. Louis, MO, USA.
Department of Health Services, Policy, and Practice, The Alpert Medical School of Brown University, Providence, RI, USA; Department of Emergency Medicine, The Alpert Medical School of Brown University, Providence, RI.
Institute for Trauma Recovery, Department of Anesthesiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.
Departments of Psychiatry and Neurology, University of California San Francisco, San Francisco, CA, USA.
Department of Biomedical Informatics, Emory University School of Medicine, Atlanta, GA, USA; Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, GA, USA.
Department of Psychiatry, Harvard Medical School, Boston, MA, USA; Institute for Technology in Psychiatry, McLean Hospital, Belmont, MA, USA; The Many Brains Project, Belmont, MA, USA.
Department of Psychiatry, Harvard Medical School, Boston, MA, USA; Institute for Technology in Psychiatry, McLean Hospital, Belmont, MA, USA; Department of Psychiatry, McLean Hospital, Belmont, MA, USA.
Department of Emergency Medicine, University of Massachusetts Chan Medical School, Worcester, MA, USA.
Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, TN, USA.
Department of Emergency Medicine, Henry Ford Health System, Detroit, MI, USA.
Department of Emergency Medicine, Indiana University School of Medicine, Indianapolis, IN, USA.
Department of Emergency Medicine, University of Florida College of Medicine -Jacksonville, Jacksonville, FL, USA.
Department of Emergency Medicine, Cooper Medical School of Rowan University, Camden, NJ, USA.
Department of Emergency Medicine, Ohio State University College of Medicine, Columbus, OH, USA; Ohio State University College of Nursing, Columbus, OH, USA.
Department of Emergency Medicine, Emory University School of Medicine, Atlanta, GA, USA.
Department of Surgery, Department of Neurosurgery, University of Pennsylvania, Philadelphia, PA, USA; Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA.
Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; Department of Surgery, Division of Traumatology, Surgical Critical Care and Emergency Surgery, University of Pennsylvania, Philadelphia, PA, USA.
Department of Emergency Medicine, Einstein Medical Center, Philadelphia, PA, USA.
Department of Emergency Medicine, Wayne State University, Ascension St. John Hospital, Detroit, MI, USA.
Department of Emergency Medicine, Massachusetts General Hospital, Boston, MA, USA.
Department of Emergency Medicine, Brigham and Women's Hospital, Boston, MA, USA.
Department of Emergency Medicine, Trinity Health-Ann Arbor, Ypsilanti, MI, USA.
Department of Emergency Medicine, University of Massachusetts Medical School-Baystate, Springfield, MA, USA.

Department of Emergency Medicine, Wayne State University, Detroit Receiving Hospital, Detroit, MI, USA.
Department of Emergency Medicine, McGovern Medical School at UTHealth, Houston, TX, USA.
Department of Psychological Sciences, University of Missouri - St. Louis, St. Louis, MO, USA.
Division of Biosciences, Ohio State University College of Dentistry, Columbus, OH, USA; Institute for Behavioral Medicine Research, OSU Wexner Medical Center, Columbus, OH, USA.
Department of Anesthesiology, University of Michigan Medical School, Ann Arbor, MI, USA; Department of Internal Medicine-Rheumatology, University of Michigan Medical School, Ann Arbor, MI, USA.
Department of Epidemiology, Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA, USA.
Department of Health Care Policy, Harvard Medical School, Boston, MA, USA.
Department of Emergency Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; Institute for Trauma Recovery, Department of Psychiatry, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.

BACKGROUND: Trauma is a risk factor for developing maladaptive alcohol use. Preclinical research has shown that stress alters the processing of midbrain and striatal reward and incentive signals. However, little research has been conducted on alterations in reward-related neurocircuitry post-trauma in humans. Neuroimaging markers may be particularly useful as they can provide insight into the mechanisms that may make an individual vulnerable to developing trauma-related psychopathologies. This study aimed to identify reward-related neural correlates associated with changes in alcohol use after trauma exposure. METHODS: Participants were recruited from U.S. emergency departments for the AURORA study (N=286, 178 female). Trauma-related change in alcohol use at 8 weeks post-trauma relative to pre-trauma was quantified as a change in 30-day total drinking per the PhenX Toolkit Alcohol 30-Day Quantity and Frequency Measure. Reward-related neurocircuitry activation and functional connectivity (FC) were assessed 2 weeks post-trauma using fMRI during a monetary reward task using region of interest and whole-brain voxelwise analyses. RESULTS: Greater increase in alcohol use from pre-trauma to 8 weeks post-trauma was predicted by (1) greater ventral tegmental area (VTA) and (2) greater cerebellum activation during Gain>Loss trials measured 2 weeks post-trauma and (3) greater seed-based FC between the VTA and lateral occipital cortex and precuneus. CONCLUSIONS: Altered VTA activation and FC early post-trauma may be associated with reward-seeking and processing, contributing to greater alcohol use post-trauma. These data provide novel evidence of neural correlates that underlie increased alcohol use early post-trauma that may be targeted via early interventions to prevent the development of maladaptive alcohol use.

Emergency Medicine

Nedzlek C, **Blanchett J**, **Illg Z**, **DiGiacinto G**, **Cunningham K**, **Wisniewski SJ**, and **Tuttle J**. Corticosteroid Prescribing Patterns in the Emergency Department for Acute COPD Exacerbations: A Retrospective Analysis Following an Educational Intervention. *Spartan Med Res J* 2024; 9(3):124542. PMID: 39430433. Full Text

Department of Emergency Medicine Henry Ford Wyandotte Hospital, Wyandotte, MI, USA.
College of Osteopathic Medicine Statewide Campus System, East Lansing, MI, USA Michigan State University.

INTRODUCTION: COPD is a progressive lung disease with marked airflow limitation. It has a large global prevalence and is managed with antibiotics, bronchodilators, and corticosteroids. Despite the prevalence, corticosteroid prescribing regimens differ widely amongst providers. This study aims to evaluate baseline corticosteroid prescribing patterns, the ability to change corticosteroid prescribing patterns with the utilization of an educational initiative, and to evaluate the effect of corticosteroid dose on length of stay, 30-day hospital readmission, mortality, and total hospital insulin dosing. METHODS: This study was conducted via a retrospective observational study. Providers at a single institution answered a baseline questionnaire on COPD corticosteroid prescribing patterns and subsequently received an educational presentation regarding evidence-based corticosteroid recommendations. Data were then retrospectively obtained and analyzed evaluating corticosteroid prescribing patterns both pre- and post-educational intervention. Data were analyzed using IBM SPSS Version 25. RESULTS: The provider survey revealed

that most (95.3%) administered 125 mg of methylprednisolone to patients treated for AECOPD. The most common reason a particular dose of corticosteroid was administered was due to previous teaching or practice patterns. The mean initial steroid dose of methylprednisolone decreased following the educational initiative from 114.24 mg to 72.8 mg ($p < 0.01$). This corresponded to a 69% (n=41) decrease of providers using 125 mg methylprednisolone ($p < 0.01$), and increased prescribing of 62.5 mg methylprednisolone by 42.6% (n=66). The mean LOS following hospital admission for AECOPD in the pre-intervention group was 5.80 days, while the mean LOS following the targeted educational intervention decreased to 4.82 days ($p = 0.01$). CONCLUSIONS: The implementation of an educational intervention may change provider corticosteroid prescribing patterns. Additionally, lower corticosteroid dose in the Emergency Department may decrease patient length of stay. Keywords: Corticosteroid, COPD, LOS, recommendations, steroid.

Emergency Medicine

Pokorney SD, Nemeth H, Chiswell K, Albert C, Allyn N, Blanco R, Butler J, Calkins H, Elkind MSV, Fonarow GC, Fontaine JM, Frankel DS, Fermann GJ, Gale R, Kalscheur M, Kirchhof P, Koren A, **Miller JB**, Rashkin J, Russo AM, Rutan C, Steinberg B, and Piccini JP. Design and Rationale of a Pragmatic Randomized Clinical Trial of Early Dronedarone versus Usual Care to Change and Improve Outcomes in Persons with First-Detected Atrial Fibrillation - The CHANGE AFIB Study. *Am Heart J* 2024; Epub ahead of print. PMID: 39423993. Full Text

Duke Clinical Research Institute, Durham, NC; Duke Heart Center, Duke University Medical Center, Durham, NC.
Duke Clinical Research Institute, Durham, NC.
Smidt Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA.
American Heart Association, Dallas, TX.
Baylor Scott and White Research Institute, Dallas, TX; Department of Medicine, University of Mississippi Medical Center, Jackson, MS.
Johns Hopkins Hospital, Baltimore, MD.
Division of Cardiology, Ronald Reagan-UCLA Medical Center, Los Angeles, CA.
Drexel University College of Medicine, Philadelphia, PA.
Cardiovascular Division, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA.
Department of Emergency Medicine, University of Cincinnati College of Medicine, Cincinnati, OH.
Hilton Head Island Leadership Institute, Hilton Head, SC.
Department of Medicine, University of Wisconsin, Madison, WI.
Department of Cardiology, University Heart and Vascular Center UKE Hamburg, Germany; German Center of Cardiovascular Research (DZHK), Partner site Hamburg/Kiel/Lübeck, Germany; Institute of Cardiovascular Sciences, University of Birmingham, UK.
Sanofi, Bridgewater, NJ.
Department of Emergency Medicine, Wayne State University & Henry Ford Hospital, Detroit, MI.
Division of Cardiovascular Disease, Cooper Medical School of Rowan University, Camden, NJ.
Department of Medicine, University of Utah, Salt Lake City, UT.
Duke Clinical Research Institute, Durham, NC; Duke Heart Center, Duke University Medical Center, Durham, NC. Electronic address: jonathan.piccini@duke.edu.

BACKGROUND: While there are several completed clinical trials that address treatment strategies in patients with symptomatic and recurrent atrial fibrillation (AF), there are no randomized clinical trials that address first-line rhythm control of new-onset AF. Recent data suggest that early initiation of rhythm control within 1 year can improve outcomes. METHODS: In this open-label pragmatic clinical trial nested within the Get With The Guidelines Atrial Fibrillation registry, approximately 3,000 patients with first-detected AF will be enrolled at approximately 200 sites. Participants will be randomized (1:1) to treatment with dronedarone in addition to usual care versus usual care alone. The primary endpoint will be time to first cardiovascular (CV) hospitalization or death from any cause through 12 months from randomization. Secondary endpoints will include a WIN ratio (all-cause death, ischemic stroke or systemic embolism, heart failure hospitalization, acute coronary hospitalization), CV hospitalization, and all-cause mortality. Patient reported outcomes will be analyzed based on change in Atrial Fibrillation Effect on Quality of Life

(AFEQT) and change in Mayo AF-Specific Symptom Inventory (MAFSI) from baseline to 12 months. CONCLUSION: CHANGE AFIB will determine if treatment with dronedarone in addition to usual care is superior to usual care alone for the prevention of CV hospitalization or death from any cause in patients with first-detected AF. The trial will also determine whether initiation of rhythm control at the time of first-detected AF affects CV events or improves patient reported outcomes. CLINICALTRIALS: GOV #: - NCT05130268.

Emergency Medicine

VandenBerg J, **Moss H**, Wechsler C, Johnson C, McRae M, Sloan S, Dimitrijevski T, Kouyoumjian S, Kline JA, and Messman A. The evaluation of video-assisted debriefing for improving performance in simulated medical student resuscitations. *AEM Educ Train* 2024; 8(5):e11029. PMID: 39398865. Full Text

Department of Emergency Medicine Lewis Katz School of Medicine at Temple University Philadelphia Pennsylvania USA.
Department of Emergency Medicine Wayne State University School of Medicine Detroit Michigan USA.
Department of Emergency Medicine Henry Ford Hospital Detroit Michigan USA.
Department of Emergency Medicine Covenant Emergency Care Center Saginaw Michigan USA.
Department of Emergency Medicine Trinity Health Oakland Hospital Pontiac Michigan USA.

OBJECTIVES: Simulation-based training is commonly used in medical education. However, there is a gap in knowledge regarding best practices in debriefing. We aimed to identify novel solutions to this by adapting video-assisted debriefing (VAD) methodologies used in athletic training. We hypothesized that utilizing VAD would lead to improvements in performance during advanced cardiac life support (ACLS)-based simulations compared to traditional verbal debriefing (VD). METHODS: The study was conducted at a single medical school. Participants were fourth-year medical students engaging in ACLS simulation-based training as part of their emergency medicine rotation. After completing an ACLS-based simulation, participants received either VD or VAD and then completed a second simulation scenario. Our primary outcome was ACLS performance, graded by blinded reviewers utilizing a previously developed modified checklist. Secondary outcomes included time from cardiac arrest to initiation of cardiopulmonary resuscitation (CPR) and first defibrillation. Measurements were made before and after the interventional debrief, referred to as pre- and postdebrief. A modified Likert-scale survey was used to subjectively assess the student's overall experience. RESULTS: Forty-six groups of 275 students were included in the study. Mean ACLS performance score for VD and VAD postdebrief were 85% and 82%, respectively ($p = 0.27$). Mean time from arrest to CPR initiation for VD and VAD postdebrief groups were 20 and 24 s, respectively ($p = 0.46$). Mean time from arrest to defibrillation for VD and VAD postdebrief groups were 50 and 59 s, respectively ($p = 0.39$). For the Likert surveys, 85% or more of participants in both groups indicated that the session was "very helpful" in all survey categories. CONCLUSIONS: VD and VAD both led to improvements in ACLS performance, time to initiation of CPR, and defibrillation among fourth-year medical students. Though postdebrief results were not statistically significantly different by comparison, overall VD led to greater improvement overall across all outcomes.

Endocrinology and Metabolism

Kruger D, Magwire M, and Urquhart S. Icodec ONWARDS: A review of the first once-weekly diabetes treatment for nurse practitioners and physician assistants. *J Am Assoc Nurse Pract* 2024; Epub ahead of print. PMID: 39412407. Full Text

Division of Endocrinology, Diabetes, Bone and Mineral Disease, Henry Ford Health System, Detroit, Michigan.
Saint Luke's Michael & Marlys Haverty Cardiometabolic Center of Excellence, Kansas City, Kansas.
Diabetes and Thyroid Associates, Fredericksburg, Virginia.

BACKGROUND: Diabetes management is challenged by the complexity of treatment regimens and the need for frequent injections, affecting patient adherence and quality of life. Insulin icodec, a once-weekly basal insulin analog, represents a significant innovation, potentially simplifying diabetes care and improving outcomes. OBJECTIVES: This review aims to evaluate the safety, efficacy, and clinical implications of insulin icodec for individuals with type 1 and type 2 diabetes, highlighting its potential to

affect current treatment paradigms. DATA SOURCES: A review was conducted comparing once-weekly insulin icodec with daily basal insulin analogs using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines to ensure transparent reporting of systematic reviews. A search was performed in the following databases: PubMed, Google Scholar, Embase, and ClinicalTrials.gov, focusing on efficacy and safety outcomes. CONCLUSIONS: Insulin icodec has demonstrated effective glycemic management and a safety profile comparable to daily basal insulins. Its extended half-life and steady-state glucose-lowering effect have the potential to reduce the burden of daily injections and improve patient adherence. IMPLICATIONS FOR PRACTICE: The introduction of once-weekly insulin icodec represents an advancement in diabetes care. For front-line clinicians, this innovation aligns with the need for more straightforward medication regimens. Coupled with continuous glucose monitoring systems, it enables a more personalized and efficient approach to diabetes management, with the potential to improve patient satisfaction and clinical outcomes. This underscores the impact of integrating such advancements into practice, highlighting the role of nurse practitioners and physician assistants in adopting these innovations to optimize patient care.

Endocrinology and Metabolism

Moretti B, Livecchi R, Taylor SR, Pitt SC, Gay BL, Haymart MR, **Bhan A**, Perkins J, and Papaleontiou M. Physician-reported barriers and facilitators to thyroid hormone deprescribing in older adults. *J Am Geriatr Soc* 2024; Epub ahead of print. PMID: 39392046. Full Text

Division of Metabolism, Endocrinology and Diabetes, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA.
Department of Internal Medicine, Mercy Health - St. Vincent Medical Center, Toledo, Ohio, USA.
Division of Endocrine Surgery, Department of General Surgery, University of Michigan, Ann Arbor, Michigan, USA.
Division of Endocrinology, Diabetes, Bone and Mineral Disorders, Department of Internal Medicine, Henry Ford Health System, Detroit, Michigan, USA.
Division of Endocrinology and Metabolism, Department of Medicine and Surgery, University of California San Francisco, San Francisco, California, USA.
Institute of Gerontology, University of Michigan, Ann Arbor, Michigan, USA.

BACKGROUND: Thyroid hormone is one of the most commonly prescribed medications in the United States. Misuse of and overtreatment with thyroid hormone is common in older adults and can lead to cardiovascular and skeletal adverse events. Even though deprescribing can reduce inappropriate care, no studies have yet explored specific barriers and facilitators to guide thyroid hormone deprescribing in older adults (defined as discontinuation of thyroid hormone when initiated without an appropriate indication or dose reduction in those overtreated). METHODS: We conducted semi-structured interviews with 19 endocrinologists, geriatricians, and primary care physicians who prescribe thyroid hormone. Interviews were completed between July 2020 and December 2021 via two-way video conferencing. We used both an inductive and deductive content analysis guided by the Theoretical Domains Framework to evaluate transcribed and coded participant responses. Thematic analysis characterized themes related to barriers and facilitators to thyroid hormone deprescribing practices in older adults. RESULTS: The most commonly reported barriers to thyroid hormone deprescribing were related to patient-level factors, followed by physician- and system-level factors. Patient factors included patients' perceived need for thyroid hormone use and patient anxiety/concerns about potential side effects related to thyroid hormone dose reduction, patient lack of knowledge, and misinformation regarding deprescribing. Physician- and system-level barriers included clinic visit time constraints, physician inertia, physician lack of knowledge about deprescribing, perceived lack of sufficient patient follow-up, and electronic health record limitations. The most prominent physician-reported facilitators to thyroid hormone deprescribing were effective physician-to-patient communication, and positive physician-patient relationship, including patients' trust in their treating physician. CONCLUSION: Barriers and facilitators to thyroid hormone deprescribing in older adults were reported at multiple levels including patient-, physician-, and system-level factors. Interventions to improve thyroid hormone deprescribing in older adults should aim to improve patient education and expectations, increase multidisciplinary physician awareness, and overcome physician inertia.

Gastroenterology
Alomari A, Althunibat I, **Obri MS**, **Curran J**, Aldroubi B, **Davis W**, and **Pompa R**. A Case of Metastatic Seminoma Mimicking a Primary Pancreatic Tumor. *Cureus* 2024; 16(9):e70329. PMID: 39463534. Request Article

Internal Medicine, Henry Ford Health System, Detroit, USA.
Internal Medicine, Saint Michael's Medical Center, Newark, USA.
Gastroenterology and Hepatology, Henry Ford Health System, Detroit, USA.
Medical College, Tishreen University, Lattakia, SYR.

Metastatic seminoma to the pancreas is exceedingly rare, with few reported cases in medical literature. We present a case of a 66-year-old male, six years post-remission from testicular seminoma, who presented with obstructive jaundice and a pancreatic mass mimicking primary malignancy. Diagnostic workup including endoscopic ultrasound-guided biopsy confirmed metastatic seminoma. He underwent successful treatment with four cycles of cisplatin and etoposide, achieving complete remission. This case underscores the diagnostic challenge of pancreatic metastases and emphasizes the role of biopsy in guiding appropriate management. Awareness of such presentations is crucial for timely intervention and improved patient outcomes.

Gastroenterology
Gonzalez HC, **Myers DT**, and **Venkat D**. Successful Implementation of a Multidisciplinary Weight Loss Program Including GLP1 Receptor Agonists for Liver Transplant Candidates With High Body Mass Index. *Transplantation* 2024; 108(11):2233-2237. PMID: 39466197. Full Text

Department of Gastroenterology and Hepatology, Henry Ford Health, Detroit, MI.
Department of Medicine, Wayne State University School of Medicine, Detroit, MI.
Department of Radiology, Henry Ford Health, Detroit, MI.
Department of Radiology, Wayne State University School of Medicine, Detroit, MI.

BACKGROUND: Body mass index (BMI) >40 is considered a relative contraindication to liver transplant. However, there is little research regarding best practices for weight loss in this population. We hypothesized that providing multidisciplinary support, including the use of glucagon-like protein 1 receptor agonists would facilitate patients' achievement of weight loss necessary for transplant eligibility. METHODS: Patients 18 y or older were referred to the Henry Ford Health Liver Metabolic Clinic from August 2019 to September 2023, with either BMI >40 or >35 with abdominal adiposity that would complicate surgery. Patients were provided individualized support from hepatologists, dieticians, and counselors, as well as prescribed antiobesity medication and monitored closely for weight loss progress. RESULTS: Among 19 patients referred to the Liver Metabolic Clinic, median baseline BMI was 42 (range, 34.6-48.8) with median goal weight loss of 14.1 kg (range, 4.1-31.4). Sixteen patients (84%) had metabolic dysfunction-associated steatohepatitis and 3 patients had alcohol-associated liver disease. Seven had comorbid hepatocellular carcinoma. Median Model for End-stage Liver Disease score was 14 (range, 7-22). Fifteen patients were treated with a glucagon-like peptide 1 receptor agonist (6 patients received liraglutide, 8 received semaglutide, and 1 received tirzepatide) and 4 received phentermine. Median weight loss was 11.7 kg for all 19 patients (range, 0-33). Eight patients received a transplant and 4 more patients were waitlisted. Time from baseline to waitlisting was ~5.5 mo (median 166 d; range, 68-840). Three patients remained on treatment, whereas 4 were deceased due to progressive liver disease or infection. CONCLUSIONS: Providing high BMI patients with individualized dietary and medical support can facilitate weight loss necessary to achieve liver transplant eligibility.

Graduate Medical Education
Harfmann BD, Bhaskaran S, Zubek J, Gordish K, **Butcko A**, Liu R, Vranish JR, Della-Moretta J, Westercamp CM, Chung CS, and Elmer SJ. 11th Annual Michigan Physiological Society Meeting: June 24-25, 2024. *Adv Physiol Educ* 2024; 48(4):833-835. PMID: 39392686. Full Text

Department of Integrative Physiology and Health Science, Alma College, Alma, Michigan, United States. ROR: https://ror.org/02pdzen98

Department of Biological Sciences, Oakland University, Rochester, Michigan, United States.
Department of Physiology, Michigan State University, East Lansing, Michigan, United States.
Department of Physiology, Wayne State University, Detroit, Michigan, United States.
Henry Ford Health System, Detroit, Michigan, United States.
Department of Biomedical Sciences, Grand Valley State University, Allendale, Michigan, United States.
Alma Public Schools, Alma, Michigan, United States.
Department of Biological Sciences, Ferris State University, Big Rapids, Michigan, United States.
Department of Kinesiology and Integrative Physiology, Michigan Technological University, Houghton, Michigan, United States.
Doctor of Physical Therapy Program, St. Catherine University, St. Paul, Minnesota, United States.

Graduate Medical Education

Nedzlek C, **Blanchett J**, **Illg Z**, **DiGiacinto G**, **Cunningham K**, **Wisniewski SJ**, and **Tuttle J**. Corticosteroid Prescribing Patterns in the Emergency Department for Acute COPD Exacerbations: A Retrospective Analysis Following an Educational Intervention. *Spartan Med Res J* 2024; 9(3):124542. PMID: 39430433. Full Text

Department of Emergency Medicine Henry Ford Wyandotte Hospital, Wyandotte, MI, USA.
College of Osteopathic Medicine Statewide Campus System, East Lansing, MI, USA Michigan State University.

INTRODUCTION: COPD is a progressive lung disease with marked airflow limitation. It has a large global prevalence and is managed with antibiotics, bronchodilators, and corticosteroids. Despite the prevalence, corticosteroid prescribing regimens differ widely amongst providers. This study aims to evaluate baseline corticosteroid prescribing patterns, the ability to change corticosteroid prescribing patterns with the utilization of an educational initiative, and to evaluate the effect of corticosteroid dose on length of stay, 30-day hospital readmission, mortality, and total hospital insulin dosing. METHODS: This study was conducted via a retrospective observational study. Providers at a single institution answered a baseline questionnaire on COPD corticosteroid prescribing patterns and subsequently received an educational presentation regarding evidence-based corticosteroid recommendations. Data were then retrospectively obtained and analyzed evaluating corticosteroid prescribing patterns both pre- and post-educational intervention. Data were analyzed using IBM SPSS Version 25. RESULTS: The provider survey revealed that most (95.3%) administered 125 mg of methylprednisolone to patients treated for AECOPD. The most common reason a particular dose of corticosteroid was administered was due to previous teaching or practice patterns. The mean initial steroid dose of methylprednisolone decreased following the educational initiative from 114.24 mg to 72.8 mg ($p < 0.01$). This corresponded to a 69% (n=41) decrease of providers using 125 mg methylprednisolone ($p < 0.01$), and increased prescribing of 62.5 mg methylprednisolone by 42.6% (n=66). The mean LOS following hospital admission for AECOPD in the pre-intervention group was 5.80 days, while the mean LOS following the targeted educational intervention decreased to 4.82 days ($p = 0.01$). CONCLUSIONS: The implementation of an educational intervention may change provider corticosteroid prescribing patterns. Additionally, lower corticosteroid dose in the Emergency Department may decrease patient length of stay. Keywords: Corticosteroid, COPD, LOS, recommendations, steroid.

Graduate Medical Education

Singh IK, **Espinosa ML**, **Lim HW**, and **Mohammad TF**. A review of therapies for hyperpigmentation modulating the synthesis of eumelanin to pheomelanin. *Arch Dermatol Res* 2024; 316(9):668. PMID: 39382722. Full Text

Michigan State University College of Osteopathic Medicine, East Lansing, MI, USA.
Division of Photobiology and Photomedicine, Department of Dermatology, Henry Ford Health, 3031 W Grand Blvd, Suite 800 Dermatology, Detroit, MI, 48202, USA.
Division of Photobiology and Photomedicine, Department of Dermatology, Henry Ford Health, 3031 W Grand Blvd, Suite 800 Dermatology, Detroit, MI, 48202, USA. tmohamm2@hfhs.org.

There are significant psychosocial burdens in patients with hyperpigmentation, which emphasizes the importance of treatment. Current gold standard for treatment is hydroquinone; however, alternatives have been developed given the concern for side effects of hydroquinone. Melanogenesis is responsible for the production of eumelanin and pheomelanin; there are many factors that will determine whether eumelanin or pheomelanin will be produced. Eumelanin is known for its photoprotective qualities, while pheomelanin is implicated in photocarcinogenesis and photoaging. Multiple treatment modalities for hyperpigmentation that shift eumelanin to pheomelanin synthesis exist. Cysteamine, glutathione, kojic acid, and methyl sulfonyl methane are four agents used to treat hyperpigmentation by shifting the production of eumelanin to pheomelanin. It is critical to discuss photoprotection with patients to help reduce the potential impact of increased pheomelanin production and to expand research in this area.

Hematology-Oncology

Gerke JA, Odron SF, Kim J, Dutta N, Clarke JG, **Media J**, Coppage DA, Oorloff M, Alcala A, Garcia G, Kang MEF, Gerke CL, Peterson JC, Morris JD, Higuchi-Sanabria R, **Valeriote FA**, Crews P, and Johnson TA. Further Probing the Properties of a Unique Sponge-derived Alkaloid Through the Isolation of a New (-)-(5E)-(8R)-(14Z)-Mycothiazole Analogue. *J Nat Prod* 2024; 87(10):2523-2529. PMID: 39348562. Request Article

Department of Natural Sciences & Mathematics, Dominican University of California, San Rafael, California 94901, United States.
Leonard Davis School of Gerontology, University of Southern California, Los Angeles, California 90089, United States.
Josephine Ford Cancer Center, Division of Hematology and Oncology, Department of Internal Medicine, Henry Ford Health System, Detroit, Michigan 48202, United States.
Department of Chemistry, One Shields Ave, University of California, Davis, California 95616, United States.
Department of Chemistry and Biochemistry, University of California Santa Cruz, Santa Cruz, California 95064, United States.

Scale-up isolation of (+)-(5Z)-(8S)-(14Z)-mycothiazole (1) from Vanuatu specimens of C. mycofijiensis to semisynthesize (+)-(5Z)-(8S)-8-O-acetyl-(14Z)-mycothiazole (2) revealed a new diastereomer, (-)-(5E)-(8R)-(14Z)-mycothiazole (4). The structure of 4 was determined using HRMS, NMR, and comparing optical rotation to (-)-(5Z)-(8R)-(14Z)-mycothiazole (3) and 2. The maximum tolerated dose of 2 in mice was 0.1 mg/kg. The IC(50) of 4 in PANC-1 and HepG2 cancer cell lines was 111.6 and 115.0 nM. Evaluation of 4 in C. elegans showed similar oxygen consumption compared to 1-2, and all compounds significantly increased the lifespan. The Z orientation at Δ(5,6) is crucial for picomolar cytotoxicity but not for mitochondrial inhibition.

Hematology-Oncology

Jacob B, **Jamil M**, **Raslan S**, **Springer K**, **Nasser Z**, and **Kuriakose P**. Infusion Reactions With Alternative Therapies During the National Shortage of Iron Dextran. *Eur J Haematol* 2024; Epub ahead of print. PMID: 39385426. Full Text

Henry Ford Health, Detroit, Michigan, USA.

Prior to the national shortage of iron dextran in early 2023, it was the most commonly administered intravenous iron infusion at our institution. After the shortage impacted the health system, alternatives such as iron sucrose and sodium ferric gluconate/sucrose were required that utilized lower doses given at more frequent patient visits. Coinciding with their more prevalent use, an increase in iron infusion reactions was observed. Our study analyzed 880 patients who received iron infusions in three Henry Ford Hospital clinics in metropolitan Detroit, Michigan, from July 2022-June 2023. The 74 reactions that occurred were most commonly associated with iron sucrose at the 500 mg dose (41/74, 55.41%, $p < 0.0001$). Most reactions observed across all iron formulations and doses were mild, with 83.7% being Grade 0 or 1 as defined by the United States Drug Allergy Registry (USDAR) grading scale for immediate reactions. Patients who experienced an infusion reaction were less likely to complete their infusion plans (OR 0.004 for iron dextran, OR 0.128 for iron sucrose, $p < 0.0001$), with infusions most commonly being

completely discontinued thereafter, with a minority pursuing alternative options. More patients with lower number of doses scheduled for iron dextran completed their infusion schedules than those with more doses, but the opposite was seen for iron sucrose. We assessed the impact of the national shortage of iron dextran examining infusion reactions with various iron infusions and doses.

Hematology-Oncology
Jiagge EM. Genetic African ancestry modifies the biology of acute myeloid leukemia. *Nat Genet* 2024; Epub ahead of print. PMID: 39367244. Full Text

Department of Hematology/Oncology, Henry Ford Health, Detroit, MI, USA. ejiagge1@hfhs.org.

Hematology-Oncology
Lessard S, Rimmelé P, Ling H, Moran K, Vieira B, Lin YD, Rajani GM, Hong V, Reik A, Boismenu R, Hsu B, Chen M, Cockroft BM, Uchida N, Tisdale J, **Alavi A**, Krishnamurti L, Abedi M, Galeon I, Reiner D, Wang L, Ramezi A, Rendo P, Walters MC, Levasseur D, Peters R, Harris T, and Hicks A. Zinc finger nuclease-mediated gene editing in hematopoietic stem cells results in reactivation of fetal hemoglobin in sickle cell disease. *Sci Rep* 2024; 14(1):24298. PMID: 39414860. Full Text

Rare Blood Disorders, Sanofi, Waltham, MA, 02451, USA. samuel.lessard@sanofi.com.
Precision Medicine and Computational Biology, Sanofi, Cambridge, MA, 02141, USA. samuel.lessard@sanofi.com.
Rare Blood Disorders, Sanofi, Waltham, MA, 02451, USA.
Sangamo Therapeutics, Richmond, CA, 94804, USA.
Cellular and Molecular Therapeutics Branch, National Heart, Lung, and Blood Institutes/National Institute of Diabetes and Digestive and Kidney Diseases, National Heart, National Institutes of Health (NIH), Bethesda, MD, USA.
Henry Ford Cancer Institute, Detroit, MI, USA.
Emory University, Aflac Cancer and Blood Disorders Center, Children's Healthcare of Atlanta, Atlanta, GA, USA.
University of California-Davis Medical Center, Sacramento, CA, USA.
University of California San Francisco Benioff Children's Hospital, Oakland, CA, USA.
Immunology and Inflammation, Sanofi, Cambridge, MA, 02141, USA.

BIVV003 is a gene-edited autologous cell therapy in clinical development for the potential treatment of sickle cell disease (SCD). Hematopoietic stem cells (HSC) are genetically modified with mRNA encoding zinc finger nucleases (ZFN) that target and disrupt a specific regulatory GATAA motif in the BCL11A erythroid enhancer to reactivate fetal hemoglobin (HbF). We characterized ZFN-edited HSC from healthy donors and donors with SCD. Results of preclinical studies show that ZFN-mediated editing is highly efficient, with enriched biallelic editing and high frequency of on-target indels, producing HSC capable of long-term multilineage engraftment in vivo, and express HbF in erythroid progeny. Interim results from the Phase 1/2 PRECIZN-1 study demonstrated that BIVV003 was well-tolerated in seven participants with SCD, of whom five of the six with more than 3 months of follow-up displayed increased total hemoglobin and HbF, and no severe vaso-occlusive crises. Our data suggest BIVV003 represents a compelling and novel cell therapy for the potential treatment of SCD.

Hematology-Oncology
Puri S, Aldhahi M, Chin LMK, Guccione AA, Jain V, and Herrick JE. Increased fatigability and impaired skeletal muscle microvascular reactivity in adults with obstructive sleep apnea: a cross-sectional study. *Eur J Med Res* 2024; 29(1):506. PMID: 39428454. Full Text

Cancer, Clinical and Translational Research Office, Henry Ford Health System, Detroit, MI, 48202, USA. shiprapuriphd85@gmail.com.
Department of Rehabilitation Sciences, College of Health and Rehabilitation Sciences, Princess Nourah Bint Abdulrahman University (PNU), P.O. Box 84428, 11671, Riyadh, Saudi Arabia.
Rehabilitation Medicine Department, Clinical Center, National Institutes of Health, Bethesda, MD, 20892, USA.

George Mason University, Professor Emeritus, Fairfax, VA, 22030, USA.
Division of Pulmonary, Critical Care and Sleep Disorders Medicine, George Washington School of Medicine & Health Sciences, Washington, DC, 20037, USA.
Department of Exercise Physiology, College of Health Sciences, University of Lynchburg, Lynchburg, VA, 24451, USA.

BACKGROUND: Sympathetic nervous system hyperactivity and chronic intermittent nocturnal hypoxia in individuals with obstructive sleep apnea (OSA) predispose them to microvascular impairment, which may contribute to increased daytime muscle fatigue. This study aimed to assess microvascular reactivity of the skeletal muscle, examine fatigability, and determine the relationship between fatigability and microvascular reactivity in adults with OSA. METHODS: Twenty-six participants were allocated into two groups-those with OSA and those without i.e. non-OSA. Each group comprised of 13 individuals who underwent an arterial occlusion test on their non-dominant leg. The percentage change of maximal hyperemic response (MHR) and the time to achieve MHR (tM) of both the total myoglobin/hemoglobin (∆[Hbtot]) and the oxygenated myoglobin/hemoglobin (∆[HbO(2)]) signals from near-infrared spectroscopy were calculated to examine microvascular reactivity. In addition, a 10-min walk test was performed to assess performance and perceived fatigability. RESULTS: The OSA group demonstrated a reduced in ∆[Hbtot]MHR (150.9 ± 16.2% vs. 235.8 ± 72.7%, p = 0.006), ∆[HbO(2)]MHR (131.4 ± 8% vs. 161.7 ± 10.6%, p = 0.001) and increased ∆[Hbtot]tM (80.5 ± 13.1 s vs. 47.7 ± 9.9 s, p < 0.001), ∆[HbO(2)]tM (85.2 ± 22.4 s vs. 52.1 ± 5.9 s, p = 0.001) compared to the non-OSA group. In addition, participants in the OSA group experienced greater perceived (6 ± 1 vs. 2.8 ± 0.1, p = 0.001) and performance fatigability (1.1 ± 0.1 vs. 0.9 ± 0.1, p = 0.001) compared to adults in the non-OSA group. Moreover, both performance and perceived fatigability were significantly associated with microvascular reactivity parameters (all p < 0.05). CONCLUSION: Microvascular dysfunction, as determined by an attenuated post-occlusive reactive hyperemia, is observed in individuals with OSA that may contribute to increased fatigability in these individuals.

Hematology-Oncology

Thoidingjam S, **Sriramulu S**, **Hassan O**, **Brown SL**, **Siddiqui F**, **Movsas B**, **Gadgeel S**, and **Nyati S**. BUB1 Inhibition Overcomes Radio- and Chemoradiation Resistance in Lung Cancer. *Cancers (Basel)* 2024; 16(19). PMID: 39409911. Full Text

Department of Radiation Oncology, Henry Ford Health, Detroit, MI 48202, USA.
Department of Surgical Pathology, Henry Ford Cancer Institute, Henry Ford Health, Detroit, MI 48202, USA.
Henry Ford Health + Michigan State University Health Sciences, Detroit, MI 48202, USA.
Department of Radiology, Michigan State University, East Lansing, MI 48824, USA.
Division of Hematology/Oncology, Department of Medicine, Henry Ford Health, Detroit, MI 48202, USA.

Background: Despite advances in targeted therapies and immunotherapies, traditional treatments like microtubule stabilizers (paclitaxel, docetaxel), DNA-intercalating platinum drugs (cisplatin), and radiation therapy remain essential for managing locally advanced and metastatic lung cancer. Identifying novel molecular targets could enhance the efficacy of these treatments. Hypothesis: We hypothesize that BUB1 (Ser/Thr kinase) is overexpressed in lung cancers and its inhibition will sensitize lung cancers to chemoradiation. Methods: BUB1 inhibitor (BAY1816032) was combined with cisplatin, paclitaxel, a PARP inhibitor olaparib, and radiation in cell proliferation and radiation-sensitization assays. Biochemical and molecular assays evaluated the impact on DNA damage signaling and cell death. Results: Immunostaining of lung tumor microarrays (TMAs) confirmed higher BUB1 expression in non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) compared to normal tissues. In NSCLC, BUB1 overexpression correlated directly with the expression of TP53 mutations and poorer overall survival in NSCLC and SCLC patients. BAY1816032 synergistically sensitized lung cancer cell lines to paclitaxel and olaparib and enhanced cell killing by radiation in both NSCLC and SCLC. Molecular analysis indicated a shift towards pro-apoptotic and anti-proliferative states, evidenced by altered BAX, BCL2, PCNA, and Caspases-9 and -3 expressions. Conclusions: Elevated BUB1 expression is associated with poorer survival in lung cancer. Inhibiting BUB1 sensitizes NSCLC and SCLC to chemotherapies (cisplatin, paclitaxel), targeted therapy (olaparib), and radiation. Furthermore, we present the novel finding that

BUB1 inhibition sensitized both NSCLC and SCLC to radiotherapy and chemoradiation. Our results demonstrate BUB1 inhibition as a promising strategy to sensitize lung cancers to radiation and chemoradiation therapies.

Hypertension and Vascular Research

Maskey D, **Liao TD**, **Potter DL**, and **Ortiz PA**. The FSGS protein actinin-4 (ACTN4) interacts with NKCC2 to regulate Thick Ascending Limb (TAL) NaCl reabsorption. *Am J Physiol Renal Physiol* 2024; Epub ahead of print. PMID: 39446130. Full Text

Hypertension and Vascular division, Internal Medicine, Henry Ford Hospital, Detroit, MI, United States.
Division of Hypertension and Vascular Research, Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, United States. ROR: https://ror.org/0193sb042
Hypertension & Vascular Research Division, Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, United States. ROR: https://ror.org/0193sb042

In the kidney, the thick Ascending Limb (TAL) of the loop of Henle is crucial for NaCl homeostasis and blood pressure regulation. In animal models of salt-sensitive hypertension, NaCl reabsorption via the apical Na+/K+/2Cl cotransporter (NKCC2) is abnormally increased in the TAL. We showed that NaCl reabsorption is controlled by the presence of NKCC2 at the apical surface of TALs. However, the molecular mechanisms that maintain the steady-state levels of NKCC2 at the apical surface are not clearly understood. Here, we report that NKCC2 interacts with the F-actin cross-linking protein actinin-4 (ACTN4). We find that ACTN4 is expressed in TALs by Western blot and immunofluorescence microscopy. ACTN4 immunoprecipitated with NKCC2 and recombinant GST-ACTN4 pulled down NKCC2 from TAL lysates. ACTN4 is involved in endocytosis in other cells. Therefore, we hypothesized that ACTN4 binds apical NKCC2 and regulates its trafficking. To study this, we silenced ACTN4 in vivo via shRNA or CRISPR/Cas9 system to decrease ACTN4 expression in TALs. We observed that silencing ACTN4 in vivo via shRNA or CRISPR/Cas9 system increased the amount NKCC2 at the apical surface of TALs. Bumetanide-induced diuresis and natriuresis were enhanced by 35% after silencing of ACTN4 in vivo (AV-NKCC2-Cas9: 3841±709 vs AAV-gRNA-ACTN4: 5546±622 µmols Na/8h, n=5, $p<0.05$). We conclude that ACTN4, binds NKCC2 to regulate its surface expression. Selective depletion of ACTN4 in TALs using shRNA or CRISPR/Cas9 enhances surface NKCC2 and TAL NaCl reabsorption, indicating that regulation of the ACTN4-NKCC2 interaction is important for renal NaCl reabsorption and could be related to hypertension.

Infectious Diseases

Bennis SL, **Yared NF**, Horvath KJ, Baker JV, Waterboer T, Thyagarajan B, and Kulasingam S. HPV Vaccination Status in HIV-Negative MSM and Its Association with High-Risk HPV Detection Using HPV Serology and Anorectal Swabs. *Vaccines (Basel)* 2024; 12(10). PMID: 39460321. Full Text

Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis, MN 55455, USA.
Division of Infectious Diseases, Department of Medicine, Henry Ford Health, Detroit, MI 48202, USA.
Department of Psychology, San Diego State University, San Diego, CA 92182, USA.
Division of Infectious Diseases, Hennepin Healthcare, Minneapolis, MN 55415, USA.
Department of Medicine, University of Minnesota, Minneapolis, MN 55455, USA.
Infections and Cancer Epidemiology, German Cancer Research Center (DKFZ), 69120 Heidelberg, Germany.
Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, MN 55455, USA.

Background/Objective: The aim of this study was to determine the prevalence of high-risk (HR) human papillomavirus (HPV) types by HPV vaccination status and the feasibility of using HPV L1 serology to identify HIV-negative men who have sex with men (MSM) who may be at risk for anal cancer. Methods: This cross-sectional study recruited HIV-negative MSM from a US metropolitan area. The prevalence of HR, quadrivalent, and nonavalent anorectal HPV DNA and HPV L1 serum antibodies was estimated. McNemar's chi-square and kappa statistics were used to determine significant differences in HPV

detection between anorectal DNA swabs and HPV L1 serology. Results: Eighty-two men had adequate anorectal swabs and serology samples for analysis. Men who self-reported receipt of the HPV vaccine (35.6%) had detectable L1 HPV antibodies (93.1%) and a lower prevalence of active anal HPV infections (20.7%) compared to those who reported none. Conclusions: If confirmed in larger prospective studies, a combination of HPV vaccination status or HPV L1 serology and anorectal swabs for HR HPV types could identify HIV-negative MSM who do not need to undergo follow-up anal testing.

Infectious Diseases
Campillo Terrazas W, **Kenney RM**, **Argyris A**, **Shallal AB**, and **Veve MP**. Judicious Use of Benzathine Penicillin G in Response to a Medication Alert During a Critical Drug Shortage. *J Pharm Technol* 2024. PMID: Not assigned. Full Text

M.P. Veve, Department of Pharmacy, Henry Ford Hospital, Detroit, MI, United States

Purpose: To evaluate judicious antibiotic prescribing of benzathine penicillin G (BPG) after implementation of an electronic health record-based medication shortage alert during a critical drug shortage. Methods: This was an institutional review board–approved retrospective cohort study of patients aged ≥3 months who received BPG between May 9, 2023, and February 28, 2024. The study included inpatient and outpatient visits after implementing a BPG medication shortage alert; patients with severe penicillin allergy, neurosyphilis, or congenital syphilis were excluded. Judicious BPG use was defined as use in patients diagnosed with primary, secondary, or latent syphilis or if they were prescribed a BPG alternative in response to the medication shortage alert; nonjudicious use included BPG for alternative diagnoses. Social determinants of health were assessed as exposure variables of interest. A separate cohort of syphilis patients receiving BPG or alternative therapy (i.e., doxycycline) was described. Results: A total of 453 patients were included. Most patients were non-Hispanic Black (n = 273, 60%) men (n = 272, 60%) with a median (interquartile range) age of 32 (22–44) years. Of these, 318 (70%) received judicious BPG, whereas 135 (30%) received nonjudicious BPG. The most nonjudicious diagnosis was streptococcal pharyngitis (n = 128, 95%). Variables associated with judicious use included age >32 years (adjusted odds ratio [adjOR], 2.273; 95% CI, 1.488–3.472), male sex (adjOR, 1.835; 95% CI, 1.206–2.792), and black race (adjOR, 1.847; 95% CI, 1.212–2.815). Among a cohort of 128 syphilis patients who received BPG (n = 64, 50%) or doxycycline (n = 64, 50%), those who received doxycycline were more likely be uninsured (35 [54.7%] vs 43 [67.2%]; P =.15) and receive outpatient treatment (3 [4.7%] vs 12 [18.7%]; P =.13). Conclusion: Despite implementing an electronic health record drug shortage alert, 30% of BPG use was nonjudicious and mostly for pharyngitis.

Infectious Diseases
Malviya M, **Kale-Pradhan P**, **Coyle M**, **Giuliano C**, and **Johnson LB**. Clinical and Drug Resistance Characteristics of Providencia Infections. *Microorganisms* 2024; 12(10). PMID: 39458394. Full Text

Division of Infectious Diseases, Henry Ford St. John Hospital, 22101 Morsoss Road, Detroit, MI 48236, USA.
Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI 48201, USA.
Henry Ford St. John Hospital, Detroit, MI 48236, USA.
Division of Infectious Diseases, Department of Internal Medicine, Henry Ford St. John Hospital, 22101 Moross Road, Detroit, MI 48236, USA.
Infection Prevention and Antimicrobial Stewardship, Ascension Michigan 22101 Morsoss Road, Detroit, MI 48236, USA.
School of Medicine, Wayne State University, 540 E Canfield St, Detroit, MI 48201, USA.

Background:Providencia is a G ram-negative bacillus that most frequently colonizes the urinary tract and is often resistant to many antimicrobials. This study aimed to evaluate the resistance patterns of Providencia spp. and clinical outcomes due to the paucity of data. Methods: A multi-center, descriptive, retrospective chart review of adult patients with Providencia spp. infections was conducted from 1 January 2020 to 31 May 2022. The primary outcome was to describe the drug resistance patterns of Providencia spp. isolates. This study's secondary outcome was to evaluate the clinical outcomes of

patients with Providencia spp. infections. Results: Of the 312 patients screened, 244 were excluded primarily for polymicrobial infections. The mean age was 70 years, and 39 (56.5%) were males. Of the 68 included cases, 46 (67.6%) were P. stuartii, 20 (29.4%) were P. rettgeri, and 2 (2.9%) were P. alcalifaciens. The most common infections were bacteremia 38 (55.8%), followed by 27 (39.7%) urinary tract infections and 3 (4.4%) wound infections. In this study, 45 patients (65.2%) had urinary catheters. The primary antibiotics used for treatment consisted of ceftriaxone (25 (36.2%)), cefepime (20 (29%)), and meropenem (10 (14.5%)). Only 5 of 68 (7.2%) cases were multidrug- resistant and required meropenem. In total, 19 patients (27.1%) died during their admission, but none were related to Providencia infections. A total of 10 of the 68 patients (14.5%) were readmitted within 30 days for reasons unrelated to the progression or recurrence of Providencia infections. Conclusions:Providencia bacteremia is predominantly seen in elderly patients. Third- generation cephalosporins remain an appropriate choice of antibiotics for Providencia spp. Providencia stuartii was the only species with multidrug resistance.

Infectious Diseases

Mulbah JL, **Kenney RM**, **Tibbetts RJ**, **Shallal AB**, and **Veve MP**. Ceftriaxone versus cefepime or carbapenems for definitive treatment of low-risk AmpC-Harboring Enterobacterales bloodstream infections in hospitalized adults: A retrospective cohort study. *Diagn Microbiol Infect Dis* 2024; 111(1):116557. PMID: 39427451. Full Text

Department of Pharmacy, Henry Ford Hospital, Detroit, MI, USA.
Department of Microbiology, Henry Ford Hospital, Detroit, MI, USA.
Department of Infectious Diseases, Henry Ford Hospital, Detroit, MI, USA.
Department of Pharmacy, Henry Ford Hospital, Detroit, MI, USA; Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI, USA. Electronic address: mpveve@wayne.edu.

OBJECTIVE: To compare outcomes of ceftriaxone to AmpC-stable therapies in patients with bacteremia caused by low-risk AmpC harboring Enterobacterales. METHODS: IRB-approved, retrospective cohort of hospitalized patients ≥18 years old with Serratia marcescens, Morganella morganii, or Providencia spp. bacteremia from 1/1/2017-2/28/2024. Patients were compared by definitive therapy with ceftriaxone vs AmpC-stable therapy (cefepime, carbapenem). The primary endpoint was 30-day all-cause mortality; secondary endpoints were clinical failure and development of ceftriaxone resistance. RESULTS: 163 patients were included; 33.1 % received ceftriaxone, 66.9 % AmpC-stable therapies. 30-day all-cause mortality was 9.3 % ceftriaxone vs 10.1 % AmpC stable patients (P = 0.87); ceftriaxone definitive therapy was not associated with 30-day all-cause mortality (adjOR, 0.79; 95 %CI, 0.23-2.3). There were no differences in clinical failure (9.3 % vs 21.1 %, P = 0.059) or relapsing infection (5.6 % vs 9.3 %, P = 0.55) between ceftriaxone and AmpC-stable treated patients. CONCLUSIONS: Patients treated with definitive ceftriaxone for low-risk AmpC Enterobacterales bacteremia had similar outcomes to AmpC stable therapies.

Internal Medicine

Al Jebaje Z, **Jabri A**, **Mishra T**, **Halboni A**, **Ayyad A**, **Alameh A**, **Ellauzi R**, **Alexandrino FB**, **Alaswad K**, and **Basir MB**. Use of mechanical circulatory support in high-risk percutaneous coronary interventions. *Prog Cardiovasc Dis* 2024; Epub ahead of print. PMID: 39442599. Full Text

Henry Ford Health System, Detroit, MI, USA. Electronic address: zaljeb1@hfhs.org.
Henry Ford Health System, Detroit, MI, USA.

As the field of percutaneous coronary intervention grows in volume, expertise, and available tools, interventional cardiologists are increasingly performing more complex and higher-risk coronary artery procedures. Mechanical circulatory support devices, previously used only in urgent situations, are now being utilized as supplementary tools to enhance outcomes in elective complex cases. This shift has sparked significant discussions about patient and device selection, as well as the potential risks involved. In this article, we explore the various devices and their distinct features. Additionally, we also introduce algorithms for device selection, placement and weaning to help guide physicians during their care for their high-risk PCI patients.

Internal Medicine
Alomari A, Althunibat I, **Obri MS**, **Curran J**, Aldroubi B, **Davis W**, and **Pompa R**. A Case of Metastatic Seminoma Mimicking a Primary Pancreatic Tumor. *Cureus* 2024; 16(9):e70329. PMID: 39463534. Request Article

Internal Medicine, Henry Ford Health System, Detroit, USA.
Internal Medicine, Saint Michael's Medical Center, Newark, USA.
Gastroenterology and Hepatology, Henry Ford Health System, Detroit, USA.
Medical College, Tishreen University, Lattakia, SYR.

Metastatic seminoma to the pancreas is exceedingly rare, with few reported cases in medical literature. We present a case of a 66-year-old male, six years post-remission from testicular seminoma, who presented with obstructive jaundice and a pancreatic mass mimicking primary malignancy. Diagnostic workup including endoscopic ultrasound-guided biopsy confirmed metastatic seminoma. He underwent successful treatment with four cycles of cisplatin and etoposide, achieving complete remission. This case underscores the diagnostic challenge of pancreatic metastases and emphasizes the role of biopsy in guiding appropriate management. Awareness of such presentations is crucial for timely intervention and improved patient outcomes.

Internal Medicine
AlRawashdeh MM, **Ishak A**, Al-Bunnia A, Agouridis AP, Lytras T, Spernovasilis N, and Tsioutis C. Patient Experiences and Perceptions with Infections Due to Multidrug-Resistant Organisms: A Systematic Review. *Pathogens* 2024; 13(9). PMID: 39339008. Full Text

School of Medicine, European University Cyprus, 2404 Nicosia, Cyprus.
Department of Internal Medicine, Henry Ford Health System, Detroit, MI 48202, USA.
Department of Internal Medicine, German Medical Institute, 4108 Limassol, Cyprus.
Department of Infectious Diseases, German Medical Institute, 4108 Limassol, Cyprus.

Infections by multidrug-resistant organisms (MDROs) pose significant public health challenges, including increased mortality rates, healthcare costs, and significant impacts on the quality of life for patients. Utilizing a systematic review methodology adhering to PRISMA guidelines, we performed a comprehensive search across three databases, identifying 20 relevant studies that investigated the psychological effects of infections due to MDROs on hospitalized adults. The primary outcomes examined included depression, anxiety, and other psychosocial impacts, while secondary outcomes included patient and caregiver understanding of the infection. Findings revealed consistent associations between contact isolation due to MDRO infections and heightened levels of depression and anxiety among patients, although evidence regarding the impact on anger was mixed. Other psychological aspects, such as feelings of stigmatization and reduced healthcare provider interactions, were also recorded. The current systematic review highlights the importance of addressing these psychological effects through holistic, patient-centered care approaches, emphasizing the need for better communication and comprehensive education for both patients and healthcare providers. Our findings suggest that mitigating the psychological burden of MDROs can enhance overall patient care and outcomes and call for further research to optimize care strategies for patients hospitalized for infections due to MDROs.

Internal Medicine
Ayyad A, **Fadel R**, **Kollman P**, **Parson A**, **Almajed MR**, **Shadid AM**, **Jabri A**, **Basir MB**, and **Alqarqaz M**. Surviving venoarterial extracorporeal membrane oxygenation (VA-ECMO): The roles of severity scores and post-operative lactate clearance. *Cardiovasc Revasc Med* 2024; Epub ahead of print. PMID: 39477754. Full Text

Henry Ford Hospital, Internal Medicine Department, Detroit, MI, USA. Electronic address: asemayyad96@gmail.com.
Henry Ford Hospital, Cardiology Department, Detroit, MI, USA.
Wayne State University, Detroit, MI, USA.

Henry Ford Hospital, Internal Medicine Department, Detroit, MI, USA.

BACKGROUND: This study investigated the association of the Survival After VA-ECMO (SAVE) score, Sequential Organ Failure Assessment (SOFA) score, and post-cannulation lactate levels with mortality among patients treated with veno-arterial extra-corporeal membrane oxygenation (VA-ECMO) for refractory cardiogenic shock (CS). METHODS: We performed a retrospective review of adult patients who underwent peripheral VA-ECMO cannulation from January 2018 to September 2022 at a quaternary care center. All-cause in-hospital mortality was assessed and compared to predicted mortality by SAVE and SOFA scores prior to cannulation, with adjusted odds ratio of risk factors for mortality identified by multivariate logistic regression analysis. Additionally, the prognostic value of 8-h post-cannulation serum lactate levels was analyzed by receiver operating characteristic (ROC) curve and Kaplan Meier analysis of 30-day survival. RESULTS: 244 patients were included in final analysis. All-cause in-hospital mortality was 70 %, and 54 % of patients died while on ECMO or within 24 h of decannulation. Pre-cannulation SAVE score (OR 0.93 per unit increase, 95 % CI 0.86-0.99, p = 0.008), SOFA score (OR 1.54 per unit increase, 95 % CI 1.32-1.75), and 8-h post-cannulation lactate levels (OR 1.20 per mmol/L increase, 95 % CI 1.04-1.36, p = 0.008) were independently associated with all-cause in-hospital mortality. 8-h post-cannulation lactate levels ≥5.3 mmol/L demonstrated high specificity for in-hospital mortality (90.0 %), while levels ≥7.8 mmol/L were demonstrated high specificity for VA-ECMO death (91.1 %). These thresholds were significantly associated with 30-day all-cause mortality (p < 0.001). CONCLUSION: Pre-cannulation SAVE and SOFA scores are useful prognostic tools in patients with CS. 8-h post-cannulation serum lactate levels are a pragmatic biomarker and can further assist in prognostication of patients on VA-ECMO, and the cutoffs of 5.3 mmol/L and 7.8 mmol/L have high specificity for all-cause mortality and VA-ECMO mortality, respectively. The development of accurate prognostic tools is critical in managing and optimizing care for patients with CS.

Internal Medicine

Fu C, **Wang J**, Ma T, **Yin C**, **Zhou L**, Clausen BE, **Mi QS**, and **Jiang A**. GSK-3β in Dendritic Cells Exerts Opposite Functions in Regulating Cross-Priming and Memory CD8 T Cell Responses Independent of β-Catenin. *Vaccines (Basel)* 2024; 12(9). PMID: 39340067. Full Text

Center for Cutaneous Biology and Immunology, Department of Dermatology, Henry Ford Health, Detroit, MI 48202, USA.
Immunology Program, Henry Ford Cancer Institute, Henry Ford Health, Detroit, MI 48202, USA.
Department of Medicine, College of Human Medicine, Michigan State University, East Lansing, MI 48824, USA.
Department of Computer Science and Engineering, School of Engineering and Computer Science, Oakland University, Rochester, MI 48309, USA.
Department of Internal Medicine, Henry Ford Health, Detroit, MI 48202, USA.
Institute for Molecular Medicine, Paul Klein Center for Immune Intervention, University Medical Center of the Johannes Gutenberg-University Mainz, Langenbeckstrasse 1, 55131 Mainz, Germany.

GSK-3β plays a critical role in regulating the Wnt/β-catenin signaling pathway, and manipulating GSK-3β in dendritic cells (DCs) has been shown to improve the antitumor efficacy of DC vaccines. Since the inhibition of GSK-3β leads to the activation of β-catenin, we hypothesize that blocking GSK-3β in DCs negatively regulates DC-mediated CD8 T cell immunity and antitumor immunity. Using CD11c-GSK-3β(-/-) conditional knockout mice in which GSK-3β is genetically deleted in CD11c-expressing DCs, we surprisingly found that the deletion of GSK-3β in DCs resulted in increased antitumor immunity, which contradicted our initial expectation of reduced antitumor immunity due to the presumed upregulation of β-catenin in DCs. Indeed, we found by both Western blot and flow cytometry that the deletion of GSK-3β in DCs did not lead to augmented expression of β-catenin protein, suggesting that GSK-3β exerts its function independent of β-catenin. Supporting this notion, our single-cell RNA sequencing (scRNA-seq) analysis revealed that GSK-3β-deficient DCs exhibited distinct gene expression patterns with minimally overlapping differentially expressed genes (DEGs) compared to DCs with activated β-catenin. This suggests that the deletion of GSK-3β in DCs is unlikely to lead to upregulation of β-catenin at the transcriptional level. Consistent with enhanced antitumor immunity, we also found that CD11c-GSK-3β(-/-) mice exhibited significantly augmented cross-priming of antigen-specific CD8 T cells following DC-

targeted vaccines. We further found that the deletion of GSK-3β in DCs completely abrogated memory CD8 T cell responses, suggesting that GSK-3β in DCs also plays a negative role in regulating the differentiation and/or maintenance of memory CD8 T cells. scRNA-seq analysis further revealed that although the deletion of GSK-3β in DCs positively regulated transcriptional programs for effector differentiation and function of primed antigen-specific CD8 T cells in CD11c-GSK-3β(-/-) mice during the priming phase, it resulted in significantly reduced antigen-specific memory CD8 T cells, consistent with diminished memory responses. Taken together, our data demonstrate that GSK-3β in DCs has opposite functions in regulating cross-priming and memory CD8 T cell responses, and GSK-3β exerts its functions independent of its regulation of β-catenin. These novel insights suggest that targeting GSK-3β in cancer immunotherapies must consider its dual role in CD8 T cell responses.

Internal Medicine

Ishak A, Mazonakis N, Spernovasilis N, Akinosoglou K, and Tsioutis C. Bactericidal versus bacteriostatic antibacterials: clinical significance, differences and synergistic potential in clinical practice. *J Antimicrob Chemother* 2024; Epub ahead of print. PMID: 39471409. Full Text

Department of Internal Medicine, 48202 Henry Ford Hospital, Detroit, MI, USA.
Department of Internal Medicine, Thoracic Diseases General Hospital Sotiria, 11527 Athens, Greece.
Department of Infectious Diseases, German Oncology Centre, 4108 Limassol, Cyprus.
School of Medicine, University of Crete, 71500 Heraklion, Greece.
School of Medicine, University of Patras, 26504 Rio, Greece.
Department of Internal Medicine and Infectious Diseases, University General Hospital of Patras, 26504 Rio, Greece.
School of Medicine, European University Cyprus, 6 Diogenes str, Nicosia 2404, Cyprus.

Antibacterial activity can be classified as either bactericidal or bacteriostatic, using methods such as the MBC/MIC ratio and time-kill curves. However, such categorization has proven challenging in clinical practice, as these definitions only apply under specific laboratory conditions, which may differ from clinical settings. Several factors, such as the specific bacteria or infectious medium, can affect the action of antibiotics, with many antibacterials exerting both activities. These definitions have also led to the belief that bactericidal antibacterials are superior to bacteriostatic, especially in more severe cases, such as endocarditis, neutropenia and bacteraemia. Additionally, current dogma dictates against the combination of bactericidal and bacteriostatic antibacterials in clinical practice, due to potential antagonism. This review aimed to assess the differences in antibacterial activity of bactericidal and bacteriostatic antibacterials based on in vitro and in vivo studies and examine their antagonistic or synergistic effects. Our findings show that specific bacteriostatic agents, such as linezolid and tigecycline, are clinically non-inferior to bactericidals in multiple infections, including pneumonia, intra-abdominal infections, and skin and soft tissue infections. Studies also support using several bacteriostatic agents as salvage therapies in severe infections, such as neutropenic fever and endocarditis. Additionally, not all combinations of bacteriostatic and bactericidal agents appear to be antagonistic, with many combinations, such as linezolid and rifampicin, already being used. The findings should be interpreted with caution, as most evidence is from observational studies and there is a need for randomized controlled trials to assess their effectiveness and combinations, especially within the context of rising antimicrobial resistance.

Internal Medicine

Jacob B, **Jamil M**, **Raslan S**, **Springer K**, **Nasser Z**, and **Kuriakose P**. Infusion Reactions With Alternative Therapies During the National Shortage of Iron Dextran. *Eur J Haematol* 2024; Epub ahead of print. PMID: 39385426. Full Text

Henry Ford Health, Detroit, Michigan, USA.

Prior to the national shortage of iron dextran in early 2023, it was the most commonly administered intravenous iron infusion at our institution. After the shortage impacted the health system, alternatives such as iron sucrose and sodium ferric gluconate/sucrose were required that utilized lower doses given at more frequent patient visits. Coinciding with their more prevalent use, an increase in iron infusion reactions was observed. Our study analyzed 880 patients who received iron infusions in three Henry Ford

Hospital clinics in metropolitan Detroit, Michigan, from July 2022-June 2023. The 74 reactions that occurred were most commonly associated with iron sucrose at the 500 mg dose (41/74, 55.41%, $p < 0.0001$). Most reactions observed across all iron formulations and doses were mild, with 83.7% being Grade 0 or 1 as defined by the United States Drug Allergy Registry (USDAR) grading scale for immediate reactions. Patients who experienced an infusion reaction were less likely to complete their infusion plans (OR 0.004 for iron dextran, OR 0.128 for iron sucrose, $p < 0.0001$), with infusions most commonly being completely discontinued thereafter, with a minority pursuing alternative options. More patients with lower number of doses scheduled for iron dextran completed their infusion schedules than those with more doses, but the opposite was seen for iron sucrose. We assessed the impact of the national shortage of iron dextran examining infusion reactions with various iron infusions and doses.

Internal Medicine

Kumar A, **Ellauzi R**, Anavekar NS, and Kalra A. Twenty-year trend of mortality from concomitant sepsis and acute myocardial infarction (Type 1 or Type 2) in the United States. *Cardiovasc Revasc Med* 2024; Epub ahead of print. PMID: 39443254. Full Text

Department of Internal Medicine, Cleveland Clinic Akron General, Akron, OH, USA.
Department of Internal Medicine, Henry Ford Health, Detroit, MI, USA.
Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN, USA.
Franciscan Health, Lafayette, IN, USA; Krannert Cardiovascular Research Center, Indiana University School of Medicine, Indianapolis, IN, USA. Electronic address: akalra@alumni.harvard.edu.

Internal Medicine

Malviya M, **Kale-Pradhan P**, **Coyle M**, **Giuliano C**, and **Johnson LB**. Clinical and Drug Resistance Characteristics of Providencia Infections. *Microorganisms* 2024; 12(10). PMID: 39458394. Full Text

Division of Infectious Diseases, Henry Ford St. John Hospital, 22101 Morsoss Road, Detroit, MI 48236, USA.
Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI 48201, USA.
Henry Ford St. John Hospital, Detroit, MI 48236, USA.
Division of Infectious Diseases, Department of Internal Medicine, Henry Ford St. John Hospital, 22101 Moross Road, Detroit, MI 48236, USA.
Infection Prevention and Antimicrobial Stewardship, Ascension Michigan 22101 Morsoss Road, Detroit, MI 48236, USA.
School of Medicine, Wayne State University, 540 E Canfield St, Detroit, MI 48201, USA.

Background:Providencia is a G ram-negative bacillus that most frequently colonizes the urinary tract and is often resistant to many antimicrobials. This study aimed to evaluate the resistance patterns of Providencia spp. and clinical outcomes due to the paucity of data. Methods: A multi-center, descriptive, retrospective chart review of adult patients with Providencia spp. infections was conducted from 1 January 2020 to 31 May 2022. The primary outcome was to describe the drug resistance patterns of Providencia spp. isolates. This study's secondary outcome was to evaluate the clinical outcomes of patients with Providencia spp. infections. Results: Of the 312 patients screened, 244 were excluded primarily for polymicrobial infections. The mean age was 70 years, and 39 (56.5%) were males. Of the 68 included cases, 46 (67.6%) were P. stuartii, 20 (29.4%) were P. rettgeri, and 2 (2.9%) were P. alcalifaciens. The most common infections were bacteremia 38 (55.8%), followed by 27 (39.7%) urinary tract infections and 3 (4.4%) wound infections. In this study, 45 patients (65.2%) had urinary catheters. The primary antibiotics used for treatment consisted of ceftriaxone (25 (36.2%)), cefepime (20 (29%)), and meropenem (10 (14.5%)). Only 5 of 68 (7.2%) cases were multidrug- resistant and required meropenem. In total, 19 patients (27.1%) died during their admission, but none were related to Providencia infections. A total of 10 of the 68 patients (14.5%) were readmitted within 30 days for reasons unrelated to the progression or recurrence of Providencia infections. Conclusions:Providencia bacteremia is predominantly seen in elderly patients. Third- generation cephalosporins remain an appropriate choice of antibiotics for Providencia spp. Providencia stuartii was the only species with multidrug resistance.

Internal Medicine

Masmoum MD, Khan S, Usmani WA, Chaudhry R, Ray R, **Mahmood A**, Afzal M, and Mirza MSS. The Effectiveness of Exercise in Reducing Cardiovascular Risk Factors Among Adults: A Systematic Review and Meta-Analysis. *Cureus* 2024; 16(9):e68928. PMID: 39381478. Full Text

General Practice, Alfaisal University College of Medicine, Riyadh, SAU.
Medicine, Fatima Jinnah Medical University, Lahore, PAK.
Medicine, Ziauddin University, Karachi, PAK.
Medicine, Baylor College of Medicine, Houston, USA.
Internal Medicine, Bankura Sammilani Medical College and Hospital, Bankura, IND.
Internal Medicine, Henry Ford Health System, Detroit, USA.
Medical Office, Allama Iqbal Medical College, Lahore, PAK.
Internal Medicine, Shandong University School of Medicine, Jinan, CHN.

Cardiovascular disease (CVD) remains one of the major causes of sickness and death in the world. However, lifestyle modifications, such as exercise, can significantly reduce the risk of this disease. This study aimed to assess the effectiveness of various forms of physical activity in reducing CVD risk factors among adults. A comprehensive search of the databases PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Central Register of Controlled Trials (CENTRAL), and Excerpta Medica Database (EMBASE) databases was conducted between January 1, 2014, and May 31, 2024, as per Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Randomized controlled trials (RCTs), cohort studies, and observational studies on the impact of aerobic, resistance, or combined training on cardiovascular risk factors in adults (≥18 years) were considered for inclusion. Data relating to primary outcomes, including stroke and myocardial infarction rates, BP, cholesterol levels, and BMI were collected. The Cochrane risk-of-bias tool and the Methodological Index for Non-Randomized Studies (MINORS) checklist were used for quality and bias assessment. Meta-analyses were performed using the RevMan software, with heterogeneity evaluated by I^2 statistics; 17 studies, including 11 RCTs and six cohort studies, met the inclusion criteria. There was a significant reduction in the mean systolic BP (SBP) by 3.32 mmHg [95% confidence interval (CI): 0.85-5.78 mmHg; $p<0.0001$] and mean diastolic BP (DBP) by 2.99 mmHg (95% CI: 2.34-3.64 mmHg; $p<0.00001$) after exercise interventions. Moreover, cholesterol levels and BMI values improved with exercise. Those who exercised had a lower risk of stroke or heart attack compared with the controls [odds ratio (OR): 0.57; 95% CI: 0.28-1.14; $p>0.0001$], although there was substantial heterogeneity in effect size across the studies ($I^2=98\%$). Different types of physical activity (i.e., aerobic, resistance, or combined exercise) can effectively reduce key cardiovascular risk factors, including BP, cholesterol levels, and BMI values. Regular physical activity is still regarded as the most effective preventive measure against CVD, despite inconsistencies in research findings. Future studies should aim to identify optimal exercise programs and their long-term effects on diverse populations.

Internal Medicine

Miller-Matero LR, **Hecht LM**, **Gavrilova L**, **Haage B**, **Autio K**, **Tobin ET**, and **Ahmedani BK**. Utilizing primary care to engage underserved patients in a psychological intervention for chronic pain. *Prim Health Care Res Dev* 2024; 25:e54. PMID: 39450755. Full Text

Henry Ford Health, Behavioral Health, Detroit, MI, USA.
Henry Ford Health, Center for Health Policy & Health Services Research, Detroit, MI, USA.
Michigan State University, East Lansing, MI, USA.
Henry Ford Health, Public Health Sciences, Detroit, MI, USA.
Henry Ford Health, Internal Medicine, Detroit, MI, USA.

BACKGROUND: Although psychological interventions can be used to improve chronic pain management, underserved individuals (i.e., racially minoritized and socioeconomically disadvantaged) may be less likely to engage in such services. The purpose of this study was to examine whether offering a psychological intervention for chronic pain in a primary care clinic could be a method in which to successfully engage underserved patients. METHODS: There were 220 patients with chronic pain in a primary care clinic located in a socioeconomically and racially diverse city who were approached to

discuss enrolment in a pilot randomized controlled trial of a five-session psychological intervention for chronic pain. Patients were introduced to the study by their primary care provider using the warm handoff model. We compared whether there were sociodemographic differences between those who enrolled in the study and those who declined to enrol. RESULTS: There were no differences between those who enrolled and those who declined enrolment with regard to race, age, insurance type, and household income. However, females were more likely to enrol in the study compared to males. CONCLUSIONS: Recruiting patients to participate in a trial of a psychological intervention for chronic pain in a primary care clinic appeared to be effective for engaging Black patients, patients with lower income, and those with government insurance. Thus, offering a psychological intervention for chronic pain in a primary care clinic may encourage engagement among racially minoritized individuals and those with lower socioeconomic status.

Internal Medicine

Mojaddedi S, Jamil J, Abraham A, **Jamil D**, Mansoor H, and Elgendy IY. Venous thromboembolism during pregnancy and postpartum period: an updated review. *Minerva Med* 2024; Epub ahead of print. PMID: 39392291. Request Article

Graduate Medical Education, University of Central Florida College of Medicine, Orlando, FL, USA.
Internal Medicine Residency Program, HCA Florida North Florida Hospital, Gainesville, FL, USA.
College of Medicine, Gulf Medical University, Ajman, United Arab Emirates.
Internal Medicine Residency Program, Henry Ford Hospital, Detroit, MI, USA.
Department of Pharmacy Practice and Science, College of Pharmacy, University of Kentucky, Lexington, KY, USA.
Division of Cardiovascular Medicine, Gill Heart Institute, University of Kentucky, Lexington, KY, USA - iyelgendy@gmail.com.

Venous thromboembolism (VTE) is a leading cause of maternal mortality. The risk of VTE in pregnant and postpartum women is ~ five times higher compared with non-pregnant women. There is a physiological tendency to a hypercoagulable state, from conception to the postpartum period. Several non-obstetric risk factors independently increase the risk of VTE. Since most signs and symptoms of VTE might mimic those of a normal pregnancy, a high index of suspicion is warranted to establish the diagnosis. D-dimer, ultrasonography and computed tomography pulmonary angiography are the primary tools for VTE diagnosis. Management mainly revolves around systemic anticoagulation with heparin. Advanced therapy options exist, but these can be considered for selected high-risk cases.

Internal Medicine

Wilson SJ, **Gelovani D**, Von A, **Kaatz S**, and Grant PJ. Medical Clinics of North America-Periprocedural Antithrombotics: Prophylaxis and Interruption. *Med Clin North Am* 2024; 108(6):1017-1037. PMID: 39341611. Full Text

Michigan Medicine, Department of Internal Medicine, 1500 E. Medical Center Drive, UH South, Unit 4, SPC 5220, Ann Arbor, MI 48109, USA. Electronic address: wilsonst@med.umich.edu.
Henry Ford Health, Department of Internal Medicine, 2799 W Grand Boulevard, Detroit, MI 48202, USA.
Emory University School of Medicine, Department of Internal Medicine, 1364 Clifton Road NE, Suite N-305, Atlanta, GA 30322, USA.
Michigan Medicine, Department of Internal Medicine, 1500 E. Medical Center Drive, UH South, Unit 4, SPC 5220, Ann Arbor, MI 48109, USA.

Anticoagulation management in the surgical patient requires clinical expertise and careful attention. For patients already receiving anticoagulation for a defined indication (ie, stroke prevention for atrial fibrillation, treatment of venous thromboembolism (VTE), or presence of a mechanical heart valve), understanding how to manage these agents by weighing the risks of thromboembolic events and bleeding is paramount. Additionally, prevention of VTE in the surgical patient involves the identification of patient-specific and procedure-specific risk factors for both VTE and bleeding. With this information, as well as familiarity with the several antithrombotic options available, an appropriate prophylaxis strategy can be employed.

Neurology

Alhashimi I, Zoghoul S, Khalil SK, Yousif ZB, **Jumah A**, and Alkailani Y. Neuroimaging Characteristics as Diagnostic Tools in Joubert Syndrome and Related Disorders: A Case Report and Literature Review. *Cureus* 2024; 16(9):e69872. PMID: 39435230. Request Article

Radiology, Hamad Medical Corporation, Doha, QAT.
Internal Medicine, Hamad Medical Corporation, Doha, QAT.
Neurology, Henry Ford Health System, Detroit, USA.
Neuroradiology Section, Neuroscience Institute, Hamad Medical Corporation, Doha, QAT.

Joubert syndrome and related disorders (JSRD) present diagnostic challenges due to their varied clinical features. Neuroimaging, particularly MRI and CT, is critical for identifying the distinctive "molar tooth sign" and other neuroanatomical abnormalities. This case report and literature review emphasize the role of neuroimaging in diagnosing JSRD. Our search targeted pediatric cases with terms like "Joubert anomaly" and "diagnostic imaging." Key findings include cerebellar vermal agenesis, ataxia, developmental delay, and oculomotor apraxia. Cognitive impairment ranges widely, complicating assessment. CT scans reveal dysplastic or absent cerebellar vermis, while MRI shows the characteristic "molar tooth" sign and additional abnormalities such as malformed cerebellar peduncles and enlarged posterior fossa. Accurate diagnosis of JSRD depends on correlating clinical symptoms with specific radiological findings. A multidisciplinary approach is vital for managing this complex disorder.

Neurology

Ata N, **Zahoor I**, **Hoda N**, Adnan SM, Vijayakumar S, Louis F, **Poisson L**, **Rattan R**, Kumar N, **Cerghet M**, and **Giri S**. Artificial neural network-based prediction of multiple sclerosis using blood-based metabolomics data. *Mult Scler Relat Disord* 2024; 92:105942. PMID: 39471746. Full Text

Department of Neurology, Henry Ford Health, Detroit, MI, 48202, USA.
Faculty of Engineering, Aligarh Muslim University, Aligarh, 202002, India.
IEEE Senior Member, Dallas, TX, 75063, USA.
Public Health Services, Henry Ford Health, Detroit, MI, 48202, USA.
Women's Health Services, Henry Ford Health, Detroit, MI, 48202, USA.
Department of Microbiology, Jaipur National University, Jaipur, 302017, India.
Department of Neurology, Henry Ford Health, Detroit, MI, 48202, USA. Electronic address: sgiri1@hfhs.org.

Multiple sclerosis (MS) remains a challenging neurological condition for diagnosis and management and is often detected in late stages, delaying treatment. Artificial intelligence (AI) is emerging as a promising approach to extracting MS information when applied to different patient datasets. Given the critical role of metabolites in MS profiling, metabolomics data may be an ideal platform for the application of AI to predict disease. In the present study, a machine-learning (ML) approach was used for a detailed analysis of metabolite profiles and related pathways in patients with MS and healthy controls (HC). This approach identified unique alterations in biochemical metabolites and their correlation with disease severity parameters. To enhance the efficiency of using metabolic profiles to determine disease severity or the presence of MS, we trained an AI model on a large volume of blood-based metabolomics datasets. We constructed this model using an artificial neural network (ANN) architecture with perceptrons. Data were divided into training, validation, and testing sets to determine model accuracy. After training, accuracy reached 87 %, sensitivity was 82.5 %, specificity was 89 %, and precision was 77.3 %. Thus, the developed model seems highly robust, generalizable with a wide scope and can handle large amounts of data, which could potentially assist neurologists. However, a large multicenter cohort study is necessary for further validation of large-scale datasets to allow the integration of AI in clinical settings for accurate diagnosis and improved MS management.

Neurology

Boura I, Giannopoulou IA, Pavlaki V, Xiromerisiou G, **Mitsias P**, and Spanaki C. FIG4-Related Parkinsonism and the Particularities of the I41T Mutation: A Review of the Literature. *Genes (Basel)* 2024; 15(10). PMID: 39457468. Full Text

School of Medicine, University of Crete, Crete, 70013 Heraklion, Greece.
Department of Basic and Clinical Neuroscience, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London SE5 9RT, UK.
Department of Neurology, University General Hospital of Heraklion, Crete, 71500 Heraklion, Greece.
School of Medicine, University of Thessaly, 41500 Larissa, Greece.
Department of Neurology, University General Hospital of Larissa, 41334 Larissa, Greece.
Department of Neurology, Henry Ford Hospital, Detroit, MI 48202, USA.
School of Medicine, Wayne State University, Detroit, MI 48202, USA.

Background/Objectives: The genetic underpinnings of Parkinson's disease (PD) and parkinsonism have drawn increasing attention in recent years. Mutations in the Factor-Induced Gene 4 (FIG4) have been implicated in various neurological disorders, including Charcot-Marie-Tooth disease type 4J (CMT4J), amyotrophic lateral sclerosis (ALS), and Yunis-Varón syndrome. This review aims to explore the association between FIG4 mutations and parkinsonism, with a specific focus on the rare missense mutation p.Ile41Thr (I41T). Methods: We identified 12 cases from 10 different families in which parkinsonism was reported in conjunction with CMT4J polyneuropathy. All cases involved the I41T mutation in a compound heterozygous state, combined with a FIG4 loss-of-function mutation. Data from clinical observations, neuroimaging studies, and genetic analyses were evaluated to understand the characteristics of parkinsonism in these patients. Results: In all 12 cases, parkinsonism developed either concurrently or following the onset of CMT4J neuropathy, but was never observed in isolation. Cases of both early- and late-onset parkinsonism were identified, reflecting similarities to genetic forms of parkinsonism with autosomal recessive inheritance. Imaging studies, including Dopamine transporter Single Photon Emission Computed Tomography (DaTscan) and brain magnetic resonance imaging (MRI), revealed abnormalities indicative of neurodegeneration, consistent with findings in other neurodegenerative disorders. Conclusions: The co-occurrence of parkinsonism with CMT4J in patients carrying the I41T mutation suggests an expanded spectrum of FIG4-related disorders, potentially implicating the same molecular mechanisms seen in other neurodegenerative disorders. Further research into FIG4-mediated pathways may offer valuable insights into potential therapeutic targets for disorders of both the central and peripheral nervous systems.

Neurology

Datta I, **Zahoor I**, **Ata N**, **Rashid F**, **Cerghet M**, **Rattan R**, **Poisson LM**, and **Giri S**. Utility of an Untargeted Metabolomics Approach Using a 2D GC-GC-MS Platform to Distinguish Relapsing and Progressive Multiple Sclerosis. *Metabolites* 2024; 14(9). PMID: 39330500. Full Text

Department of Public Health Sciences, Henry Ford Health, Detroit, MI 48202, USA.
Department of Neurosurgery, Henry Ford Health, Detroit, MI 48202, USA.
Department of Neurology, Henry Ford Health, Detroit, MI 48202, USA.
Women's Health Services, Henry Ford Health, Detroit, MI 48202, USA.

Multiple sclerosis (MS) is the most common inflammatory neurodegenerative disease of the central nervous system (CNS) in young adults and results in progressive neurological defects. The relapsing-remitting phenotype (RRMS) is the most common disease course in MS, which ultimately progresses to secondary progressive MS (SPMS), while primary progressive MS (PPMS) is a type of MS that worsens gradually over time without remissions. There is a gap in knowledge regarding whether the relapsing form can be distinguished from the progressive course, or healthy subjects (HS) based on an altered serum metabolite profile. In this study, we performed global untargeted metabolomics with the 2D GC-GC-MS platform to identify altered metabolites between RRMS, PPMS, and HS. We profiled 235 metabolites in the serum of patients with RRMS (n = 41), PPMS (n = 31), and HS (n = 91). A comparison of RRMS and HS patients revealed 22 significantly altered metabolites at $p < 0.05$ (false-discovery rate [FDR] = 0.3). The PPMS and HS comparisons revealed 28 altered metabolites at $p < 0.05$ (FDR = 0.2). Pathway

analysis using MetaboAnalyst revealed enrichment of four metabolic pathways in both RRMS and PPMS (hypergeometric test $p < 0.05$): (1) galactose metabolism; (2) amino sugar and nucleotide sugar metabolism; (3) phenylalanine, tyrosine, and tryptophan biosynthesis; and (4) aminoacyl-tRNA biosynthesis. The Qiagen IPA enrichment test identified the sulfatase 2 (SULF2) ($p = 0.0033$) and integrin subunit beta 1 binding protein 1 (ITGB1BP1) ($p = 0.0067$) genes as upstream regulators of altered metabolites in the RRMS vs. HS groups. However, in the PPMS vs. HS comparison, valine was enriched in the neurodegeneration of brain cells ($p = 0.05$), and heptadecanoic acid, alpha-ketoisocaproic acid, and glycerol participated in inflammation in the CNS ($p = 0.03$). Overall, our study suggests that RRMS and PPMS may contribute metabolic fingerprints in the form of unique altered metabolites for discriminating MS disease from HS, with the potential for constructing a metabolite panel for progressive autoimmune diseases such as MS.

Neurology

Singh S, Singh PK, Ahmad Z, Das S, Foretz M, Viollet B, **Giri S**, and Kumar A. Myeloid Cell-Specific Deletion of AMPKα1 Worsens Ocular Bacterial Infection by Skewing Macrophage Phenotypes. *J Immunol* 2024; Epub ahead of print. PMID: 39413004. Full Text

Department of Ophthalmology, Visual and Anatomical Sciences, Kresge Eye Institute, Wayne State University School of Medicine, Detroit, MI.
Department of Ophthalmology, Mason Eye Institute, University of Missouri School of Medicine, Columbia, MO.
Université Paris Cité, CNRS, INSERM, Institut Cochin, Paris, France.
Department of Neurology, Henry Ford Health System, Detroit, MI.
Department of Biochemistry, Microbiology, and Immunology, Wayne State University School of Medicine, Detroit, MI.

AMP-activated protein kinase (AMPK) plays a crucial role in governing essential cellular functions such as growth, proliferation, and survival. Previously, we observed increased vulnerability to bacterial (Staphylococcus aureus) endophthalmitis in global AMPKα1 knockout mice. In this study, we investigated the specific involvement of AMPKα1 in myeloid cells using LysMCre;AMPKα1fl mice. Our findings revealed that whereas endophthalmitis resolved in wild-type C57BL/6 mice, the severity of the disease progressively worsened in AMPKα1-deficient mice over time. Moreover, the intraocular bacterial load and inflammatory mediators (e.g., IL-1β, TNF-α, IL-6, and CXCL2) were markedly elevated in the LysMCre;AMPKα1fl mice. Mechanistically, the deletion of AMPKα1 in myeloid cells skewed macrophage polarization toward the inflammatory M1 phenotype and impaired the phagocytic clearance of S. aureus by macrophages. Notably, transferring AMPK-competent bone marrow from wild-type mice to AMPKα1 knockout mice preserved retinal function and mitigated the severity of endophthalmitis. Overall, our study underscores the role of myeloid-specific AMPKα1 in promoting the resolution of inflammation in the eye during bacterial infection. Hence, therapeutic strategies aimed at restoring or enhancing AMPKα1 activity could improve visual outcomes in endophthalmitis and other ocular infections.

Neurosurgery

Datta I, **Zahoor I**, **Ata N**, **Rashid F**, **Cerghet M**, **Rattan R**, **Poisson LM**, and **Giri S**. Utility of an Untargeted Metabolomics Approach Using a 2D GC-GC-MS Platform to Distinguish Relapsing and Progressive Multiple Sclerosis. *Metabolites* 2024; 14(9). PMID: 39330500. Full Text

Department of Public Health Sciences, Henry Ford Health, Detroit, MI 48202, USA.
Department of Neurosurgery, Henry Ford Health, Detroit, MI 48202, USA.
Department of Neurology, Henry Ford Health, Detroit, MI 48202, USA.
Women's Health Services, Henry Ford Health, Detroit, MI 48202, USA.

Multiple sclerosis (MS) is the most common inflammatory neurodegenerative disease of the central nervous system (CNS) in young adults and results in progressive neurological defects. The relapsing-remitting phenotype (RRMS) is the most common disease course in MS, which ultimately progresses to secondary progressive MS (SPMS), while primary progressive MS (PPMS) is a type of MS that worsens gradually over time without remissions. There is a gap in knowledge regarding whether the relapsing form

can be distinguished from the progressive course, or healthy subjects (HS) based on an altered serum metabolite profile. In this study, we performed global untargeted metabolomics with the 2D GC-GC-MS platform to identify altered metabolites between RRMS, PPMS, and HS. We profiled 235 metabolites in the serum of patients with RRMS (n = 41), PPMS (n = 31), and HS (n = 91). A comparison of RRMS and HS patients revealed 22 significantly altered metabolites at $p < 0.05$ (false-discovery rate [FDR] = 0.3). The PPMS and HS comparisons revealed 28 altered metabolites at $p < 0.05$ (FDR = 0.2). Pathway analysis using MetaboAnalyst revealed enrichment of four metabolic pathways in both RRMS and PPMS (hypergeometric test $p < 0.05$): (1) galactose metabolism; (2) amino sugar and nucleotide sugar metabolism; (3) phenylalanine, tyrosine, and tryptophan biosynthesis; and (4) aminoacyl-tRNA biosynthesis. The Qiagen IPA enrichment test identified the sulfatase 2 (SULF2) ($p = 0.0033$) and integrin subunit beta 1 binding protein 1 (ITGB1BP1) ($p = 0.0067$) genes as upstream regulators of altered metabolites in the RRMS vs. HS groups. However, in the PPMS vs. HS comparison, valine was enriched in the neurodegeneration of brain cells ($p = 0.05$), and heptadecanoic acid, alpha-ketoisocaproic acid, and glycerol participated in inflammation in the CNS ($p = 0.03$). Overall, our study suggests that RRMS and PPMS may contribute metabolic fingerprints in the form of unique altered metabolites for discriminating MS disease from HS, with the potential for constructing a metabolite panel for progressive autoimmune diseases such as MS.

Neurosurgery
Eide JG, **Mason W**, **Mackie H**, **Cook B**, **Ray A**, **Asmaro K**, **Robin A**, **Rock J**, and **Craig JR**. Diagnostic Accuracy of Beta-2 Transferrin Gel Electrophoresis for Detecting Cerebrospinal Fluid Rhinorrhea. *Laryngoscope* 2024; Epub ahead of print. PMID: 39400322. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, Detroit, Michigan, U.S.A.
Department of Pathology, Henry Ford Health, Detroit, Michigan, U.S.A.
Department of Neurosurgery, Henry Ford Health, Detroit, Michigan, U.S.A.

OBJECTIVE: Unilateral thin clear rhinorrhea (UTCR) may represent a variety of pathologies including cerebrospinal fluid (CSF) rhinorrhea. Beta-2 transferrin (B2Tf) gel electrophoresis (GE) has become the preferred testing modality due to reportedly high sensitivity (87%-100%) and specificity (71%-100%). However, there have been relatively few studies assessing its diagnostic accuracy. The purpose of this single-institution study was to determine the accuracy of B2Tf GE in detecting CSF rhinorrhea. METHODS: A single-center retrospective review was conducted from 2016 and 2024 for all patients who presented with UTCR and underwent B2Tf GE. Institutional review board approval was obtained. The gold standard for diagnostic confirmation of true and false positives (TP, FP) as well as false negatives (FN) was endoscopic exploration. The gold standard for true negative (TN) was response to medical therapy. RESULTS: A total of 105 patients underwent 149 B2Tf GE tests. 40 (38.1%) patients were diagnosed with CSF rhinorrhea. Of the 149 B2-Tf GE tests, there were 51 TPs, 72 TNs, 20 FPs, and 6 FNs yielding 89.5% sensitivity, 78.3% specificity, 71.8% positive predictive value, and 92.3% negative predictive value, respectively. Of the false results the most common causes for error were purulent sinusitis (n = 6, 23.1%), possible mucous contamination from nose-blowing during collection (n = 3, 11.5%), patient collection error (n = 3, 11.5%), and blood contamination (n = 1, 3.8%). CONCLUSION: Although these single-institutional data demonstrate test accuracy within ranges previously reported in the literature, they also demonstrate diagnostic limitations. Future studies should explore reasons for erroneous B2Tf GE results and how these may change clinical decision-making. LEVEL OF EVIDENCE: IV Laryngoscope, 2024.

Neurosurgery
Holdhoff M, Ye X, Strowd RE, Nabors B, **Walbert T**, Lieberman FS, Bagley SJ, Fiveash JB, Fisher JD, Desideri S, Surakus T, Engelhardt M, Kaindl T, Lane HA, Litherland K, Grossman SA, and Kleinberg LR. Lisavanbulin (BAL101553), a novel microtubule inhibitor, plus radiation in patients with newly diagnosed, MGMT promoter unmethylated glioblastoma. *Neurooncol Adv* 2024; 6(1):vdae150. PMID: 39371261. Full Text

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, Maryland, USA.
Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA.

University of Alabama, Birmingham, Alabama, USA.
Henry Ford Hospital, Detroit, Michigan, USA.
University of Pittsburgh, Pittsburgh, Pennsylvania, USA.
University of Pennsylvania, Philadelphia, Pennsylvania, USA.
Basilea Pharmaceutica International Ltd, Allschwil, Switzerland.

BACKGROUND: Lisavanbulin (BAL101553) is a small, lipophilic, oral microtubule destabilizer with promising antitumoral activity observed in preclinical glioblastoma (GBM) models. METHODS: This multicenter phase 1 study sought to determine the MTD of oral Lisavanbulin in combination with standard RT (60 Gy/30 fractions) but without temozolomide in patients with newly diagnosed MGMT promoter unmethylated GBM (uGBM). Dose escalation followed a modified 3 + 3 design. Secondary objectives included estimation of OS and PFS and pharmacokinetic analysis. RESULTS: Twenty-six patients with uGBM (median age, 63 years, 42.3% male, 61.5% with gross total resection, median Karnofsky performance status 80) were enrolled; 2 tumors had an IDH1 mutation. Predefined dose levels of Lisavanbulin, administered daily concomitantly with RT, were: 4 mg (5 pts), 6 mg (5 pts), 8 mg (7 pts), 12 mg (5 pts), and 15 mg (4 pts). The initial starting dose was 8 mg. Due to grade 4 aseptic meningoencephalitis in the first patient, the dose was decreased to 4 mg. Dose escalation resumed and continued to 15 mg with dose-limiting toxicities of grade 2 confusion and memory impairment observed at 12 mg. Avanbulin exposures increased in a relatively dose-proportional manner with increasing oral dose of Lisavanbulin from 4 to 15 mg. CONCLUSIONS: Lisavanbulin in combination with RT was considered safe up to the highest predefined oral dose level of 15 mg daily.

Neurosurgery
Kim BD, Mondal SK, Kenyon E, Chen M, Mallett CL, **deCarvalho AC**, Medarova Z, and Moore A. Nanoparticle Delivery of an Oligonucleotide Payload in a Glioblastoma Multiforme Animal Model. *J Vis Exp* 2024; Epub ahead of print. (211). PMID: 39400152. Request Article

Precision Health Program, Michigan State University; Department of Biomedical Engineering, College of Engineering, Michigan State University.
Precision Health Program, Michigan State University; Department of Radiology, College of Human Medicine, Michigan State University.
Department of Radiology, College of Human Medicine, Michigan State University; Institute for Quantitative Health Science and Engineering, Michigan State University.
Henry Ford Health.
Transcode Therapeutics Inc.
Precision Health Program, Michigan State University; Department of Radiology, College of Human Medicine, Michigan State University; moorea57@msu.edu.

Glioblastoma multiforme (GBM) is the most common and aggressive form of primary brain malignancy for which there is no cure. The blood-brain barrier is a significant hurdle in the delivery of therapies to GBM. Reported here is an image-guided, iron oxide-based therapeutic delivery nano platform capable of bypassing this physiological barrier by virtue of size and accumulating in the tumor region, delivering its payload. This 25 nm nano platform consists of crosslinked dextran-coated iron oxide nanoparticles labeled with Cy5.5 fluorescent dye and containing antisense oligonucleotide as a payload. The magnetic iron oxide core enables tracking of the nanoparticles through in vivo magnetic resonance imaging, while Cy5.5 dye allows tracking by optical imaging. This report details the monitoring of the accumulation of this nanoparticle platform (termed MN-anti-miR10b) in orthotopically implanted glioblastoma tumors following intravenous injection. In addition, it provides insight into the in vivo delivery of RNA oligonucleotides, a problem that has hampered the translation of RNA therapeutics into the clinic.

Neurosurgery
Rodriguez A, Ahluwalia MS, Bettegowda C, Brem H, Carter BS, Chang S, Das S, Eberhart C, Garzon-Muvdi T, Hadjipanayis CG, Hawkins C, Jacques TS, Khalessi AA, McDermott MW, **Mikkelsen T**, Orr BA, Phillips JJ, **Rosenblum M**, Shelton WJ, Solomon DA, von Deimling A, Woodworth GF, and Rutka JT. Toward standardized brain tumor tissue processing protocols in neuro-oncology: a perspective for gliomas and beyond. *Front Oncol* 2024; 14:1471257. PMID: 39376983. Full Text

Department of Neurosurgery, College of Medicine, University of Arkansas for Medical Sciences, Little Rock, AR, United States.
Department of Medical Oncology, Miami Cancer Institute, Baptist Health South Florida, Miami, FL, United States.
Department of Neurosurgery, Johns Hopkins Hospital, Baltimore, MD, United States.
Department of Neurosurgery, Massachusetts General Hospital and Harvard Medical School, Boston, MA, United States.
Division of Neuro-Oncology, Department of Neurosurgery, University of California San Francisco, San Francisco, CA, United States.
Division of Neurosurgery, St. Michael's Hospital, University of Toronto, Toronto, ON, Canada.
Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD, United States.
Department of Neurosurgery, Emory University, Atlanta, GA, United States.
Department of Neurological Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA, United States.
Division of Pathology, Hospital for Sick Children, Toronto, ON, Canada.
Developmental Biology and Cancer Programme, UCL GOS Institute of Child Health and Department of Histopathology, Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom.
Department of Radiology and Neurosciences, Don and Karen Cohn Chancellor's Endowed Chair of Neurological Surgery, University of California, San Diego, San Diego, CA, United States.
Division of Neurosurgery, Miami Neuroscience Institute, Miami, FL, United States.
Department of Neurosurgery, Hermelin Brain Tumor Center, Henry Ford Health System, Detroit, MI, United States.
Department of Pathology, St. Jude Children's Research Hospital, Memphis, TN, United States.
Department of Neurological Surgery, University of California, San Francisco, San Francisco, CA, United States.
Neuropathology Division, Department of Pathology, University of California, San Francisco, San Francisco, CA, United States.
Department of Neurosurgery, Omics Laboratory, Hermelin Brain Tumor Center, Henry Ford Health System, Detroit, MI, United States.
Division of Neuropathology, Department of Pathology and Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, San Francisco, CA, United States.
Department of Neuropathology, Institute of Pathology, Ruprecht-Karls-University of Heidelberg, Heidelberg, Germany.
Department of Neurosurgery, University of Maryland School of Medicine, Baltimore, MD, United States.
Division of Neurosurgery, Chair Emeritus, Hospital for Sick Children, Toronto, ON, Canada.

Implementation of standardized protocols in neurooncology during the surgical resection of brain tumors is needed to advance the clinical treatment paradigms that use tissue for diagnosis, prognosis, bio-banking, and treatment. Currently recommendations on intraoperative tissue procurement only exist for diffuse gliomas but management of other brain tumor subtypes can also benefit from these protocols. Fresh tissue from surgical resection can now be used for intraoperative diagnostics and functional precision medicine assays. A multidisciplinary neuro-oncology perspective is critical to develop the best avenues for practical standardization. This perspective from the multidisciplinary Oncology Tissue Advisory Board (OTAB) discusses current advances, future directions, and the imperative of adopting standardized protocols for diverse brain tumor entities. There is a growing need for consistent operating room practices to enhance patient care, streamline research efforts, and optimize outcomes.

Obstetrics, Gynecology and Women's Health Services

Ata N, **Zahoor I**, **Hoda N**, Adnan SM, Vijayakumar S, Louis F, **Poisson L**, **Rattan R**, Kumar N, **Cerghet M**, and **Giri S**. Artificial neural network-based prediction of multiple sclerosis using blood-based metabolomics data. *Mult Scler Relat Disord* 2024; 92:105942. PMID: 39471746. Full Text

Department of Neurology, Henry Ford Health, Detroit, MI, 48202, USA.
Faculty of Engineering, Aligarh Muslim University, Aligarh, 202002, India.
IEEE Senior Member, Dallas, TX, 75063, USA.

Public Health Services, Henry Ford Health, Detroit, MI, 48202, USA.
Women's Health Services, Henry Ford Health, Detroit, MI, 48202, USA.
Department of Microbiology, Jaipur National University, Jaipur, 302017, India.
Department of Neurology, Henry Ford Health, Detroit, MI, 48202, USA. Electronic address: sgiri1@hfhs.org.

Multiple sclerosis (MS) remains a challenging neurological condition for diagnosis and management and is often detected in late stages, delaying treatment. Artificial intelligence (AI) is emerging as a promising approach to extracting MS information when applied to different patient datasets. Given the critical role of metabolites in MS profiling, metabolomics data may be an ideal platform for the application of AI to predict disease. In the present study, a machine-learning (ML) approach was used for a detailed analysis of metabolite profiles and related pathways in patients with MS and healthy controls (HC). This approach identified unique alterations in biochemical metabolites and their correlation with disease severity parameters. To enhance the efficiency of using metabolic profiles to determine disease severity or the presence of MS, we trained an AI model on a large volume of blood-based metabolomics datasets. We constructed this model using an artificial neural network (ANN) architecture with perceptrons. Data were divided into training, validation, and testing sets to determine model accuracy. After training, accuracy reached 87 %, sensitivity was 82.5 %, specificity was 89 %, and precision was 77.3 %. Thus, the developed model seems highly robust, generalizable with a wide scope and can handle large amounts of data, which could potentially assist neurologists. However, a large multicenter cohort study is necessary for further validation of large-scale datasets to allow the integration of AI in clinical settings for accurate diagnosis and improved MS management.

Obstetrics, Gynecology and Women's Health Services

Chan-Sui R, Kruger RE, Cho E, Padmanabhan V, **Moravek M**, and Shikanov A. Reproductive Health in Trans and Gender Diverse Patients: Effects of transmasculine gender-affirming hormone therapy on future reproductive capacity: clinical data, animal models, and gaps in knowledge. *Reproduction* 2024; 168(5). PMID: 39190001. Full Text

Department of Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, USA.
Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, Michigan, USA.
Department of Pediatrics, University of Michigan, Ann Arbor, Michigan, USA.
Department of Molecular & Integrative Physiology, University of Michigan, Ann Arbor, Michigan, USA.
Department of Urology, University of Michigan, Ann Arbor, Michigan, USA.
Cellular and Molecular Biology Program, University of Michigan, Ann Arbor, Michigan, USA.
Department of Women's Heath, Henry Ford Health, Rochester Hills, Michigan, USA.

IN BRIEF: Animal studies are needed to inform clinical guidance on the effects of testosterone gender-affirming hormone therapy (T-GAHT) on fertility. This review summarizes current animal models of T-GAHT and identifies gaps in knowledge for future study. ABSTRACT: Testosterone gender affirming hormone therapy (T-GAHT) is frequently used by transgender and gender-diverse individuals assigned female at birth to establish masculinizing characteristics. Although many seek parenthood, particularly as a gestational parent or through surrogacy, the current standard guidance of fertility counseling for individuals on testosterone (T) lacks clarity. At this time, individuals are typically recommended to undergo fertility preservation or stop treatment, associating T-therapy with a loss of fertility; however, there is an absence of consistent information regarding the true fertility potential for transgender and gender-diverse adults and adolescents. This review evaluates recent studies that utilize animal models of T-GAHT to relate to findings from clinical studies, with a more specific focus on fertility. Relevant literature based on murine models in post- and pre-pubertal populations has suggested reversibility of the impacts of T-GAHT, alone or following gonadotropin-releasing hormone agonist (GnRHa), on reproduction. These studies reported changes in clitoral area and ovarian morphology, including corpora lutea, follicle counts, and ovarian weights from T-treated mice. Future studies should aim to determine the impact of the duration of T-treatment and cessation on fertility outcomes, as well as establish animal models that are clinically representative of these outcomes with respect to gender diverse populations.

Obstetrics, Gynecology and Women's Health Services

Datta I, **Zahoor I**, **Ata N**, **Rashid F**, **Cerghet M**, **Rattan R**, **Poisson LM**, and **Giri S**. Utility of an Untargeted Metabolomics Approach Using a 2D GC-GC-MS Platform to Distinguish Relapsing and Progressive Multiple Sclerosis. *Metabolites* 2024; 14(9). PMID: 39330500. Full Text

Department of Public Health Sciences, Henry Ford Health, Detroit, MI 48202, USA.
Department of Neurosurgery, Henry Ford Health, Detroit, MI 48202, USA.
Department of Neurology, Henry Ford Health, Detroit, MI 48202, USA.
Women's Health Services, Henry Ford Health, Detroit, MI 48202, USA.

Multiple sclerosis (MS) is the most common inflammatory neurodegenerative disease of the central nervous system (CNS) in young adults and results in progressive neurological defects. The relapsing-remitting phenotype (RRMS) is the most common disease course in MS, which ultimately progresses to secondary progressive MS (SPMS), while primary progressive MS (PPMS) is a type of MS that worsens gradually over time without remissions. There is a gap in knowledge regarding whether the relapsing form can be distinguished from the progressive course, or healthy subjects (HS) based on an altered serum metabolite profile. In this study, we performed global untargeted metabolomics with the 2D GC-GC-MS platform to identify altered metabolites between RRMS, PPMS, and HS. We profiled 235 metabolites in the serum of patients with RRMS (n = 41), PPMS (n = 31), and HS (n = 91). A comparison of RRMS and HS patients revealed 22 significantly altered metabolites at $p < 0.05$ (false-discovery rate [FDR] = 0.3). The PPMS and HS comparisons revealed 28 altered metabolites at $p < 0.05$ (FDR = 0.2). Pathway analysis using MetaboAnalyst revealed enrichment of four metabolic pathways in both RRMS and PPMS (hypergeometric test $p < 0.05$): (1) galactose metabolism; (2) amino sugar and nucleotide sugar metabolism; (3) phenylalanine, tyrosine, and tryptophan biosynthesis; and (4) aminoacyl-tRNA biosynthesis. The Qiagen IPA enrichment test identified the sulfatase 2 (SULF2) ($p = 0.0033$) and integrin subunit beta 1 binding protein 1 (ITGB1BP1) ($p = 0.0067$) genes as upstream regulators of altered metabolites in the RRMS vs. HS groups. However, in the PPMS vs. HS comparison, valine was enriched in the neurodegeneration of brain cells ($p = 0.05$), and heptadecanoic acid, alpha-ketoisocaproic acid, and glycerol participated in inflammation in the CNS ($p = 0.03$). Overall, our study suggests that RRMS and PPMS may contribute metabolic fingerprints in the form of unique altered metabolites for discriminating MS disease from HS, with the potential for constructing a metabolite panel for progressive autoimmune diseases such as MS.

Obstetrics, Gynecology and Women's Health Services

Sanses TVD, **Kim S**, and Davis DL. Pelvic Floor Muscle Evaluation in Older Women with Urinary Incontinence: A Feasibility Study. *Int Urogynecol J* 2024; Epub ahead of print. PMID: 39373912. Full Text

Department of Obstetrics and Gynecology, Howard University College of Medicine, Howard University Hospital, 2041 Georgia Ave. NW, OBGYN 3C-16, Washington, DC, 20060, USA. tatiana.sanses@howard.edu.
Department of Obstetrics and Gynecology, Henry Ford Hospital, Detroit, MI, USA.
Department of Department of Diagnostic Radiology and Nuclear Medicine, University of Maryland School of Medicine, Baltimore, MD, USA.

INTRODUCTION AND HYPOTHESIS: The objective of this feasibility study was to characterize the pelvic floor muscles (PFMs) in older women with urinary incontinence (UI) via clinical and magnetic resonance imaging (MRI) evaluation. METHODS: This cross-sectional study included women aged ≥ 70 years with symptomatic UI confirmed by a 3-day bladder diary. Clinical evaluation of the PFMs included the Modified Oxford Scale strength assessment (grade 0-5). PFM defects were also characterized as none/normal, minor, and major based on MRI evaluation. Descriptive statistics were utilized. Spearman's correlation with 95% confidence intervals was calculated between PFMs strength, MRI defects, and age. RESULTS: Participants (n = 20) were 76.6 ± 4.7 years. Clinical evaluation demonstrated poor PFM strength in 95% (n = 19) of participants with the following grades: 15% (n = 3) grade 0, 45% (n = 9) grade 1, and 35% (n = 7) grade 2. MRI evaluation demonstrated PFMs= defects in 100% of participants with 45% (n = 9) minor and 55% (n = 11) major defects. The correlation coefficients between PFM strength and MRI defects, MRI defects and age, and PFM strength and age were -0.29 (95% CI -0.64, 0.18; p = 0.22), -0.01

(95% CI = -0.44, 0.44; p = 0.99), and 0.04 (95% CI = -0.41, 0.47; p = 0.88) respectively. CONCLUSION: Clinical and MRI evaluation of PFMs in older women with UI is feasible. Clinical evaluation of PFMs demonstrated poor strength in 95% of women, and MRI revealed PFM defects in all participants.

Obstetrics, Gynecology and Women's Health Services

Wong TY, Adzibolosu NK, Mattei LH, **Speak AC**, Morris RT, and Polan RM. Disparities in contemporary human papilloma virus vaccination uptake among adult women living in the United States: An All of Us Research Program study. *Gynecol Oncol* 2024; 191:100-105. PMID: 39383630. Full Text

Department of Gynecologic Oncology, Barbara Ann Karmanos Cancer Institute, Detroit, MI, USA.
C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, USA.
Department of Obstetrics and Gynecology, Henry Ford Hospital, Detroit, MI, USA.
Department of Gynecologic Oncology, Barbara Ann Karmanos Cancer Institute, Detroit, MI, USA.
Electronic address: rosa.m.polan@gmail.com.

OBJECTIVE: Age-adjusted rates of new cervical cancer diagnoses in the United States have remained stable despite increasing availability of Human Papilloma Virus (HPV) vaccination. As it is well established that sociodemographic factors drive cervical cancer care inequity, we aimed to evaluate their impact on catch-up HPV vaccination rates in adults. METHODS: The All of Us (AoU) Research Program is a longitudinal cohort study sponsored by the National Institutes of Health. All participants ages 18-47 assigned female sex at birth enrolled between May 2018 and April 2023 were included in this analysis. Primary outcome was receipt of HPV vaccination. Bivariable and multivariable tests were used to examine associations. RESULTS: A total of 113,344 participants were identified in the AoU program, with 53 % (n = 60,594) self-identifying as a racial or ethnic minority. Only 3575 participants (3.2 %) were documented as having received HPV vaccination. Median age of vaccination was 26 and participants ages 18-27 were more likely to be vaccinated. Participants without health insurance (OR = 0.32, 95 % CI 0.26-0.40), stable employment (OR = 0.85, 95 % CI 0.79-0.91), and those who reported lower income (OR = 0.87, 95 % CI 0.79-0.97) were significantly less likely to have received HPV vaccination. Participants who described cost as a barrier to healthcare were also less likely to have received HPV vaccination (OR = 0.82, 95 % CI 0.73-0.93). CONCLUSION: Sociodemographic factors including low income, lack of health insurance, and lack of stable employment were all associated with lower likelihood of catch-up HPV vaccination among adult women living in the United States.

Ophthalmology and Eye Care Services

Dossantos J, **Riddering AT**, Ndjonko LCM, Choudhry HS, Gasquet N, Kong X, Ramulu PY, and Kaleem MA. Assessing Eye Clinic Accessibility: A Study Validating and Applying the SiteWise Survey. *Transl Vis Sci Technol* 2024; 13(10):37. PMID: 39470469. Full Text

School of Medicine and Health Sciences, George Washington University, Washington, DC, USA.
Wilmer Eye institute, Johns Hopkins School of Medicine, Baltimore, MD, USA.
Henry Ford Health, Department of Ophthalmology, Detroit, MI, USA.
Department of Biological Sciences, Northwestern University, Evanston, IL, USA.
Rutgers New Jersey Medical School, Newark, NJ, USA.

PURPOSE: To validate the SiteWise survey as a reliable tool for assessing the accessibility of outpatient ophthalmology clinics for visually impaired patients and to compare accessibility between hospital-based and satellite clinics. METHODS: This quality improvement study, conducted from January to December 2023, used the SiteWise survey to assess design features in seven satellite and two hospital-based clinics within the Wilmer Eye Institute network. Independent surveyors evaluated elements such as parking, sidewalks, entrances, and interior areas. Reliability was measured using Krippendorf's alpha, and accessibility scores were compared using generalized estimated equations, analyses of variance, and t tests. RESULTS: The SiteWise survey demonstrated high reliability with a Krippendorf's alpha of 0.99. Hospital-based clinics had higher accessibility scores (mean 78.9%) compared to satellite clinics (mean 71.3%, P < 0.05). Areas such as hallways (mean 89%) and waiting areas (mean 87%) scored highest, whereas parking lots/sidewalks (mean 61%) and stairways (mean 61%) scored lowest, indicating

significant room for improvement in these areas. CONCLUSIONS: The SiteWise tool is reliable and effective in identifying accessibility deficiencies in outpatient ophthalmology clinics. Although indoor areas generally scored well, outdoor and transitional spaces require significant enhancements to improve accessibility for visually impaired patients. TRANSLATIONAL RELEVANCE: This study bridges the gap between basic research and clinical care by providing a validated tool to assess and improve the accessibility of eye care facilities, ensuring they meet the needs of visually impaired patients.

Ophthalmology and Eye Care Services
Kuo BL, Muste JC, Russell MW, **Wu AK**, Valentim CCS, and Singh RP. Evidence for the Hepato-Retinal Axis: A Systematic Review. *Ophthalmic Surg Lasers Imaging Retina* 2024; 55(10):587-596. PMID: 39037358. Request Article

BACKGROUND AND OBJECTIVE: Liver health has been reported to be associated with retinal pathology in various ways. These include deposition of retino-toxins, neovascular drive, and disruption of the blood-retina barrier. Extrahepatic synthesis of implicated molecules and hemodynamic changes in liver dysfunction are also considered. The objective was to review the current evidence for and against a hepato-retinal axis that may guide further areas of preclinical and clinical investigation. METHODS: This was a systematic review. PubMed and Cochrane were queried for English language studies examining the connection between hepatic dysfunction and retinal pathology. RESULTS: Fourteen studies were included and examined out of 604 candidate publications. The studies selected include preclinical studies as well as clinical case series and studies. CONCLUSIONS: Several liver pathologies may be linked to retinal pathology as mediated by hepatically synthesized molecules. The hepato-retinal axis may be present and further, targeted studies of the axis are warranted. [Ophthalmic Surg Lasers Imaging Retina 2024;55:587-596.].

Ophthalmology and Eye Care Services
Trivedi V, You Q, Me R, Lee PS, **Le K**, Tran D, and Lin X. TEMPORARY AMNIOTIC MEMBRANE GRAFT PLACEMENT FOR TREATMENT OF REFRACTORY MACULAR HOLES. *Retin Cases Brief Rep* 2024; Epub ahead of print. PMID: 39454066. Full Text

Kresge Eye Institute/Wayne State University School of Medicine Department of Ophthalmology, Detroit, MI.
Henry Ford Hospital Department of Ophthalmology, Detroit, MI.

PURPOSE: To report two patient cases demonstrating the management of refractory macular holes through the application of temporary thin amniotic membrane grafts, followed by subsequent graft removal upon achieving hole closure. METHODS: Comprehensive chart and literature review was conducted utilizing the PubMed database. RESULTS: We describe two patients who underwent repeat pars plana vitrectomy for treatment of refractory macular holes. In both cases, the epi-retinal placement of a thin amniotic membrane graft (AMG) was done to achieve hole closure. Following a period of retinal stabilization, the amniotic membranes were removed due to the healthy appearance of the outer retinal layers and the ellipsoid zone, ultimately resulting in an improved final visual acuity in both patients. CONCLUSION: This case series demonstrates a new approach of using a temporary AMG to close refractory macular holes. After graft removal, both patients reported enhanced visual acuity and subjective visual improvement, accompanied by the stable closure of macular holes on serial OCT scans.

Orthopedics/Bone and Joint Center
Gaudiani MA, **Castle JP**, **Abbas MJ**, **Myhand MJ**, Sprys-Tellner TJ, **McConnell JT**, **Pratt BA**, and **Lynch TS**. High Return to Play and Variable Salary Impact After Hip Arthroscopy in National Hockey League Players. *Arthrosc Sports Med Rehab* 2024. PMID: Not assigned. Full Text

M.A. Gaudiani, Department of Orthopaedic Surgery, Henry Ford Health, 2799 W Grand Blvd, Detroit, MI, United States

Purpose: To assess the impact of hip arthroscopy for femoroacetabular impingement syndrome (FAIS) on National Hockey League (NHL) player performance, career length, and salary. Methods: Through a

retrospective review, all NHL players who underwent hip arthroscopy for FAIS from 2003 to 2023 were identified from a public online database. A 2:1 matched control cohort was used for comparison. Game use and performance metrics were collected and compared at 1 season and 3 seasons before and after the index season. Game use, performance, and salary were compared between operatively managed players and healthy controls. Performance measures and financial data were recorded. Results: Of the 75 NHL players who underwent hip arthroscopy, 66 (88%) returned to play and were matched to 132 healthy controls. At 1 season after the index season, the operative cohort of NHL players showed a significantly decreased Corsi percentage compared with the year prior (48.4% ± 5.2% vs 50.8% ± 4.2%, P = .024). The control cohort showed an increased Corsi percentage (51.6% ± 5.1% vs 48.9% ± 8.1%, P = .011) and increased Fenwick percentage (51.3% ± 4.6% vs 48.8% ± 8.0%, P = .013) at 1 season after the index season. On financial analysis, by season, injured players in the lower salary group showed lower earnings at season 2 ($1,360,000 ± $910,000 vs $3,950,000 ± $3,300,000; P = .012). However, by cumulative earnings, the total injured cohort showed higher earnings at season 4 ($17,300,000 ± $7,760,000 vs $12,960,000 ± $8,100,000; P = .041), driven by higher cumulative earnings in the highest salary group in seasons 3 and 4. Conclusions: After hip arthroscopy for FAIS, 88% of NHL players successfully return to play. Career length was found to be similar between the injured and matched groups. One season after surgery, NHL players showed worse performance compared with their prior season, but this returned to baseline 3 seasons after surgery. Lower-salary players in the injured group showed decreased salaries at 2 seasons after the index season compared with controls, whereas no differences were found in cumulative salaries. Level of Evidence: Level III, retrospective cohort study.

Orthopedics/Bone and Joint Center

Khlopas A, Wright LT, Hao KA, Reddy A, Beason A, Simcox T, King JJ, Wright JO, Schoch BS, Farmer KW, and Wright TW. The effect of socioeconomic status on clinical outcomes and implant survivorship after primary anatomic and reverse total shoulder arthroplasty. *J Shoulder Elbow Surg* 2024; Epub ahead of print. PMID: 39326656. Full Text

Department of Orthopedic Surgery, Henry Ford Health System, Detroit, MI, USA.
College of Medicine, University of Florida, Gainesville, FL, USA.
Department of Orthopaedic Surgery & Sports Medicine, University of Florida, Gainesville, FL, USA.
Department of Orthopaedic Surgery & Sports Medicine, University of Florida, Gainesville, FL, USA.
Electronic address: kingjj@ortho.ufl.edu.
Department of Orthopaedic Surgery & Sports Medicine, Mayo Clinic, Jacksonville, FL, USA.

BACKGROUND: Low socioeconomic status has been shown to contribute to poor outcomes in patients undergoing joint replacement surgery. However, there is a paucity of studies investigating shoulder arthroplasty. The purpose of this study was to evaluate the effect of socioeconomic status on baseline and postoperative outcome scores and implant survivorship after anatomic and reverse primary total shoulder arthroplasty (TSA). METHODS: A retrospective review of a prospectively collected single-institution database was performed to identify patients who underwent primary TSA. Zip codes were collected and converted to Area Deprivation Index (ADI) scores. We performed a correlation analysis between national ADI scores and preoperative, postoperative, and preoperative to postoperative improvement in range of motion (ROM), shoulder strength, and functional outcome scores in patients with minimum 2-year follow-up. Patients were additionally grouped into groups according to their national ADI. Achievement of the minimum clinically important difference (MCID), substantial clinical benefit (SCB), and patient acceptable symptom state (PASS) and revision-free survivorship were compared between groups. RESULTS: A total of 1148 procedures including 415 anatomic and 733 reverse total shoulder arthroplasties with a mean age of 64 ± 8.2 and 69.9 ± 8.0 years, respectively, were included. The mean follow-up was 6.3 ± 3.6 years for anatomic and 4.9 ± 2.7 years for reverse total shoulder arthroplasty. We identified a weak negative correlation between national ADI and most functional outcome scores and ROM preoperatively (R range 0.07-0.16), postoperatively (R range 0.09-0.14), and preoperative to postoperative improvement (R range 0.01-0.17). Thus, greater area deprivation was weakly associated with poorer function preoperatively, poorer final outcomes, and poorer improvement in outcomes. There was no difference in the proportion of each ADI group achieving MCID, SCB, and PASS in the anatomic total shoulder arthroplasty cohort. However, in the reverse total shoulder arthroplasty cohort, the proportion of patients achieving MCID, SCB, and PASS decreased with greater deprivation. There was no

difference in survivorship between ADI groups. CONCLUSIONS: We found a negative effect of low socioeconomic status on baseline and postoperative patient outcomes and ROM; however, the correlations were relatively weak. Patients that reside in socioeconomically deprived areas have poorer functional outcomes before and after TSA and achieve less improvement from surgery. We should strive to identify modifiable factors to improve the success of TSA in socioeconomically deprived areas.

Orthopedics/Bone and Joint Center

Mansour DT, Court TA, Bishop CR, and Vaidya R. Management of Bleeding Diathesis in Elective and Orthopaedic Trauma: A Review. *J Am Acad Orthop Surg* 2024; Epub ahead of print. PMID: 39378371. Full Text

From the Wayne State University, School of Medicine, Detroit, MI (Mansour, Court, Bishop, Vaidya), Department of Orthopedic Surgery (Mansour, Court, Vaidya), and Department of Hematology and Oncology (Bishop), Detroit Medical Center, Detroit, MI.

There is a general need among orthopaedic surgeons for practical advice on managing patients with bleeding disorders. Appropriate diagnosis and management of these disorders is paramount once discovered before, during, or after the patient's surgical course. Bleeding disorders disrupt the body's ability to control bleeding, commonly through platelet function and blood clotting. Normally, the vessel contracts and retracts once disruption of blood vessels occurs, limiting blood loss. Blood platelets adhere to exposed collagen, aggregate at the site, and obstruct blood loss. Because platelet aggregates are temporary, blood clotting is needed to back up the platelet plug and provide a milieu for the healing process that completes the hemostatic events. Disorders that interfere with any of these events can result in hemorrhage, drainage, or rebleeding. Bleeding disorders are a group of conditions, either hereditary or acquired, marked by abnormal or excessive bleeding and/or bruising. The most effective methods for assessing coagulation disorders include a detailed history and a series of blood tests. Clinical examination findings are notable but may be less specific. If a surgical patient has a bleeding disorder discovered preoperatively, postoperatively, or intraoperatively, treatments exist with medications, surgical management, interventional radiology procedures, and replacement therapy.

Otolaryngology – Head and Neck Surgery

Babatunde OA, Gonzalez K, Osazuwa-Peters N, Adams SA, Hughes Halbert C, Clark F, Nagar A, Obeysekare J, and **Adjei Boakye E**. Adverse Childhood Events Significantly Impact Depression and Mental Distress in Adults with a History of Cancer. *Cancers (Basel)* 2024; 16(19). PMID: 39409912. Full Text

Department of Psychiatry, Prisma Health, Greer, SC 29650, USA.
School of Medicine, California University of Science and Medicine, Colton, CA 92324, USA.
Department of Head and Neck Surgery & Communication Sciences, Duke University School of Medicine, Durham, NC 27710, USA.
Department of Population Health Sciences, Duke University School of Medicine, Durham, NC 27710, USA.
Duke Cancer Institute, Durham, NC 27701, USA.
Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, 915 Greene Street, Columbia, SC 29208, USA.
Biobehavioral Health and Nursing Science Department, College of Nursing, University of South Carolina, 1601 Greene Street, Columbia, SC 29208, USA.
Department of Population and Public Health Sciences, University of Southern California, Los Angeles, CA 90032, USA.
Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA 90089, USA.
School of Medicine-Greenville, University of South Carolina, Greenville, SC 29605, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI 48202, USA.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System, Detroit, MI 48202, USA.
Henry Ford Health + Michigan State University Health Sciences, Detroit, MI 48202, USA.

Department of Epidemiology and Biostatistics, Michigan State University College of Human Medicine, East Lansing, MI 48824, USA.

Objectives: Adverse childhood experiences (ACEs) are linked to a heightened risk of depression. We explored the relationship between ACEs and both depression and mental distress among cancer survivors. Methods: This was a cross-sectional analysis using the 2022 Behavioral Risk Factor Surveillance System database of cancer survivors aged ≥18 (n = 14,132). The primary outcome was self-reported history of depression, and the secondary outcome was mental distress. The exposure variable was the number of ACEs, classified as 0, 1-2, and ≥3. Weighted multivariable logistic regression models assessed the association between the number of ACEs and depression and mental distress while adjusting for covariates. Results: Approximately 22% of respondents reported experiencing ≥3 ACEs. The prevalence of depression was 21.8%, and mental distress was 15.4%. Compared with cancer survivors who had experienced 0 ACEs, those who had experienced ≥3 (aOR = 3.94; 95% CI, 3.04-5.10) or 1-2 (aOR = 1.85; 95% CI, 1.47-2.32) ACEs had a higher likelihood of reporting depression. Compared with cancer survivors who had experienced 0 ACEs, those who had experienced ≥3 (aOR = 0.67; 95% CI, 0.48-0.93) had a lower likelihood of reporting mental distress. Conclusions: This study highlights the impact of ACEs on depression in adulthood among cancer survivors.

Otolaryngology – Head and Neck Surgery
Craig JR. Doing the Rhinologic Work, From Humans to Mice to Robots. *Am J Rhinol Allergy* 2024; 38(6):364-365. PMID: 39438151. Full Text

Division Head, Rhinology and Endoscopic Skull Base Surgery, Henry Ford Health-Michigan State University College of Human Medicine, Detroit, MI, USA Email: JCraig1@hfhs.org.

Otolaryngology – Head and Neck Surgery
Craig JR, and Hopkins C. Sinus Pathophysiology of Odontogenic Sinusitis. *Otolaryngol Clin North Am* 2024; 57(6):1007-1018. PMID: 39428205. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202, USA. Electronic address: jcraig1@hfhs.org.
Department of Otolaryngology-Head and Neck Surgery, Guy's and St Thomas' Hospitals, UK.

Odontogenic sinusitis (ODS) is distinct pathophysiologically from nonodontogenic rhinosinusitis. ODS refers to bacterial sinusitis secondary to infectious dental pathology or procedures. Sinus mucosal inflammation in ODS is severe, mostly lymphocytic, and is driven by Th1 or Th17 inflammation. The sinus's respiratory mucosa maintains its structure and function, contrary to significant epithelial barrier dysfunction seen in some forms of chronic rhinosinusitis. The severe inflammation and infection of ODS help explain certain unique clinical features like foul-smelling drainage, frequent purulence, and papillary edema on nasal endoscopy. Appreciating the unique pathophysiology of ODS facilitates its recognition and selection of optimal interventions.

Otolaryngology – Head and Neck Surgery
Craig JR, Saibene AM, and Felisati G. Sinusitis Management in Odontogenic Sinusitis. *Otolaryngol Clin North Am* 2024; 57(6):1157-1171. PMID: 39428206. Full Text

Rhinology, Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, 2799 West Grand Boulevard, Detroit, MI 48202, USA. Electronic address: jcraig1@hfhs.org.
Otolaryngology Unit, Department of Health Sciences, San Paolo and Carlo Hospital, University of Milan, Milan, Italy.

For odontogenic sinusitis (ODS), appropriately treating the infectious dental pathology and sinusitis leads to disease resolution in greater than 90% of cases. Importantly, managing the sinusitis of ODS is distinct from non-odontogenic rhinosinusitis. The main factors affecting ODS management decision-making include whether patients present with complicated ODS (extrasinus infectious spread), whether they have treatable dental pathology, and whether they have high dental versus sinusitis symptom burdens. This

article will provide an evidence-based approach to the multidisciplinary management necessary to manage the purulent sinusitis characteristic of ODS.

Otolaryngology – Head and Neck Surgery
Craig JR, Tataryn RW, and Saibene AM. The Future of Odontogenic Sinusitis. *Otolaryngol Clin North Am* 2024; 57(6):1173-1181. PMID: 39428207. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202, USA. Electronic address: jcraig1@hfhs.org.
Private Practice Endodontics, Spokane, WA, USA; Department of Endodontics, Loma Linda University, Loma Linda, CA, USA.
Otolaryngology Unit, Department of Health Sciences, Santi Paolo and Carlo Hospital, Università degli Studi di Milano, Milan, Italy. Electronic address: https://twitter.com/ent_ams.

This article discusses the exciting future of odontogenic sinusitis (ODS) in the context of recent advancements in ODS understanding. It emphasizes the importance of integrating ODS into the broader framework of sinonasal diseases and highlights the need for multidisciplinary collaboration among otolaryngologists and dental specialists to optimize clinical outcomes, research, and education. Key challenges include refining dental and sinus pathophysiologic understandings, establishing widely accepted diagnostic criteria, and optimizing multidisciplinary treatment pathways. The article provides also some tips for how to develop interdisciplinary networks both to improve clinical care and research endeavors.

Otolaryngology – Head and Neck Surgery
Di Ponio AP, **Samad MN**, Pellizzari R, Mackie H, **Deeb RH**, and **Craig JR**. Outcomes after Functional Nasal Surgery in Patients with Versus without Rhinitis Medicamentosa. *Laryngoscope* 2024; Epub ahead of print. PMID: 39387236. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, Detroit, Michigan, U.S.A. Michigan State University College of Human Medicine, East Lansing, Michigan, U.S.A.

OBJECTIVE: Topical nasal decongestants (TNDs) are used to reduce nasal soft tissue edema and obstruction. However, after frequent TND use, patients can develop rhinitis medicamentosa (RM) with rebound nasal edema and obstruction. Management of RM has centered largely on TND cessation ± intranasal corticosteroids. The purpose of this study was to compare nasal obstruction outcomes following nasal obstruction surgery in patients with versus without RM. METHODS: A retrospective case-control study was conducted with adult patients who underwent bilateral inferior turbinate reduction (ITR) with or without septoplasty and nasal valve repair. Patients with versus without RM were assessed. RM was defined as at least daily TND use for ≥4 weeks. Preoperative and postoperative Nasal Obstruction Symptom Evaluation (NOSE) scores, and long-term TND cessation rates were collected. NOSE score changes were compared between patients with versus without RM. RESULTS: Of the 36 RM patients, mean age was 52.0 years, and 63.9% were male. Of 116 non-RM patients, mean age was 41.6 years, and 46.6% were male. Postoperative NOSE scores were collected at a mean 972.1 days postoperatively for RM patients, and 565.0 days for non-RM patients. Mean NOSE score reductions were - 9.8 for RM and - 8.6 for non-RM patients, both of which were significant ($p < 0.0001$). NOSE score reductions were not significantly between the two groups ($p = 0.2438$). Long-term TND cessation was maintained in 86.1% of RM patients. CONCLUSION: Patients with and without RM achieved similar long-term significant NOSE score reductions following nasal obstruction surgery, and 86.1% of RM patients maintained long-term TND cessation. LEVEL OF EVIDENCE: Level 3 evidence Laryngoscope, 2024.

Otolaryngology – Head and Neck Surgery
Eide JG, **Mason W**, **Mackie H**, **Cook B**, **Ray A**, **Asmaro K**, **Robin A**, **Rock J**, and **Craig JR**. Diagnostic Accuracy of Beta-2 Transferrin Gel Electrophoresis for Detecting Cerebrospinal Fluid Rhinorrhea. *Laryngoscope* 2024; Epub ahead of print. PMID: 39400322. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, Detroit, Michigan, U.S.A.
Department of Pathology, Henry Ford Health, Detroit, Michigan, U.S.A.
Department of Neurosurgery, Henry Ford Health, Detroit, Michigan, U.S.A.

OBJECTIVE: Unilateral thin clear rhinorrhea (UTCR) may represent a variety of pathologies including cerebrospinal fluid (CSF) rhinorrhea. Beta-2 transferrin (B2Tf) gel electrophoresis (GE) has become the preferred testing modality due to reportedly high sensitivity (87%-100%) and specificity (71%-100%). However, there have been relatively few studies assessing its diagnostic accuracy. The purpose of this single-institution study was to determine the accuracy of B2Tf GE in detecting CSF rhinorrhea. METHODS: A single-center retrospective review was conducted from 2016 and 2024 for all patients who presented with UTCR and underwent B2Tf GE. Institutional review board approval was obtained. The gold standard for diagnostic confirmation of true and false positives (TP, FP) as well as false negatives (FN) was endoscopic exploration. The gold standard for true negative (TN) was response to medical therapy. RESULTS: A total of 105 patients underwent 149 B2Tf GE tests. 40 (38.1%) patients were diagnosed with CSF rhinorrhea. Of the 149 B2-Tf GE tests, there were 51 TPs, 72 TNs, 20 FPs, and 6 FNs yielding 89.5% sensitivity, 78.3% specificity, 71.8% positive predictive value, and 92.3% negative predictive value, respectively. Of the false results the most common causes for error were purulent sinusitis (n = 6, 23.1%), possible mucous contamination from nose-blowing during collection (n = 3, 11.5%), patient collection error (n = 3, 11.5%), and blood contamination (n = 1, 3.8%). CONCLUSION: Although these single-institutional data demonstrate test accuracy within ranges previously reported in the literature, they also demonstrate diagnostic limitations. Future studies should explore reasons for erroneous B2Tf GE results and how these may change clinical decision-making. LEVEL OF EVIDENCE: IV Laryngoscope, 2024.

Otolaryngology – Head and Neck Surgery
Fridman I, **Neslund-Dudas C**, Barrow LCJ, Dunn MR, Jones R, Kinlaw AC, Smith AB, Stein JN, **Tam S**, Wood WA, and Lafata JE. Telephone Survey-Reported Perceptions of Telehealth Visits Among Black and Non-Black Patients Diagnosed With Cancer. *JCO Oncol Pract* 2024; Op2400307. Epub ahead of print. PMID: 39475625. Full Text

University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC.
Department of Public Health Sciences, Henry Ford Health, Detroit, MI.
Department of Epidemiology and Biostatistics, College of Human Medicine, Michigan State University, East Lansing, MI.
University of North Carolina Eshelman School of Pharmacy, Chapel Hill, NC.
Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.
Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC.
Patient and Family Advisory Council, UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC.
Cecil G. Sheps Center for Health Services Research, University of North Carolina at Chapel Hill, Chapel Hill, NC.
Department of Urology, University of North Carolina School of Medicine, Chapel Hill, NC.
Division of Oncology, University of North Carolina School of Medicine, Chapel Hill, NC.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, Detroit, MI.
Department of Surgery, College of Human Medicine, Michigan State University, East Lansing, MI.
Division of Hematology-Oncology, University of North Carolina School of Medicine, Chapel Hill, NC.

PURPOSE: Empirical evidence underscores both benefits of telehealth visits and persistent disparities in use for Black adults. Guided by the Technology Acceptance Model, we evaluated perceptions regarding telehealth visits among Black and Non-Black adults receiving cancer care from two academic health systems. METHODS: Between April 2022 and October 2023, a survey was conducted among adult patients treated for cancer in the past 3 years. Survey recruitment was stratified by visit type (telehealth or in-person) and race. Before a scheduled oncology visit, respondents completed a telephone survey to assess their perceptions of usefulness, ease of use, and attitudes toward telehealth visits. Frequency differences were estimated using chi-square tests, and prevalence differences using logistic regression.

RESULTS: The survey was completed by 773 respondents (42% Black) with a 15% response rate. Black respondents were younger and less likely to report male sex, being married, having a college education, comfortable income, or confidence in medical and e-literacy. Compared with Non-Black respondents, Black respondents perceived telehealth visits as less useful for determining health needs (37% v 48%) and asking questions (9% v 15%). They thought that telehealth visits were less easy with regard to understanding their health care provider (14% v 21%) and the ability to connect (23% v 30%). Black respondents expressed more concern about internet access (26% v 15%), access to electronic devices (17% v 9%), and finding assistance for connecting (24% v 12%). They also found telehealth visits to be less private (19% v 34%). CONCLUSION: Racial differences in telehealth ease of use and usefulness perceptions highlight the need for oncology practices to couple connectivity support with effective communication strategies to avoid disparities in oncology telehealth services.

Otolaryngology – Head and Neck Surgery

Prince ADP, **Oslin K**, Forner D, Smith JD, Hershey E, Chionis L, Allevato M, Prince MEP, and Chinn SB. Patient-Initiated Communication After Parotidectomy. *Laryngoscope* 2024; Epub ahead of print. PMID: 39415645. Full Text

Department of Otolaryngology Head and Neck Surgery, University of Michigan Health System, Ann Arbor, Michigan, U.S.A.
Now at Department of Otolaryngology Head and Neck Surgery, Henry Ford Hospital, Detroit, Michigan, U.S.A.
Now at Dartmouth Hitchcock Medical Center, Section of Otolaryngology Head and Neck Surgery, Lebanon, New Hampshire, U.S.A.
Now at Kaiser Permanente Oakland Medical Center, Oakland, California, U.S.A.

OBJECTIVES: We sought to study the incidence of patient-initiated communication after parotidectomy, identify patient and surgical factors associated with patient-initiated communication, and evaluate trends and possible areas for improvement. METHODS: A retrospective cohort study of patients who underwent parotidectomy without combined procedures from 2018 to 2022 in a single tertiary-care institution was performed. We reviewed all patient communications documented within the electronic medical record within 30 days of discharge. We categorized patient communications as requiring an action by the surgeon, instruction by support staff, or reassurance. RESULTS: A total of 363 patients were included. Most patients were women (55.4%), Caucasian (78.8%), and had an average age of 56 years ± 16. We found 123 (33.9%) patients initiated postoperative communications. Swelling (47.2%) was the most common concern followed by wound concerns (15.4%). Switching from planned inpatient to outpatient surgery increased (OR = 2.635; 95% CI = 1.200-6.146, p = 0.026) propensity for postoperative communication. We found 31 (25.2%) postoperative communications required an action by the surgeon, 40 (32.5%) required instruction by the support staff, and the other 52 (42.3%) required reassurance or clarification. Multivariate analysis showed swelling (OR = 6.5, CI = 2.2-19, p < 0.001), male sex (OR = 3.27, CI = 1.127-9.459, p = 0.029), previous smoking (OR = 3.468, CI = 1.181-10.185, p = 0.024), and cancer (OR = 6.862, CI = 1.757-26.804, p = 0.006) were predictive of requiring an action by the surgeon. CONCLUSIONS: This is the first study to evaluate patient-initiated communication after parotidectomy and found it occurred 33.4% of the time. We found significant opportunities to improve perioperative care, enhance patient satisfaction, and reduce the overall burden on medical personnel. LEVEL OF EVIDENCE: Level IV Laryngoscope, 2024.

Pathology and Laboratory Medicine

Abbas O, and **Al-Obaidy KI**. TFE3-Rearranged PEComa-like Neoplasm of the Kidney: A Case Report and Letter to the Editor. *Am J Surg Pathol* 2024; Epub ahead of print. PMID: 39371039. Full Text

Department of Pathology and Laboratory Medicine Henry Ford Health, Detroit.
Department of Medicine, College of Human Medicine, Michigan State University, East Lansing, MI
Conflicts of Interest and Source of Funding: The authors have disclosed that they have no significant relationships with, or financial interest in, any commercial companies pertaining to this article.

Pathology and Laboratory Medicine

Eide JG, **Mason W**, **Mackie H**, **Cook B**, **Ray A**, **Asmaro K**, **Robin A**, **Rock J**, and **Craig JR**. Diagnostic Accuracy of Beta-2 Transferrin Gel Electrophoresis for Detecting Cerebrospinal Fluid Rhinorrhea. *Laryngoscope* 2024; Epub ahead of print. PMID: 39400322. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, Detroit, Michigan, U.S.A.
Department of Pathology, Henry Ford Health, Detroit, Michigan, U.S.A.
Department of Neurosurgery, Henry Ford Health, Detroit, Michigan, U.S.A.

OBJECTIVE: Unilateral thin clear rhinorrhea (UTCR) may represent a variety of pathologies including cerebrospinal fluid (CSF) rhinorrhea. Beta-2 transferrin (B2Tf) gel electrophoresis (GE) has become the preferred testing modality due to reportedly high sensitivity (87%-100%) and specificity (71%-100%). However, there have been relatively few studies assessing its diagnostic accuracy. The purpose of this single-institution study was to determine the accuracy of B2Tf GE in detecting CSF rhinorrhea. METHODS: A single-center retrospective review was conducted from 2016 and 2024 for all patients who presented with UTCR and underwent B2Tf GE. Institutional review board approval was obtained. The gold standard for diagnostic confirmation of true and false positives (TP, FP) as well as false negatives (FN) was endoscopic exploration. The gold standard for true negative (TN) was response to medical therapy. RESULTS: A total of 105 patients underwent 149 B2Tf GE tests. 40 (38.1%) patients were diagnosed with CSF rhinorrhea. Of the 149 B2-Tf GE tests, there were 51 TPs, 72 TNs, 20 FPs, and 6 FNs yielding 89.5% sensitivity, 78.3% specificity, 71.8% positive predictive value, and 92.3% negative predictive value, respectively. Of the false results the most common causes for error were purulent sinusitis (n = 6, 23.1%), possible mucous contamination from nose-blowing during collection (n = 3, 11.5%), patient collection error (n = 3, 11.5%), and blood contamination (n = 1, 3.8%). CONCLUSION: Although these single-institutional data demonstrate test accuracy within ranges previously reported in the literature, they also demonstrate diagnostic limitations. Future studies should explore reasons for erroneous B2Tf GE results and how these may change clinical decision-making. LEVEL OF EVIDENCE: IV Laryngoscope, 2024.

Pathology and Laboratory Medicine

Kadiyala D, **Sly M**, **Montecalvo J**, and **Vummidi D**. Benign Metastasizing Leiomyoma in a Patient With No Known History of Uterine Leiomyomas. *Cureus* 2024; 16(8):e68314. PMID: 39350828. Full Text

Department of Radiology, Wayne State University School of Medicine, Detroit, USA.
Department of Radiology, Henry Ford Health System, Detroit, USA.
Department of Pathology, Henry Ford Health System, Detroit, USA.

Benign metastasizing leiomyoma (BML) is a rare medical condition characterized by metastasis of fibroid tissue from uterine leiomyomas to other areas of the body, most commonly the lungs. While BML is mostly prevalent in women with a prior history of uterine leiomyomas who underwent surgical intervention, this case report explores the case of a 50-year-old female who was diagnosed with pulmonary benign metastasizing leiomyoma (PBML) with no prior history of confirmed leiomyomas. After initially presenting with worsening cough and congestion, chest radiograph and computed tomography revealed multiple bilateral pulmonary nodules, initially raising concerns for malignancy. Further, a workup with bronchoscopy with fine needle aspiration and pulmonary lesion biopsy revealed the presence of smooth muscle tissue suggestive of PBML. Subsequent uterine ultrasonography revealed a 3-cm intramural uterine fibroid, supporting the diagnosis. This case highlights the diagnostic challenge posed by PBML due to its asymptomatic manifestation and radiological similarity with other serious conditions such as malignancy and sarcoidosis. The case further highlights the importance of recognizing typical radiological features of PBML and the necessity of histological examination for accurate diagnosis. Finally, the critical role of a multidisciplinary approach in managing such rare conditions and the need for individualized treatment are also explored.

Pathology and Laboratory Medicine

Mulbah JL, **Kenney RM**, **Tibbetts RJ**, **Shallal AB**, and **Veve MP**. Ceftriaxone versus cefepime or carbapenems for definitive treatment of low-risk AmpC-Harboring Enterobacterales bloodstream infections in hospitalized adults: A retrospective cohort study. *Diagn Microbiol Infect Dis* 2024; 111(1):116557. PMID: 39427451. Full Text

Department of Pharmacy, Henry Ford Hospital, Detroit, MI, USA.
Department of Microbiology, Henry Ford Hospital, Detroit, MI, USA.
Department of Infectious Diseases, Henry Ford Hospital, Detroit, MI, USA.
Department of Pharmacy, Henry Ford Hospital, Detroit, MI, USA; Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI, USA. Electronic address: mpveve@wayne.edu.

OBJECTIVE: To compare outcomes of ceftriaxone to AmpC-stable therapies in patients with bacteremia caused by low-risk AmpC harboring Enterobacterales. METHODS: IRB-approved, retrospective cohort of hospitalized patients ≥18 years old with Serratia marcescens, Morganella morganii, or Providencia spp. bacteremia from 1/1/2017-2/28/2024. Patients were compared by definitive therapy with ceftriaxone vs AmpC-stable therapy (cefepime, carbapenem). The primary endpoint was 30-day all-cause mortality; secondary endpoints were clinical failure and development of ceftriaxone resistance. RESULTS: 163 patients were included; 33.1 % received ceftriaxone, 66.9 % AmpC-stable therapies. 30-day all-cause mortality was 9.3 % ceftriaxone vs 10.1 % AmpC stable patients (P = 0.87); ceftriaxone definitive therapy was not associated with 30-day all-cause mortality (adjOR, 0.79; 95 %CI, 0.23-2.3). There were no differences in clinical failure (9.3 % vs 21.1 %, P = 0.059) or relapsing infection (5.6 % vs 9.3 %, P = 0.55) between ceftriaxone and AmpC-stable treated patients. CONCLUSIONS: Patients treated with definitive ceftriaxone for low-risk AmpC Enterobacterales bacteremia had similar outcomes to AmpC stable therapies.

Pathology and Laboratory Medicine

Thoidingjam S, **Sriramulu S**, **Hassan O**, **Brown SL**, **Siddiqui F**, **Movsas B**, **Gadgeel S**, and **Nyati S**. BUB1 Inhibition Overcomes Radio- and Chemoradiation Resistance in Lung Cancer. *Cancers (Basel)* 2024; 16(19). PMID: 39409911. Full Text

Department of Radiation Oncology, Henry Ford Health, Detroit, MI 48202, USA.
Department of Surgical Pathology, Henry Ford Cancer Institute, Henry Ford Health, Detroit, MI 48202, USA.
Henry Ford Health + Michigan State University Health Sciences, Detroit, MI 48202, USA.
Department of Radiology, Michigan State University, East Lansing, MI 48824, USA.
Division of Hematology/Oncology, Department of Medicine, Henry Ford Health, Detroit, MI 48202, USA.

Background: Despite advances in targeted therapies and immunotherapies, traditional treatments like microtubule stabilizers (paclitaxel, docetaxel), DNA-intercalating platinum drugs (cisplatin), and radiation therapy remain essential for managing locally advanced and metastatic lung cancer. Identifying novel molecular targets could enhance the efficacy of these treatments. Hypothesis: We hypothesize that BUB1 (Ser/Thr kinase) is overexpressed in lung cancers and its inhibition will sensitize lung cancers to chemoradiation. Methods: BUB1 inhibitor (BAY1816032) was combined with cisplatin, paclitaxel, a PARP inhibitor olaparib, and radiation in cell proliferation and radiation-sensitization assays. Biochemical and molecular assays evaluated the impact on DNA damage signaling and cell death. Results: Immunostaining of lung tumor microarrays (TMAs) confirmed higher BUB1 expression in non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) compared to normal tissues. In NSCLC, BUB1 overexpression correlated directly with the expression of TP53 mutations and poorer overall survival in NSCLC and SCLC patients. BAY1816032 synergistically sensitized lung cancer cell lines to paclitaxel and olaparib and enhanced cell killing by radiation in both NSCLC and SCLC. Molecular analysis indicated a shift towards pro-apoptotic and anti-proliferative states, evidenced by altered BAX, BCL2, PCNA, and Caspases-9 and -3 expressions. Conclusions: Elevated BUB1 expression is associated with poorer survival in lung cancer. Inhibiting BUB1 sensitizes NSCLC and SCLC to chemotherapies (cisplatin, paclitaxel), targeted therapy (olaparib), and radiation. Furthermore, we present the novel finding that

BUB1 inhibition sensitized both NSCLC and SCLC to radiotherapy and chemoradiation. Our results demonstrate BUB1 inhibition as a promising strategy to sensitize lung cancers to radiation and chemoradiation therapies.

Pathology and Laboratory Medicine
Tran PTC, Din NU, **Xu Z**, and **Ahsan BU**. Clinicopathological characteristics of extranodal Rosai-Dorfman disease: A retrospective case series of 25 patients. *Ann Diagn Pathol* 2024; 73:152377. PMID: 39366206. Full Text

College of Osteopathic Medicine of the Pacific, Western University of Health Sciences, Pomona, CA, USA.
Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi, Pakistan.
Department of Pathology, Henry Ford Health, Detroit, MI, USA.
Department of Pathology, Henry Ford Health, Detroit, MI, USA; Department of Medicine, Michigan State University College of Human Medicine, Detroit, MI, USA. Electronic address: bahsan1@hfhs.org.

Rosai-Dorfman disease (RDD) is a rare non-Langerhans cell histiocytosis, classically affecting the lymph nodes. Even rarer extranodal disease is diagnostically challenging due to overlapping histologic features with other entities and lack of a universally agreed set of biomarkers. Cyclin D1 immunohistochemistry (IHC) may serve as a useful adjunct in diagnosing extranodal RDD. We present a retrospective case series of patients diagnosed with extranodal RDD between January 2013 and December 2023. IHC staining for cyclin D1 was performed on archived tissue samples. Baseline IHC results for biomarkers supporting the RDD diagnosis were recorded along with patient demographic characteristics, clinical features, and disease outcomes. A total of 25 patients with extranodal RDD were included: 21 women (84 %) and 4 men (16 %). The mean age at diagnosis was 42.6 years. Cutaneous and deep tissue involvement was seen in 5 (20 %) and 20 (80 %) patients, respectively. 11 patients (44 %) had disease localized to the trunk and extremities, and 13 had disease in the head and neck region (52 %), of which 5 occurred in the nose and paranasal tissues. Available follow-up data showed most patients fully recovered (n = 11; 78.6 %). However, 1 patient had disease recurrence, 1 developed blindness, and 1 developed deafness. Cyclin D1 IHC was positive in all samples (100 %), consistent with previous studies. The clinicopathologic findings in this study highlight the spectrum of potential disease sites, possible morbid outcomes related to disease site, and the diagnostic utility of cyclin D1 IHC.

Pathology and Laboratory Medicine
Vellaichamy G, Poulik J, **Palanisamy N**, **Kis O**, **Fang X**, **Al-Obaidy KI**, **Shwayder TA**, and **Friedman BJ**. Spitz-Type Proliferative Nodules Arising Within a Large Congenital Melanocytic Nevus Harboring a Novel LMNA-RAF1 Fusion. *J Cutan Pathol* 2024; Epub ahead of print. PMID: 39462150. Full Text

Department of Dermatology, Henry Ford Health, Detroit, Michigan, USA.
Detroit Medical Center, Children's Hospital of Michigan, Detroit, Michigan, USA.
Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, Michigan, USA.
Department of Pathology & Laboratory Medicine, Henry Ford Health, Detroit, Michigan, USA.

Pathology and Laboratory Medicine
Xu Z, Aryal SC, McHugh K, **Theisen BK**, and **Yuan L**. Fine Needle Aspiration Cytology of Pancreatoblastoma in Adult/Adolescent Patients, One With Histology Mimicking NUT Carcinoma. *Diagn Cytopathol* 2024; Epub ahead of print. PMID: 39391903. Full Text

Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Pathology and Laboratory Medicine, Mayo Clinic Rochester, Rochester, Minnesota, USA.
Department of Pathology and Laboratory Medicine, Mayo Clinic Arizona, Scottsdale, Arizona, USA.

Pancreatoblastoma is a rare malignant neoplasm. Cytologic diagnosis is challenging due to the tumor's heterogeneity and requirement of the presence of squamoid nests. Commonly affects children, but the tumor rarely is seen in adult patients. We are reporting three cases from two patients. First patient was a 38-year-old male with a mass in the pancreatic body and numerous hepatic lesions. Fine-needle

aspiration (FNA) of the pancreas showed a biphasic malignancy, predominantly composed of a primitive component with intermingled squamoid nests. Subsequent Liver FNA from the same patient showed a similar biphasic malignancy. NUT carcinoma was the top differential and was ruled out by molecular testing. Second patient was a 24-year-old female with a history of pancreatoblastoma related to Gardner's syndrome initially diagnosed in 2015 at age 17, status post distal pancreatectomy and chemotherapy. Celiac lymph node FNA in 2021 showed few cohesive clusters of atypical epithelioid cells, which were highlighted by beta-catenin. Lastly, the literature was reviewed; differential diagnosis and ancillary testing were discussed.

Pharmacy

Campillo Terrazas W, **Kenney RM**, **Argyris A**, **Shallal AB**, and **Veve MP**. Judicious Use of Benzathine Penicillin G in Response to a Medication Alert During a Critical Drug Shortage. *J Pharm Technol* 2024. PMID: Not assigned. Full Text

M.P. Veve, Department of Pharmacy, Henry Ford Hospital, Detroit, MI, United States

Purpose: To evaluate judicious antibiotic prescribing of benzathine penicillin G (BPG) after implementation of an electronic health record-based medication shortage alert during a critical drug shortage. Methods: This was an institutional review board–approved retrospective cohort study of patients aged ≥3 months who received BPG between May 9, 2023, and February 28, 2024. The study included inpatient and outpatient visits after implementing a BPG medication shortage alert; patients with severe penicillin allergy, neurosyphilis, or congenital syphilis were excluded. Judicious BPG use was defined as use in patients diagnosed with primary, secondary, or latent syphilis or if they were prescribed a BPG alternative in response to the medication shortage alert; nonjudicious use included BPG for alternative diagnoses. Social determinants of health were assessed as exposure variables of interest. A separate cohort of syphilis patients receiving BPG or alternative therapy (i.e., doxycycline) was described. Results: A total of 453 patients were included. Most patients were non-Hispanic Black (n = 273, 60%) men (n = 272, 60%) with a median (interquartile range) age of 32 (22–44) years. Of these, 318 (70%) received judicious BPG, whereas 135 (30%) received nonjudicious BPG. The most nonjudicious diagnosis was streptococcal pharyngitis (n = 128, 95%). Variables associated with judicious use included age >32 years (adjusted odds ratio [adjOR], 2.273; 95% CI, 1.488–3.472), male sex (adjOR, 1.835; 95% CI, 1.206–2.792), and black race (adjOR, 1.847; 95% CI, 1.212–2.815). Among a cohort of 128 syphilis patients who received BPG (n = 64, 50%) or doxycycline (n = 64, 50%), those who received doxycycline were more likely be uninsured (35 [54.7%] vs 43 [67.2%]; P =.15) and receive outpatient treatment (3 [4.7%] vs 12 [18.7%]; P =.13). Conclusion: Despite implementing an electronic health record drug shortage alert, 30% of BPG use was nonjudicious and mostly for pharyngitis.

Pharmacy

Imlay H, **Greenlee SB**, Tritle BJ, Fino NF, and Spivak ES. In-person prospective audit and feedback on an oncology ward: development of an immunocompromised antimicrobial stewardship program. *Antimicrob Steward Healthc Epidemiol* 2024; 4(1):e173. PMID: 39430797. Full Text

Division of Infectious Diseases, Department of Internal Medicine, University of Utah Health, Salt Lake City, UT, USA.
Department of Pharmacy, University of Utah Health, Salt Lake City, UT, USA.
Department of Pharmacy, Henry Ford Macomb Hospital, Clinton Twp., MI, USA.
Division of Epidemiology, Department of Internal Medicine, University of Utah, Salt Lake City, UT, USA.

OBJECTIVE: To describe clinical syndromes, opportunities for antimicrobial optimization, and acceptance of recommendations made by an immunocompromised antimicrobial stewardship program performing in-person prospective audit and feedback (IPPAF) on inpatient oncology services. DESIGN: Retrospective cohort study. SETTING: Three inpatient oncology services including patients with solid tumor malignancies in an academic cancer center. PATIENTS: Hospitalized adults with oncologic malignancies receive antimicrobials for any indication. METHODS: We reviewed all patients receiving antimicrobials on inpatient oncology services who were included in IPPAF and prospectively documented clinical syndromes represented, most common recommendations, and acceptance rate. We also examined the

standardized antimicrobial administration ratio (SAAR) for oncology units over the study period. RESULTS: Over 34 weeks, we performed 154 interventions for 138 patients. Metastatic malignancy was common (52%) and 90-day mortality was high (43%). Diagnostic uncertainty was common (33/154, 21%), as were cases of intra-abdominal pathology (30/154, 19%), pneumonia (25/154, 16%), and urinary tract infection (12/154, 8%). The most common recommendations were changes in duration (63/154, 41%) and stopping antimicrobials for syndromes determined to be noninfectious (29/154, 19%). Acceptance of interventions was high (77% overall) and several SAARs on the primary oncology unit significantly decreased after starting IPPAF. CONCLUSIONS: We identified numerous opportunities for antimicrobial optimization among solid tumor malignancy patients. Most clinical syndromes were ones also encountered frequently in non-oncology populations, but several were unique and represented opportunities for targeted education.

Pharmacy

Malviya M, **Kale-Pradhan P**, **Coyle M**, **Giuliano C**, and **Johnson LB**. Clinical and Drug Resistance Characteristics of Providencia Infections. *Microorganisms* 2024; 12(10). PMID: 39458394. Full Text

Division of Infectious Diseases, Henry Ford St. John Hospital, 22101 Morsoss Road, Detroit, MI 48236, USA.
Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI 48201, USA.
Henry Ford St. John Hospital, Detroit, MI 48236, USA.
Division of Infectious Diseases, Department of Internal Medicine, Henry Ford St. John Hospital, 22101 Moross Road, Detroit, MI 48236, USA.
Infection Prevention and Antimicrobial Stewardship, Ascension Michigan 22101 Morsoss Road, Detroit, MI 48236, USA.
School of Medicine, Wayne State University, 540 E Canfield St, Detroit, MI 48201, USA.

Background:Providencia is a G ram-negative bacillus that most frequently colonizes the urinary tract and is often resistant to many antimicrobials. This study aimed to evaluate the resistance patterns of Providencia spp. and clinical outcomes due to the paucity of data. Methods: A multi-center, descriptive, retrospective chart review of adult patients with Providencia spp. infections was conducted from 1 January 2020 to 31 May 2022. The primary outcome was to describe the drug resistance patterns of Providencia spp. isolates. This study's secondary outcome was to evaluate the clinical outcomes of patients with Providencia spp. infections. Results: Of the 312 patients screened, 244 were excluded primarily for polymicrobial infections. The mean age was 70 years, and 39 (56.5%) were males. Of the 68 included cases, 46 (67.6%) were P. stuartii, 20 (29.4%) were P. rettgeri, and 2 (2.9%) were P. alcalifaciens. The most common infections were bacteremia 38 (55.8%), followed by 27 (39.7%) urinary tract infections and 3 (4.4%) wound infections. In this study, 45 patients (65.2%) had urinary catheters. The primary antibiotics used for treatment consisted of ceftriaxone (25 (36.2%)), cefepime (20 (29%)), and meropenem (10 (14.5%)). Only 5 of 68 (7.2%) cases were multidrug- resistant and required meropenem. In total, 19 patients (27.1%) died during their admission, but none were related to Providencia infections. A total of 10 of the 68 patients (14.5%) were readmitted within 30 days for reasons unrelated to the progression or recurrence of Providencia infections. Conclusions:Providencia bacteremia is predominantly seen in elderly patients. Third- generation cephalosporins remain an appropriate choice of antibiotics for Providencia spp. Providencia stuartii was the only species with multidrug resistance.

Pharmacy

Momper JD, Venkataramanan R, **Jantz AS**, Cibrik DM, Birdwell K, Nguyen T, Masters BM, and Patel SJ. Evaluation of Effective Half-Life and Its Impact on Time to Steady State for Oral MeltDose Tacrolimus (LCPT) in De Novo Kidney Transplant Recipients. *Ther Drug Monit* 2024; Epub ahead of print. PMID: 39446891. Full Text

Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego, La Jolla, California.
School of Pharmacy and Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania.
Department of Pharmacy, Henry Ford Health, Detroit, Michigan.

Department of Medicine, University of Kansas Health System, Kansas City, Kansas.
Division of Nephrology, Vanderbilt University Medical Center, Nashville, Tennessee; and.
Medical Affairs, Veloxis Pharmaceuticals, Inc., Cary, North Carolina.

BACKGROUND: For extended-release drug formulations, effective half-life (t1/2eff) is a relevant pharmacokinetic parameter to inform dosing strategies and time to reach steady state. Tacrolimus, an immunosuppressant commonly used for the prophylaxis of organ rejection in transplant patients, is available as both immediate- and extended-release formulations. To the best of our knowledge, the t1/2eff of tacrolimus from these different formulations has not yet been assessed. The objective of this study was to characterize the t1/2eff and terminal half-life (t1/2z) of an extended-release once-daily tacrolimus formulation (LCPT) and twice-daily immediate-release tacrolimus (IR-Tac). METHODS: A noncompartmental analysis of pharmacokinetic data obtained from a phase 2 study in de novo kidney transplant recipients receiving either LCPT or IR-Tac was conducted. Intensive blood sampling was performed on days 1, 7, and 14, and tacrolimus whole blood concentrations were measured using a validated liquid chromatography with tandem mass spectrometry method. T1/2eff was estimated using within-participant accumulation ratios. T1/2z was estimated by linear regression of the terminal phase of the concentration versus time profile. RESULTS: The median accumulation ratios of LCPT and IR-Tac on day 14 were 3.18 and 2.06, respectively.The median (interquartile range; IQR) t1/2eff for LCPT at day 14 of dosing was 48.4 (37.4-77.9) hours, whereas the t1/2z was 20.3 (17.6-22.9) hours. For IR-Tac, the median (IQR) t1/2eff and t1/2z on day 14 were 12.5 (8.8-23.0) hours and 12.2 (9.2-15.7) hours, respectively. CONCLUSIONS: Consistent with its prolonged release of tacrolimus, LCPT demonstrated a higher accumulation ratio and a longer t1/2eff compared with IR-Tac. These findings underscore the pharmacokinetic differences between different drug formulations of the same moiety and may help inform dose adjustments for LCPT in kidney transplantation.

Pharmacy

Mulbah JL, **Kenney RM**, **Tibbetts RJ**, **Shallal AB**, and **Veve MP**. Ceftriaxone versus cefepime or carbapenems for definitive treatment of low-risk AmpC-Harboring Enterobacterales bloodstream infections in hospitalized adults: A retrospective cohort study. *Diagn Microbiol Infect Dis* 2024; 111(1):116557. PMID: 39427451. Full Text

Department of Pharmacy, Henry Ford Hospital, Detroit, MI, USA.
Department of Microbiology, Henry Ford Hospital, Detroit, MI, USA.
Department of Infectious Diseases, Henry Ford Hospital, Detroit, MI, USA.
Department of Pharmacy, Henry Ford Hospital, Detroit, MI, USA; Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI, USA. Electronic address: mpveve@wayne.edu.

OBJECTIVE: To compare outcomes of ceftriaxone to AmpC-stable therapies in patients with bacteremia caused by low-risk AmpC harboring Enterobacterales. METHODS: IRB-approved, retrospective cohort of hospitalized patients ≥18 years old with Serratia marcescens, Morganella morganii, or Providencia spp. bacteremia from 1/1/2017-2/28/2024. Patients were compared by definitive therapy with ceftriaxone vs AmpC-stable therapy (cefepime, carbapenem). The primary endpoint was 30-day all-cause mortality; secondary endpoints were clinical failure and development of ceftriaxone resistance. RESULTS: 163 patients were included; 33.1 % received ceftriaxone, 66.9 % AmpC-stable therapies. 30-day all-cause mortality was 9.3 % ceftriaxone vs 10.1 % AmpC stable patients (P = 0.87); ceftriaxone definitive therapy was not associated with 30-day all-cause mortality (adjOR, 0.79; 95 %CI, 0.23-2.3). There were no differences in clinical failure (9.3 % vs 21.1 %, P = 0.059) or relapsing infection (5.6 % vs 9.3 %, P = 0.55) between ceftriaxone and AmpC-stable treated patients. CONCLUSIONS: Patients treated with definitive ceftriaxone for low-risk AmpC Enterobacterales bacteremia had similar outcomes to AmpC stable therapies.

Pharmacy

Mulugeta SG, **Mannino A**, **Aref N**, **Procopio V**, **Gendjar S**, and **Vincent S**. Thrice is Nice: Thrice Weekly versus Daily Ertapenem in Patients on Hemodialysis. *Int J Antimicrob Agents* 2024; 107355. Epub ahead of print. PMID: 39389384. Full Text

Henry Ford Health, Detroit. 2799 Grand BLVD. Detroit, MI. 48202. Electronic address: smuluge1@hfhs.org.
Henry Ford Health, Macomb. 15855 19 Mile Rd, Clinton Twp, MI 48038.
Henry Ford Health, Detroit. 2799 Grand BLVD. Detroit, MI. 48202.

Plastic Surgery

Diffley M, **Hall JMD**, **Tepper D**, and **Siddiqui A**. The Educational Benefits of Plastic Surgery Rotations for Off-Service Residents. *Adv Med Educ Pract* 2024; 15:999-1004. PMID: 39464207. Full Text

Department of General Surgery, Henry Ford Health, Detroit, MI, USA.
Division of Plastic Surgery, Henry Ford Health, Detroit, MI, USA.
Michigan State University, College of Human Medicine, Henry Ford Hospital, Detroit, MI, USA.

PURPOSE: With increasing specialization among surgical divisions, a well-rounded education during a surgical residency is often accomplished by rotating among different subspecialties. Inclusion of specific rotations in the resident curriculum can be considered as a cost-benefit calculation balancing the value of exposure to a subspecialty versus the opportunity cost of potential learning from another rotation. We find that often these decisions are based on anecdotal feedback. Our goal is to supplement these reports with a quantifiable metric of learning achieved on the plastic surgery rotation. Our hypothesis in this prospective study was that residents would demonstrate improved performance on a post-rotation test after their 1-month rotation on plastic surgery compared to the pre-rotation test. METHODS: A question bank was developed to reflect institutional curriculum objectives and clinical scenarios commonly seen on the service. The questions were developed, validated and vetted in collaboration with medical educators and attending plastic surgeons yielding 20 questions available for use. Postgraduate year 1 residents were given a 10-question test before and after their plastic surgery rotation. A one-tailed paired t-test was used to assess improvement between the pre-rotation test and the post-rotation test. RESULTS: A total of 378 tests were administered with 228 (60%) pre- and post-rotation tests completed meeting inclusion criteria. Average percentage of correct answers for the pre-rotation test was 29% and 88% for the post-rotation test showing a differential improvement of 58% ($p < 0.001$). CONCLUSION: Surgical trainee time is a limited commodity. Each clinical rotation needs proven consistent benefit for the trainees. We developed a questionnaire that documents the improvement in clinical knowledge after a one-month rotation on plastic surgery relative to before. The test results were consistent even when comparing trainees who did the rotation early versus late in the PGY-1 year. Clinical exposure reinforces and solidifies specialty learning.

Plastic Surgery

Myszenski AL, **Divine G**, **Gibson J**, Samuel P, **Diffley M**, **Wang A**, and **Siddiqui A**. Risk Categories for Discharge Planning Using AM-PAC "6-Clicks" Basic Mobility Scores in Non-Surgical Hospitalized Adults. *Cureus* 2024; 16(9):e69670. PMID: 39429401. Request Article

Rehabilitation, Henry Ford Health System, Detroit, USA.
Public Health Sciences, Henry Ford Health System, Detroit, USA.
Occupational Therapy, Wayne State University, Detroit, USA.
Plastic and Reconstructive Surgery, Henry Ford Health System, Detroit, USA.
Surgery, Henry Ford Health System, Detroit, USA.

BACKGROUND: Early discharge planning is important for safe, cost-effective, and timely hospital discharges. Patients with deconditioning are at risk for prolonged lengths of stay related to discharge needs. Functional mobility outcome measures are associated with discharge disposition. The purpose of this study is to examine the clinical usefulness of risk categories based on the Activity Measure for Post-Acute Care (AM-PAC) "6-clicks" Basic Mobility (6cBM) scores on predicting discharge destination. METHODS: A retrospective cohort study of 3739 adults admitted to general medical units at an urban, academic hospital between January 1, 2018 and February 29, 2020 who received at least two physical therapy visits and had an AM-PAC 6cBM recorded within 48 hours of admission and before discharge. The outcome variable was discharge destination dichotomized to post-acute care facilities (PACF);

inpatient rehabilitation, skilled nursing facility, or subacute rehabilitation) or home (with or without home care services). The predictor variables were 6cBM near admission and discharge. Logistic regression was used to estimate the odds of being discharged to PACF compared to home, based on the Three-level risk categorization system: (a) low (6cBM score > 20), (b) moderate (6cBM score 15-19), or (c) high (6cBM score < 14) risk. RESULTS: Analysis indicated important differences between the three risk categories in both time periods. Based on 6cBM at admission, patients in the high-risk category were nine times more likely to be discharged to PACF than those in the low-risk category. At discharge, those in the high-risk category were 29 times more likely to go to PACF than those in the low-risk category. Other characteristics differentiating patients who went to PACF were sex (males), age (older) and longer hospitalization. CONCLUSIONS: Predicting risk for discharge to a PACF using risk categories based on AM-PAC 6cBM can be useful for early discharge planning.

Public Health Sciences

Ata N, **Zahoor I**, **Hoda N**, Adnan SM, Vijayakumar S, Louis F, **Poisson L**, **Rattan R**, Kumar N, **Cerghet M**, and **Giri S**. Artificial neural network-based prediction of multiple sclerosis using blood-based metabolomics data. *Mult Scler Relat Disord* 2024; 92:105942. PMID: 39471746. Full Text

Department of Neurology, Henry Ford Health, Detroit, MI, 48202, USA.
Faculty of Engineering, Aligarh Muslim University, Aligarh, 202002, India.
IEEE Senior Member, Dallas, TX, 75063, USA.
Public Health Services, Henry Ford Health, Detroit, MI, 48202, USA.
Women's Health Services, Henry Ford Health, Detroit, MI, 48202, USA.
Department of Microbiology, Jaipur National University, Jaipur, 302017, India.
Department of Neurology, Henry Ford Health, Detroit, MI, 48202, USA. Electronic address: sgiri1@hfhs.org.

Multiple sclerosis (MS) remains a challenging neurological condition for diagnosis and management and is often detected in late stages, delaying treatment. Artificial intelligence (AI) is emerging as a promising approach to extracting MS information when applied to different patient datasets. Given the critical role of metabolites in MS profiling, metabolomics data may be an ideal platform for the application of AI to predict disease. In the present study, a machine-learning (ML) approach was used for a detailed analysis of metabolite profiles and related pathways in patients with MS and healthy controls (HC). This approach identified unique alterations in biochemical metabolites and their correlation with disease severity parameters. To enhance the efficiency of using metabolic profiles to determine disease severity or the presence of MS, we trained an AI model on a large volume of blood-based metabolomics datasets. We constructed this model using an artificial neural network (ANN) architecture with perceptrons. Data were divided into training, validation, and testing sets to determine model accuracy. After training, accuracy reached 87 %, sensitivity was 82.5 %, specificity was 89 %, and precision was 77.3 %. Thus, the developed model seems highly robust, generalizable with a wide scope and can handle large amounts of data, which could potentially assist neurologists. However, a large multicenter cohort study is necessary for further validation of large-scale datasets to allow the integration of AI in clinical settings for accurate diagnosis and improved MS management.

Public Health Sciences

Babatunde OA, Gonzalez K, Osazuwa-Peters N, Adams SA, Hughes Halbert C, Clark F, Nagar A, Obeysekare J, and **Adjei Boakye E**. Adverse Childhood Events Significantly Impact Depression and Mental Distress in Adults with a History of Cancer. *Cancers (Basel)* 2024; 16(19). PMID: 39409912. Full Text

Department of Psychiatry, Prisma Health, Greer, SC 29650, USA.
School of Medicine, California University of Science and Medicine, Colton, CA 92324, USA.
Department of Head and Neck Surgery & Communication Sciences, Duke University School of Medicine, Durham, NC 27710, USA.
Department of Population Health Sciences, Duke University School of Medicine, Durham, NC 27710, USA.
Duke Cancer Institute, Durham, NC 27701, USA.

Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, 915 Greene Street, Columbia, SC 29208, USA.
Biobehavioral Health and Nursing Science Department, College of Nursing, University of South Carolina, 1601 Greene Street, Columbia, SC 29208, USA.
Department of Population and Public Health Sciences, University of Southern California, Los Angeles, CA 90032, USA.
Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA 90089, USA.
School of Medicine-Greenville, University of South Carolina, Greenville, SC 29605, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI 48202, USA.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System, Detroit, MI 48202, USA.
Henry Ford Health + Michigan State University Health Sciences, Detroit, MI 48202, USA.
Department of Epidemiology and Biostatistics, Michigan State University College of Human Medicine, East Lansing, MI 48824, USA.

Objectives: Adverse childhood experiences (ACEs) are linked to a heightened risk of depression. We explored the relationship between ACEs and both depression and mental distress among cancer survivors. Methods: This was a cross-sectional analysis using the 2022 Behavioral Risk Factor Surveillance System database of cancer survivors aged ≥18 (n = 14,132). The primary outcome was self-reported history of depression, and the secondary outcome was mental distress. The exposure variable was the number of ACEs, classified as 0, 1-2, and ≥3. Weighted multivariable logistic regression models assessed the association between the number of ACEs and depression and mental distress while adjusting for covariates. Results: Approximately 22% of respondents reported experiencing ≥3 ACEs. The prevalence of depression was 21.8%, and mental distress was 15.4%. Compared with cancer survivors who had experienced 0 ACEs, those who had experienced ≥3 (aOR = 3.94; 95% CI, 3.04-5.10) or 1-2 (aOR = 1.85; 95% CI, 1.47-2.32) ACEs had a higher likelihood of reporting depression. Compared with cancer survivors who had experienced 0 ACEs, those who had experienced ≥3 (aOR = 0.67; 95% CI, 0.48-0.93) had a lower likelihood of reporting mental distress. Conclusions: This study highlights the impact of ACEs on depression in adulthood among cancer survivors.

Public Health Sciences

Cirulli GO, **Davis M**, **Stephens A**, **Chiarelli G**, **Finati M**, **Chase M**, **Tinsley S**, **Arora S**, Sood A, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Midlife baseline prostate-specific antigen, velocity, and doubling time association with lethal prostate cancer and mortality. *Cancer* 2024; Epub ahead of print. PMID: 39377255. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, Michigan, USA.
Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Public Health Sciences, Henry Ford Health System, Detroit, Michigan, USA.
Department of Urology, IRCCS Humanitas Research Hospital, Humanitas University, Milan, Italy.
Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
Department of Urology, The James Cancer Hospital and Solove Research Institute, The Ohio State University Wexner Medical Center, Columbus, Ohio, US.

BACKGROUND: Midlife baseline prostate-specific antigen (MB PSA), defined as a single PSA value measured between 40-59 years of age, has been proposed as a tool that can limit potential harms of PSA screening. This study aimed to examine the ability of MB PSA versus PSA doubling time (PSADT) and PSA velocity (PSAV) in assessing the likelihood of developing of lethal prostate cancer (PCa) in a diverse and contemporary North American population. METHODS: Men 40-59 years old, who received their first PSA between the years 1995 and 2019, were included. For MB PSA values, the first PSA test result was included. For PSADT, the first two PSA test results were included. For PSAV, the first three PSA test results within 30 months were included. Selection criteria resulted in a total of 77,594 patients with at least two PSA test results and 11,634 patients with at least three PSA test results. Multivariable Fine-Gray regression was used to examine the impact of the value of the PSA testing methods on the development

of lethal PCa (defined as death from PCa or development of metastatic disease either at diagnosis or during follow-up). Time-dependent receiver operating characteristic/area under the curve (AUC) at 5, 10, and 15 years were plotted. RESULTS: In the main cohort, patients were most frequently in the 50-54 age category (32.8%), had a Charlson comorbidity index of 0 (70.5%), and were White (63.2%). Of these, 9.3% had the midlife baseline PSA in the top 10th percentile, and 0.4% had a PSADT 0-6 months. Lethal PCa was diagnosed in 593 (0.8%) patients. The median (interquartile range) time to lethal PCa was 8.6 (3.2-14.9) years. In the main cohort, MB PSA and PSADT showed significant associations with the occurrence of lethal PCa, with a hazard ratio (HR) of 6.10 (95% confidence interval [CI], 4.85-7.68) and HR of 2.20 (95% CI, 1.07-4.54) for patients in the top 10th percentile MB PSA group and in the PSADT between 0 to <6 months group, respectively. In patients with three PSA results available, MB PSA and PSAV showed significant associations with the occurrence of lethal PCa, with a HR of 3.95 (95% CI, 2.29-6.79) and 3.57 (95% CI, 2.17-5.86) for patients in the top 10th percentile MB PSA group and in the in the PSAV >0.4 ng/mL/year group, respectively. PSADT and PSAV did not exhibit higher AUCs than MB PSA in assessing the likelihood of lethal PCa. Specifically, they were 0.818 and 0.708 at 10 and 15 years, respectively, for the PSADT; 0.862 and 0.756 at 10 and 15 years, respectively, for the PSAV; and 0.868 and 0.762 at 10 and 15 years, respectively, for the MB PSA (all $p > .05$). CONCLUSIONS: The study findings are that PSAV or PSADT were not superior to midlife baseline in assessing the likelihood of developing lethal PCa. This suggests that these variables may not have practical use in enhancing PSA screening strategies in a clinical setting.

Public Health Sciences

Coyne P, **Susick L**, **Schultz L**, **Santarossa S**, **Gough P**, **Rice S**, **Brewster N**, **Behrendt R**, and **Bilicki V**. Using Care Navigation to Improve Patient-Reported Outcomes Among Older Adult Patients: Preliminary Results From a Pilot Study. *J Patient Exp* 2024; 11:23743735241272152. PMID: 39484230. Full Text

Department of Public Health Sciences, Henry Ford Health, Detroit, MI, USA. RINGGOLD: 2971
Henry Ford Health + Michigan State University Health Sciences, East Lansing, MI, USA. RINGGOLD: 657020
College of Human Medicine, Michigan State University, East Lansing, MI, USA. RINGGOLD: 12268
Department of Care Experience, Henry Ford Health, Detroit, MI, USA.

Navigating health and social care in the United States can be difficult for people of all ages, but older adults often have multiple health problems, chronic illnesses, and disabilities that can increase the complexities of their care. To assist older adult patients and/or their caregivers with coordinating care, and providing information, advocacy, and resources, Henry Ford Health (HFH) implemented a Senior Care Navigation Program (SCNP). Older HFH patients or their caregivers were referred to the SCNP either by a provider or another member of their care team. A senior navigator (SN) then reached out to the patient/caregiver by telephone to discuss the SCNP and their support/care needs. The SN scheduled follow-up calls as needed. Patients/caregivers enrolled in Phase 1 of this pilot program were given the option to join the evaluation group. These patients were interviewed by an independent research interviewer at baseline, 3-, 6-, and 9-month post initial contact to complete 5 patient-reported outcomes measures. Our Phase 1 pilot has demonstrated significant improvements in the EQ5D (health-related quality of life) and two patient-reported outcomes measurement information system (PROMIS) measures (depression and anxiety) suggesting that the SCNP program at HFH is having a positive impact on older adult patients' health and well-being. In Phase 2, we will further evaluate the impact of the SCNP on healthcare utilization.

Public Health Sciences

Datta I, **Zahoor I**, **Ata N**, **Rashid F**, **Cerghet M**, **Rattan R**, **Poisson LM**, and **Giri S**. Utility of an Untargeted Metabolomics Approach Using a 2D GC-GC-MS Platform to Distinguish Relapsing and Progressive Multiple Sclerosis. *Metabolites* 2024; 14(9). PMID: 39330500. Full Text

Department of Public Health Sciences, Henry Ford Health, Detroit, MI 48202, USA.
Department of Neurosurgery, Henry Ford Health, Detroit, MI 48202, USA.
Department of Neurology, Henry Ford Health, Detroit, MI 48202, USA.

Women's Health Services, Henry Ford Health, Detroit, MI 48202, USA.

Multiple sclerosis (MS) is the most common inflammatory neurodegenerative disease of the central nervous system (CNS) in young adults and results in progressive neurological defects. The relapsing-remitting phenotype (RRMS) is the most common disease course in MS, which ultimately progresses to secondary progressive MS (SPMS), while primary progressive MS (PPMS) is a type of MS that worsens gradually over time without remissions. There is a gap in knowledge regarding whether the relapsing form can be distinguished from the progressive course, or healthy subjects (HS) based on an altered serum metabolite profile. In this study, we performed global untargeted metabolomics with the 2D GC-GC-MS platform to identify altered metabolites between RRMS, PPMS, and HS. We profiled 235 metabolites in the serum of patients with RRMS (n = 41), PPMS (n = 31), and HS (n = 91). A comparison of RRMS and HS patients revealed 22 significantly altered metabolites at $p < 0.05$ (false-discovery rate [FDR] = 0.3). The PPMS and HS comparisons revealed 28 altered metabolites at $p < 0.05$ (FDR = 0.2). Pathway analysis using MetaboAnalyst revealed enrichment of four metabolic pathways in both RRMS and PPMS (hypergeometric test $p < 0.05$): (1) galactose metabolism; (2) amino sugar and nucleotide sugar metabolism; (3) phenylalanine, tyrosine, and tryptophan biosynthesis; and (4) aminoacyl-tRNA biosynthesis. The Qiagen IPA enrichment test identified the sulfatase 2 (SULF2) ($p = 0.0033$) and integrin subunit beta 1 binding protein 1 (ITGB1BP1) ($p = 0.0067$) genes as upstream regulators of altered metabolites in the RRMS vs. HS groups. However, in the PPMS vs. HS comparison, valine was enriched in the neurodegeneration of brain cells ($p = 0.05$), and heptadecanoic acid, alpha-ketoisocaproic acid, and glycerol participated in inflammation in the CNS ($p = 0.03$). Overall, our study suggests that RRMS and PPMS may contribute metabolic fingerprints in the form of unique altered metabolites for discriminating MS disease from HS, with the potential for constructing a metabolite panel for progressive autoimmune diseases such as MS.

Public Health Sciences

Finati M, Morrison C, **Stephens A**, **Chiarelli G**, **Cirulli GO**, **Tinsley S**, **Davis M**, Sood A, **Buffi N**, **Lughezzani G**, Salonia A, Briganti A, Montorsi F, Busetto GM, Bettocchi C, **Rogers C**, Carrieri G, and **Abdollah F**. Association of race with incidence, characteristics, and mortality from incidental prostate cancer: Analysis of two North American contemporary cohorts. *Prostate* 2024; e24803. Epub ahead of print. PMID: 39465565. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health, Detroit, Michigan, USA.
Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
Wayne State University School of Medicine, Detroit, Michigan, USA.
Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA.
Department of Biomedical Sciences, Humanitas University, Milan, Italy.
Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Department of Urology, The James Cancer Hospital and Solove Research Institute, The Ohio State University Wexner Medical Center, Columbus, Ohio, USA.
Vattikuti Urology Institute, Henry Ford Health, Detroit, Michigan, USA.

BACKGROUND: Non-Hispanic Black (NHB) men are at higher risk both for incidence and mortality from prostate cancer (PCa) compared to Non-Hispanic White (NHW) men, but these findings arise from biopsy-detected PCa reports. We aimed to compare the incidence, subsequent management and cancer-specific mortality (CSM) of incidental PCa among NHB and NHW men, using two different North American cohorts. METHODS: The Surveillance, Epidemiology and End-Result (SEER: 2004-2017) and our institutional Henry Ford Health (HFH: 1995-2022) databases were queried to identify men diagnosed with incidental PCa. Cumulative incidence estimates were used to calculate CSM differences between NHB and NHW men. Competing-risk multivariable regression analysis tested the impact of race on CSM, after accounting for all available covariates. RESULTS: A total of 418 and 6,124 incidental PCa cases were recorded in HFH and SEER database respectively. No pathological differences were observed between NHB and NHW men in both the cohorts, except for prostate-specific antigen (PSA) value at diagnosis, which was higher in NHB men. At 10-years, the CSM rates were 5.5% vs 7.2% in our cohort

and 8.6% vs 10.3% in the SEER cohort for NHW and NHB men, respectively (all Gray's test p-value > 0.05). At multivariable, race was not an independent predictor of CSM in our HFH cohort (HR: 1.46, 95% CI: 0.57-3.71, p = 0.6). In the SEER cohort, NHB men were 34% less likely to die from PCa from 1 year to the next (95% CI: 0.49-0.90, p = 0.008), when compared with NHW men. CONCLUSIONS: In the comparison of incidental PCa findings between NHB and NHW men, both groups had similar pathological characteristic and survival outcomes. These findings are different from the 'conventional' screening-detected PCa and suggest that racial differences have minimal to no adverse effects on PCa-specific mortality after incidental diagnosis.

Public Health Sciences

Fridman I, **Neslund-Dudas C**, Barrow LCJ, Dunn MR, Jones R, Kinlaw AC, Smith AB, Stein JN, **Tam S**, Wood WA, and Lafata JE. Telephone Survey-Reported Perceptions of Telehealth Visits Among Black and Non-Black Patients Diagnosed With Cancer. *JCO Oncol Pract* 2024; Op2400307. Epub ahead of print. PMID: 39475625. Full Text

University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC.
Department of Public Health Sciences, Henry Ford Health, Detroit, MI.
Department of Epidemiology and Biostatistics, College of Human Medicine, Michigan State University, East Lansing, MI.
University of North Carolina Eshelman School of Pharmacy, Chapel Hill, NC.
Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.
Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC.
Patient and Family Advisory Council, UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC.
Cecil G. Sheps Center for Health Services Research, University of North Carolina at Chapel Hill, Chapel Hill, NC.
Department of Urology, University of North Carolina School of Medicine, Chapel Hill, NC.
Division of Oncology, University of North Carolina School of Medicine, Chapel Hill, NC.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, Detroit, MI.
Department of Surgery, College of Human Medicine, Michigan State University, East Lansing, MI.
Division of Hematology-Oncology, University of North Carolina School of Medicine, Chapel Hill, NC.

PURPOSE: Empirical evidence underscores both benefits of telehealth visits and persistent disparities in use for Black adults. Guided by the Technology Acceptance Model, we evaluated perceptions regarding telehealth visits among Black and Non-Black adults receiving cancer care from two academic health systems. METHODS: Between April 2022 and October 2023, a survey was conducted among adult patients treated for cancer in the past 3 years. Survey recruitment was stratified by visit type (telehealth or in-person) and race. Before a scheduled oncology visit, respondents completed a telephone survey to assess their perceptions of usefulness, ease of use, and attitudes toward telehealth visits. Frequency differences were estimated using chi-square tests, and prevalence differences using logistic regression. RESULTS: The survey was completed by 773 respondents (42% Black) with a 15% response rate. Black respondents were younger and less likely to report male sex, being married, having a college education, comfortable income, or confidence in medical and e-literacy. Compared with Non-Black respondents, Black respondents perceived telehealth visits as less useful for determining health needs (37% v 48%) and asking questions (9% v 15%). They thought that telehealth visits were less easy with regard to understanding their health care provider (14% v 21%) and the ability to connect (23% v 30%). Black respondents expressed more concern about internet access (26% v 15%), access to electronic devices (17% v 9%), and finding assistance for connecting (24% v 12%). They also found telehealth visits to be less private (19% v 34%). CONCLUSION: Racial differences in telehealth ease of use and usefulness perceptions highlight the need for oncology practices to couple connectivity support with effective communication strategies to avoid disparities in oncology telehealth services.

Public Health Sciences

Jacob B, **Jamil M**, **Raslan S**, **Springer K**, **Nasser Z**, and **Kuriakose P**. Infusion Reactions With Alternative Therapies During the National Shortage of Iron Dextran. *Eur J Haematol* 2024; Epub ahead of print. PMID: 39385426. Full Text

Henry Ford Health, Detroit, Michigan, USA.

Prior to the national shortage of iron dextran in early 2023, it was the most commonly administered intravenous iron infusion at our institution. After the shortage impacted the health system, alternatives such as iron sucrose and sodium ferric gluconate/sucrose were required that utilized lower doses given at more frequent patient visits. Coinciding with their more prevalent use, an increase in iron infusion reactions was observed. Our study analyzed 880 patients who received iron infusions in three Henry Ford Hospital clinics in metropolitan Detroit, Michigan, from July 2022-June 2023. The 74 reactions that occurred were most commonly associated with iron sucrose at the 500 mg dose (41/74, 55.41%, $p < 0.0001$). Most reactions observed across all iron formulations and doses were mild, with 83.7% being Grade 0 or 1 as defined by the United States Drug Allergy Registry (USDAR) grading scale for immediate reactions. Patients who experienced an infusion reaction were less likely to complete their infusion plans (OR 0.004 for iron dextran, OR 0.128 for iron sucrose, $p < 0.0001$), with infusions most commonly being completely discontinued thereafter, with a minority pursuing alternative options. More patients with lower number of doses scheduled for iron dextran completed their infusion schedules than those with more doses, but the opposite was seen for iron sucrose. We assessed the impact of the national shortage of iron dextran examining infusion reactions with various iron infusions and doses.

Public Health Sciences

Miller-Matero LR, **Hecht LM**, **Gavrilova L**, **Haage B**, **Autio K**, **Tobin ET**, and **Ahmedani BK**. Utilizing primary care to engage underserved patients in a psychological intervention for chronic pain. *Prim Health Care Res Dev* 2024; 25:e54. PMID: 39450755. Full Text

Henry Ford Health, Behavioral Health, Detroit, MI, USA.
Henry Ford Health, Center for Health Policy & Health Services Research, Detroit, MI, USA.
Michigan State University, East Lansing, MI, USA.
Henry Ford Health, Public Health Sciences, Detroit, MI, USA.
Henry Ford Health, Internal Medicine, Detroit, MI, USA.

BACKGROUND: Although psychological interventions can be used to improve chronic pain management, underserved individuals (i.e., racially minoritized and socioeconomically disadvantaged) may be less likely to engage in such services. The purpose of this study was to examine whether offering a psychological intervention for chronic pain in a primary care clinic could be a method in which to successfully engage underserved patients. METHODS: There were 220 patients with chronic pain in a primary care clinic located in a socioeconomically and racially diverse city who were approached to discuss enrolment in a pilot randomized controlled trial of a five-session psychological intervention for chronic pain. Patients were introduced to the study by their primary care provider using the warm handoff model. We compared whether there were sociodemographic differences between those who enrolled in the study and those who declined to enrol. RESULTS: There were no differences between those who enrolled and those who declined enrolment with regard to race, age, insurance type, and household income. However, females were more likely to enrol in the study compared to males. CONCLUSIONS: Recruiting patients to participate in a trial of a psychological intervention for chronic pain in a primary care clinic appeared to be effective for engaging Black patients, patients with lower income, and those with government insurance. Thus, offering a psychological intervention for chronic pain in a primary care clinic may encourage engagement among racially minoritized individuals and those with lower socioeconomic status.

Public Health Sciences

Myszenski AL, **Divine G**, **Gibson J**, Samuel P, **Diffley M**, **Wang A**, and **Siddiqui A**. Risk Categories for Discharge Planning Using AM-PAC "6-Clicks" Basic Mobility Scores in Non-Surgical Hospitalized Adults. *Cureus* 2024; 16(9):e69670. PMID: 39429401. Request Article

Rehabilitation, Henry Ford Health System, Detroit, USA.
Public Health Sciences, Henry Ford Health System, Detroit, USA.
Occupational Therapy, Wayne State University, Detroit, USA.
Plastic and Reconstructive Surgery, Henry Ford Health System, Detroit, USA.
Surgery, Henry Ford Health System, Detroit, USA.

BACKGROUND: Early discharge planning is important for safe, cost-effective, and timely hospital discharges. Patients with deconditioning are at risk for prolonged lengths of stay related to discharge needs. Functional mobility outcome measures are associated with discharge disposition. The purpose of this study is to examine the clinical usefulness of risk categories based on the Activity Measure for Post-Acute Care (AM-PAC) "6-clicks" Basic Mobility (6cBM) scores on predicting discharge destination. METHODS: A retrospective cohort study of 3739 adults admitted to general medical units at an urban, academic hospital between January 1, 2018 and February 29, 2020 who received at least two physical therapy visits and had an AM-PAC 6cBM recorded within 48 hours of admission and before discharge. The outcome variable was discharge destination dichotomized to post-acute care facilities (PACF); inpatient rehabilitation, skilled nursing facility, or subacute rehabilitation) or home (with or without home care services). The predictor variables were 6cBM near admission and discharge. Logistic regression was used to estimate the odds of being discharged to PACF compared to home, based on the Three-level risk categorization system: (a) low (6cBM score > 20), (b) moderate (6cBM score 15-19), or (c) high (6cBM score < 14) risk. RESULTS: Analysis indicated important differences between the three risk categories in both time periods. Based on 6cBM at admission, patients in the high-risk category were nine times more likely to be discharged to PACF than those in the low-risk category. At discharge, those in the high-risk category were 29 times more likely to go to PACF than those in the low-risk category. Other characteristics differentiating patients who went to PACF were sex (males), age (older) and longer hospitalization. CONCLUSIONS: Predicting risk for discharge to a PACF using risk categories based on AM-PAC 6cBM can be useful for early discharge planning.

Public Health Sciences

Robin G, Basappa NS, North S, **Ghosh S**, and Kolinsky M. Outcomes of First Subsequent Taxane Therapy in Patients with Metastatic Castration-Resistant Prostate Cancer Who Previously Received Docetaxel Intensification for Metastatic Castration-Sensitive Prostate Cancer. *Curr Oncol* 2024; 31(9):5080-5087. PMID: 39330003. Full Text

Department of Medicine, University of Alberta, 11230-83 Ave NW, Edmonton, AB T6G 2B7, Canada.
Department of Medical Oncology, University of Alberta, Edmonton, AB T6G 1Z2, Canada.
Cross Cancer Institute, Edmonton, AB T6G 1Z2, Canada.
Henry Ford Hospital, One Ford Place, Detroit, MI 48202, USA.

BACKGROUND: The management of advanced prostate cancer continues to evolve rapidly, particularly with the earlier use of survival-prolonging therapies in metastatic castration-sensitive prostate cancer (mCSPC). Though approved prior to the use of intensification therapy in mCSPC, taxane-based chemotherapies remain a relevant option for patients with metastatic castration-resistant prostate cancer (mCRPC). However, there is little evidence determining the outcomes of taxane chemotherapies as the first subsequent taxane (FST) in mCRPC pts who received docetaxel intensification (DI) in mCSPC. The purpose of this study is to compare outcomes between the survival-prolonging taxanes, docetaxel and cabazitaxel as FST after DI. METHODS: New patient consults seen at the Cross Cancer Institute from 1 July 2014 to 31 December 2020 were retrospectively reviewed. Pts were considered eligible if they received DI for mCSPC and then received either docetaxel or cabazitaxel in mCRPC. Variables of interest were collected from electronic medical records. The primary endpoint was ≥50% PSA response at 12 weeks relative to baseline for FST. Secondary endpoints included OS from mCSPC diagnosis, as well as PFS and OS from the FST start date. PSA responses were compared using the chi-squared test, and time-based endpoints were compared using the Kaplan-Meier method. RESULTS: In total, 34 pts were identified: docetaxel = 22 and cabazitaxel = 12 as FST. 91.2% of pts (docetaxel 95.5% vs. cabazitaxel 83.3%) received FST in 2nd line mCRPC. The median age at diagnosis (63.1 vs. 67.1 yrs, p = 0.236) and the median time to CRPC (18.6 vs. 14.2 mos, p = 0.079) were similar for docetaxel and cabazitaxel,

respectively. The median time to FST (24.1 vs. 34.6 mos, p = 0.036) and OS from mCSPC diagnosis (30.9 vs. 52.7 mos, p = 0.002) were significantly shorter for pts receiving cabazitaxel vs. docetaxel. PSA responses occurred in 40.9% of pts treated with docetaxel compared to 25.0% treated with cabazitaxel (p = 0.645). There was no significant difference in median PFS (2.7 vs. 3.5 mos, p = 0.727) or median OS (11.4 vs. 8.1 mos, p = 0.132) from the time of FST for pts treated with docetaxel vs. cabazitaxel, respectively. CONCLUSIONS: Both docetaxel and cabazitaxel demonstrated activity as FST after DI in mCSPC. Pts who received cabazitaxel had a shorter time to FST and OS from mCSPC. The reasons for this may reflect clinician preference for cabazitaxel in pts with aggressive or rapidly progressing disease. No difference was found in PSA response, PFS, or OS from FST with docetaxel compared to cabazitaxel. While limited by its retrospective nature and small sample size, this study suggests that docetaxel is active as FST despite treatment with DI in mCSPC.

Pulmonary and Critical Care Medicine

Ayyad A, **Fadel R**, **Kollman P**, **Parson A**, **Almajed MR**, **Shadid AM**, **Jabri A**, **Basir MB**, and **Alqarqaz M**. Surviving venoarterial extracorporeal membrane oxygenation (VA-ECMO): The roles of severity scores and post-operative lactate clearance. *Cardiovasc Revasc Med* 2024; Epub ahead of print. PMID: 39477754. Full Text

Henry Ford Hospital, Internal Medicine Department, Detroit, MI, USA. Electronic address: asemayyad96@gmail.com.
Henry Ford Hospital, Cardiology Department, Detroit, MI, USA.
Wayne State University, Detroit, MI, USA.
Henry Ford Hospital, Internal Medicine Department, Detroit, MI, USA.

BACKGROUND: This study investigated the association of the Survival After VA-ECMO (SAVE) score, Sequential Organ Failure Assessment (SOFA) score, and post-cannulation lactate levels with mortality among patients treated with veno-arterial extra-corporeal membrane oxygenation (VA-ECMO) for refractory cardiogenic shock (CS). METHODS: We performed a retrospective review of adult patients who underwent peripheral VA-ECMO cannulation from January 2018 to September 2022 at a quaternary care center. All-cause in-hospital mortality was assessed and compared to predicted mortality by SAVE and SOFA scores prior to cannulation, with adjusted odds ratio of risk factors for mortality identified by multivariate logistic regression analysis. Additionally, the prognostic value of 8-h post-cannulation serum lactate levels was analyzed by receiver operating characteristic (ROC) curve and Kaplan Meier analysis of 30-day survival. RESULTS: 244 patients were included in final analysis. All-cause in-hospital mortality was 70 %, and 54 % of patients died while on ECMO or within 24 h of decannulation. Pre-cannulation SAVE score (OR 0.93 per unit increase, 95 % CI 0.86-0.99, p = 0.008), SOFA score (OR 1.54 per unit increase, 95 % CI 1.32-1.75), and 8-h post-cannulation lactate levels (OR 1.20 per mmol/L increase, 95 % CI 1.04-1.36, p = 0.008) were independently associated with all-cause in-hospital mortality. 8-h post-cannulation lactate levels ≥5.3 mmol/L demonstrated high specificity for in-hospital mortality (90.0 %), while levels ≥7.8 mmol/L were demonstrated high specificity for VA-ECMO death (91.1 %). These thresholds were significantly associated with 30-day all-cause mortality (p < 0.001). CONCLUSION: Pre-cannulation SAVE and SOFA scores are useful prognostic tools in patients with CS. 8-h post-cannulation serum lactate levels are a pragmatic biomarker and can further assist in prognostication of patients on VA-ECMO, and the cutoffs of 5.3 mmol/L and 7.8 mmol/L have high specificity for all-cause mortality and VA-ECMO mortality, respectively. The development of accurate prognostic tools is critical in managing and optimizing care for patients with CS.

Pulmonary and Critical Care Medicine

Coz Yataco AO, Soghier I, Hébert PC, Belley-Cote E, Disselkamp M, Flynn D, Halvorson K, Iaccarino JM, Lim W, Lindenmeyer CC, Miller PJ, O'Neil K, Pendleton KM, Vusse LV, and **Ouellette DR**. Red Blood Cell Transfusion in Critically Ill Adults: An American College of Chest Physicians Clinical Practice Guideline. *Chest* 2024; Epub ahead of print. PMID: 39341492. Full Text

Critical Care Medicine Division and Pulmonary Medicine Division, Integrated Hospital-Care Institute, Cleveland, OH; Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH. Electronic address: cozyata@ccf.org.

Division of Pulmonary and Critical Care Medicine, Department of Medicine, Salem Hospital/Massachusetts General Brigham, Salem, MA; American College of Chest Physicians, Glenview, IL.
Bruyere Research Institute, University of Ottawa, Ottawa.
Population Health Research Institute, ON, Canada.
Department of Critical Care and Pulmonary Medicine, Lexington Veterans Affairs Healthcare System, Lexington, KY.
Boston University Chobanian & Avedisian School of Medicine, Boston, MA.
Department of Medicine, John A. Burns School of Medicine, University of Hawaii, Honolulu, HI.
American College of Chest Physicians, Glenview, IL.
Department of Medicine, McMaster University, Hamilton, ON, Canada.
Department of Gastroenterology, Hepatology and Nutrition, Cleveland Clinic, Cleveland, OH.
Section of Pulmonary, Critical Care, Allergy and Immunologic Disease, Section on Hematology and Oncology, Department of Medicine, Section on Critical Care Medicine, Department of Anesthesiology, Wake Forest School of Medicine, Winston-Salem.
Wilmington Health and MICU, Novant New Hanover Regional Medical Center, Wilmington, NC.
Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, Department of Medicine, University of Minnesota, Minneapolis, MN.
Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, University of Washington, Seattle, WA.
Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI.

BACKGROUND: Blood products frequently are administered to critically ill patients. Considering recent trials and practice variability, a comprehensive review of current evidence was deemed essential to offer pertinent guidance to critical care practitioners. This American College of Chest Physicians (CHEST) guidelines panel examined the literature on RBC transfusions among critically ill patients overall and specific subgroups, including patients with gastrointestinal bleeding, acute coronary syndrome (ACS), cardiac surgery, isolated troponin elevation, and septic shock, to provide evidence-based recommendations. STUDY DESIGN AND METHODS: A panel of experts developed 6 Population, Intervention, Comparator, and Outcome questions addressing RBC transfusions in critically ill patients and performed a comprehensive evidence review. The panel applied the Grading of Recommendations, Assessment, Development, and Evaluations approach to assess the certainty of evidence and to formulate and grade recommendations. A modified Delphi technique was used to reach consensus on the recommendations. RESULTS: The initial search identified a total of 3,082 studies, and after the initial screening, 38 articles were reviewed. Among them, 23 studies met inclusion criteria, comprising 22 randomized controlled trials and 1 cohort study. Based on the analysis of these studies, the panel formulated 2 strong and 4 conditional recommendations. The overall quality of evidence for recommendations ranged from very low to moderate. CONCLUSIONS: In most critically ill patients, a restrictive strategy was preferable to a permissive approach because it does not increase the risk of death or complications, but does decrease RBC use significantly. Data from critically ill subpopulations also supported a restrictive approach, except in patients with ACS, for whom favoring a restrictive approach could increase adverse outcomes.

Pulmonary and Critical Care Medicine
VanAken G, Wieczorek D, Rubick D, **Jabri A**, **Franco-Palacios D**, **Grafton G**, **Kelly B**, **Osinbowale O**, **Ahsan ST**, **Awdish R**, **Aronow HD**, Shore S, and **Aggarwal V**. Cardiopulmonary exercise testing following acute pulmonary embolism: Systematic review and pooled analysis of global studies. *Pulm Circ* 2024; 14(4):e12451. PMID: 39391222. Full Text

Department of Internal Medicine University of Michigan Ann Arbor Michigan USA.
University of Michigan Medical School Ann Arbor Michigan USA.
Central Michigan University College of Medicine Mount Pleasant Michigan USA.
Division of Cardiology Henry Ford Health Detroit Michigan USA.
Division of Pulmonary and Critical Care Medicine Henry Ford Health Detroit Michigan USA.
Department of Osteopathic Medical Specialties Michigan State University College of Osteopathic Medicine East Lansing Michigan USA.

Michigan State University College of Human Medicine East Lansing Michigan USA.
Division of Cardiology (Frankel Cardiovascular Center), Department of Internal Medicine University of Michigan Ann Arbor Michigan USA.

Recent reports have revealed a substantial morbidity burden associated with "post-PE syndrome" (PPES). Cardiopulmonary exercise testing (CPET) has shown promise in better characterizing these patients. In this systematic review and pooled analysis, we aim to use CPET data from PE survivors to understand PPES better. A literature search was conducted in PubMed, EMBASE, and Cochrane for studies reporting CPET results in post-PE patients without known pulmonary hypertension published before August 1, 2023. Studies were independently reviewed by two authors. CPET findings were subcategorized into (1) exercise capacity (percent predicted pVO(2) and pVO(2)) and (2) ventilatory efficiency (VE/VCO(2) slope and V(D)/V(T)). We identified 14 studies (n = 804), 9 prospective observational studies, 4 prospective case-control studies, and 1 randomized trial. Pooled analysis demonstrated a weighted mean percent predicted pVO(2) of 76.09 ± 20.21% (n = 184), with no difference between patients tested <6 months (n = 76, 81.69±26.06%) compared to ≥6 months post-acute PE (n = 88, 82.55 ± 21.47%; p = 0.817). No difference was seen in pVO(2) in those tested <6 months (n = 76, 1.67 ± 0.51 L/min) compared to ≥6 months post-acute PE occurrence (n = 144, 1.75 ± 0.57 L/min; p = 0.306). The weighted mean VE/VCO(2) slope was 32.72 ± 6.02 (n = 244), with a significant difference noted between those tested <6 months (n = 91, 36.52 ± 6.64) compared to ≥6 months post-acute PE (n = 191, 31.99 ± 5.7; p < 0.001). In conclusion, this study, which was limited by small sample sizes and few multicenter studies, found no significant difference in exercise capacity between individuals tested <6 months versus ≥6 months after acute PE. However, ventilatory efficiency was significantly improved in patients undergoing CPET ≥ 6 months compared to those <6 months from the index PE.

Radiation Oncology

Abdel-Wahab M, Giammarile F, Carrara M, Paez D, Hricak H, Ayati N, Li JJ, Mueller M, Aggarwal A, Al-Ibraheem A, **Alkhatib S**, Atun R, Bello A, Berger D, Delgado Bolton RC, Buatti JM, Burt G, Bjelac OC, Cordero-Mendez L, Dosanjh M, Eichler T, Fidarova E, Gondhowiardjo S, Gospodarowicz M, Grover S, Hande V, Harsdorf-Enderndorf E, Herrmann K, Hofman MS, Holmberg O, Jaffray D, Knoll P, Kunikowska J, Lewis JS, Lievens Y, Mikhail-Lette M, Ostwald D, Palta JR, Peristeris P, Rosa AA, Salem SA, Dos Santos MA, Sathekge MM, Shrivastava SK, Titovich E, Urbain JL, Vanderpuye V, Wahl RL, Yu JS, Zaghloul MS, Zhu H, and Scott AM. Radiotherapy and theranostics: a Lancet Oncology Commission. *Lancet Oncol* 2024; 25(11):e545-e580. PMID: 39362232. Full Text

Division of Human Health, Department of Nuclear Sciences and Applications, International Atomic Energy Agency, Vienna, Austria. Electronic address: m.abdel-wahab@iaea.org.
Division of Human Health, Department of Nuclear Sciences and Applications, International Atomic Energy Agency, Vienna, Austria.
Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; Molecular Pharmacology Program, Sloan Kettering Institute, New York, NY, USA; Department of Radiology, Weill Cornell Medical College, New York, NY, USA; Gerstner Sloan Kettering Graduate School of Biomedical Sciences, New York, NY, USA.
Centre for Health Economics, Monash Business School, Monash University, Melbourne, VIC, Australia.
WifOR Institute, Darmstadt, Germany.
Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, London, UK.
Department of Nuclear Medicine, King Hussein Cancer Center, Amman, Jordan; Division of Nuclear Medicine, Department of Radiology and Nuclear Medicine, University of Jordan, Amman, Jordan.
Department of Radiation Oncology, Henry Ford Health, Detroit, MI, USA.
Department of Global Health and Population, Harvard T H Chan School of Public Health, Boston, MA, USA; Department of Health Policy and Management, Harvard T H Chan School of Public Health, Boston, MA, USA; Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA, USA.
National Hospital, Abuja and Federal University of Health Sciences, Azare, Nigeria.
Department of Diagnostic Imaging (Radiology) and Nuclear Medicine, University Hospital San Pedro and Centre for Biomedical Research of La Rioja, Logroño, Spain; Servicio Cántabro de Salud, Santander, Spain.

Department of Radiation Oncology, Holden Comprehensive Cancer Center, Carver College of Medicine, University of Iowa, Iowa City, IA, USA.
University of Lancaster, Lancaster, UK.
University of Oxford, Oxford, UK; European Organization for Nuclear Research, Geneva, Switzerland.
Department of Radiation Oncology, Massey Cancer Center Virginia Commonwealth University, Richmond, VA, USA.
Department of Radiotherapy, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia.
Radiation Oncology, University of Toronto, Princess Margaret Cancer Centre, Toronto, ON, Canada.
Botswana-University of Pennsylvania Partnership, Gaborone, Botswana; Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA, USA.
Department of Global Health, Medicine and Welfare, Atomic Bomb Disease Institute, Nagasaki University, Nagasaki, Japan.
Department of Nuclear Medicine, University of Duisburg, Essen, Germany; German Cancer Consortium, University Hospital Essen, Essen, Germany.
Molecular Imaging and Therapeutic Nuclear Medicine, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia.
Division of Radiation, Transport and Waste Safety, Department of Nuclear Safety and Security, International Atomic Energy Agency, Vienna, Austria.
Department of Radiation Physics and Department of Imaging Physics, University of Texas MD Anderson Cancer Center, Houston, TX, USA.
Nuclear Medicine Department, Medical University of Warsaw, Warsaw, Poland.
Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; Molecular Pharmacology Program, Sloan Kettering Institute, New York, NY, USA; Department of Pharmacology, Weill Cornell Medical College, New York, NY, USA.
Department of Radiation Oncology, Ghent University Hospital and Ghent University, Ghent, Belgium.
WifOR Institute, Darmstadt, Germany; Steinbeis School of International Business and Entrepreneurship, Herrenberg, Germany.
Department of Radiation Oncology, Virginia Commonwealth University, Richmond, VA, USA.
WifOR Institute, Athens, Greece.
Radiation Oncology, Grupo Oncoclinicas, Salvador, Brazil.
Latin American Society of Radiation Oncology, Brasilia/DF, Brazil.
Department of Nuclear Medicine, University of Pretoria, Pretoria, South Africa; Steve Biko Academic Hospital, Pretoria, South Africa; Nuclear Medicine Research Infrastructure, Pretoria, South Africa.
Department of Radiation Oncology, Tata Memorial Hospital, Mumbai, India.
Department of Radiology, Division of Nuclear Medicine, Branford General Hospital, Ontario, Canada.
National Center for Radiotherapy Oncology and Nuclear Medicine Department of the Korlebu Teaching Hospital, Accra, Ghana.
Mallinckrodt Institute of Radiology, Department of Radiology, and Department of Radiation Oncology, Washington University School of Medicine, St Louis, MO, USA.
Department of Radiation Oncology and Department of Cancer Biology, Cleveland Clinic, Cleveland, OH USA.
Radiation Oncology Department, National Cancer Institute, Cairo University & Children's Cancer Hospital, Cairo, Egypt.
Department of Radiation Oncology, Fudan University Shanghai Cancer Center, Shanghai, China; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China.
Department of Molecular Imaging and Therapy, Austin Health, Melbourne, VIC, Australia; Olivia Newton-John Cancer Research Institute, Melbourne, VIC, Australia; School of Cancer Medicine, La Trobe University, Melbourne, VIC, Australia; Faculty of Medicine, University of Melbourne, Melbourne, VIC, Australia. Electronic address: andrew.scott@onjcri.org.au.

Following on from the 2015 Lancet Oncology Commission on expanding global access to radiotherapy, Radiotherapy and theranostics: a Lancet Oncology Commission was created to assess the access and availability of radiotherapy to date and to address the important issue of access to the promising field of theranostics at a global level. A marked disparity in the availability of radiotherapy machines between high-income countries and low-income and middle-income countries (LMICs) has been identified

previously and remains a major problem. The availability of a suitably trained and credentialled workforce has also been highlighted as a major limiting factor to effective implementation of radiotherapy, particularly in LMICs. We investigated initiatives that could mitigate these issues in radiotherapy, such as extended treatment hours, hypofractionation protocols, and new technologies. The broad implementation of hypofractionation techniques compared with conventional radiotherapy in prostate cancer and breast cancer was projected to provide radiotherapy for an additional 2·2 million patients (0·8 million patients with prostate cancer and 1·4 million patients with breast cancer) with existing resources, highlighting the importance of implementing new technologies in LMICs. A global survey undertaken for this Commission revealed that use of radiopharmaceutical therapy-other than (131)I-was highly variable in high-income countries and LMICs, with supply chains, workforces, and regulatory issues affecting access and availability. The capacity for radioisotope production was highlighted as a key issue, and training and credentialling of health professionals involved in theranostics is required to ensure equitable access and availability for patient treatment. New initiatives-such as the International Atomic Energy Agency's Rays of Hope programme-and interest by international development banks in investing in radiotherapy should be supported by health-care systems and governments, and extended to accelerate the momentum generated by recognising global disparities in access to radiotherapy. In this Commission, we propose actions and investments that could enhance access to radiotherapy and theranostics worldwide, particularly in LMICs, to realise health and economic benefits and reduce the burden of cancer by accessing these treatments.

Radiation Oncology

Etienne T, **Kim J**, **Thind K**, and **Chetty IJ**. Development of an EGSnrc multi-leaf collimator component module and treatment head model for a low-field MRI linear accelerator. *Med Phys* 2024; Epub ahead of print. PMID: 39388092. Full Text

Department of Radiation Oncology, Baylor Scott and White Health, Temple, Texas, USA.
Department of Radiation Oncology, Cedars-Sinai Medical Center, Los Angeles, California, USA.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, Michigan, USA.

BACKGROUND: Monte Carlo (MC) modeling of MR-guided radiotherapy (MRgRT) treatment machines enables the characterization of photon/electron interactions in the presence of a magnetic field. The EGSnrc MC code system is a well-established system for radiation dose calculations. The multi-leaf collimator (MLC) component modules presently available within the EGSnrc MC code system do not include a model of the double-focused MLC available on a low-field (0.35T) MRI linear accelerator (MR linac). PURPOSE: Here we developed and validated a new component module (CM) for the low-field MRgRT MLC using the EGSnrc/BEAMnrc/DOSXYZnrc code system. We performed detailed modeling of the treatment head and validated the model using measurements and calculations from the vendor-specific treatment planning system (TPS). METHODS: The detailed geometry of the low-field MR linac MLC and other treatment head structures were modeled using BEAMnrc. Comparisons of DOSXYZnrc simulated dose against measurements and the low-field MR linac TPS for a variety of AAPM TG-53 task group report suggested square and shaped fields, as well as a step-and-shoot intensity-modulated radiotherapy (IMRT) plan, are presented. RESULTS: Our model agrees with both measured and TPS calculated data on average within 2%/2 mm (dose/DTA) criterion for square field profiles. Output factors agreed within 1% for field sizes down to 2.49 × 2.49 cm(2) and within 2% of TPS data for the smallest field size of 0.83 × 0.83 cm(2). Shaped field and IMRT MC calculations agreed with measured and TPS data such that the gamma pass rates (3%/2 mm) were 99.5% and (3%/3 mm) 96.2%, respectively. CONCLUSIONS: We developed and validated an MLC CM (SYNCVRMLC) for the low-field MR linac using the EGSnrc MC code systems. This new CM will facilitate MC computation of fluence and dose distributions using BEAMnrc/DOSXYZnrc for patients treated on the low-field MR linac.

Radiation Oncology

Koontz BF, Koritzinsky M, Zoberi JE, **Brown SL**, Ding X, Wong J, Joiner MC, Dominello MM, and Burmeister J. Three discipline collaborative radiation therapy (3DCRT) special debate: Systemic radiotherapy using targeted isotopes is the best hope for advancing curative radiation therapy. *J Appl Clin Med Phys* 2024; e14533. Epub ahead of print. PMID: 39447139. Full Text

Department of Radiation Oncology, AdventHealth Cancer Institute, Orlando, Florida, USA.
Princess Margaret Cancer Centre, University Health Network / Department of Radiation Oncology, University of Toronto, Toronto, Ontario, Canada.
Department of Radiation Oncology, Washington University School of Medicine, Saint Louis, Missouri, USA.
Department of Radiation Oncology, Henry Ford Health, Michigan State University Health Sciences, Detroit, Michigan, USA.
Department of Radiation Oncology, William Beaumont University Hospital, Corewell Health, Royal Oak, Michigan, USA.
Department of Radiation Oncology, City of Hope Cancer Center, Duarte, California, USA.
Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan, USA.
Gershenson Radiation Oncology Center, Barbara Ann Karmanos Cancer Institute, Detroit, Michigan, USA.

Radiation Oncology
Sriramulu S, **Thoidingjam S**, Speers C, and **Nyati S**. Present and Future of Immunotherapy for Triple-Negative Breast Cancer. *Cancers (Basel)* 2024; 16(19). PMID: 39409871. Full Text

Department of Radiation Oncology, Henry Ford Cancer Institute, Henry Ford Health, Detroit, MI 48202, USA.
Department of Radiation Oncology, University of Michigan, Ann Arbor, MI 48109, USA.
Department of Radiation Oncology, UH Seidman Cancer Center, University Hospitals Case Medical Center, Case Western Reserve University, Cleveland, OH 44106, USA.
Henry Ford Health + Michigan State University Health Sciences, Detroit, MI 48202, USA.
Department of Radiology, Michigan State University, East Lansing, MI 48824, USA.

Triple-negative breast cancer (TNBC) lacks the expression of estrogen receptors (ERs), human epidermal growth factor receptor 2 (HER2), and progesterone receptors (PRs). TNBC has the poorest prognosis among breast cancer subtypes and is more likely to respond to immunotherapy due to its higher expression of PD-L1 and a greater percentage of tumor-infiltrating lymphocytes. Immunotherapy has revolutionized TNBC treatment, especially with the FDA's approval of pembrolizumab (Keytruda) combined with chemotherapy for advanced cases, opening new avenues for treating this deadly disease. Although immunotherapy can significantly improve patient outcomes in a subset of patients, achieving the desired response rate for all remains an unmet clinical goal. Strategies that enhance responses to immune checkpoint blockade, including combining immunotherapy with chemotherapy, molecularly targeted therapy, or radiotherapy, may improve response rates and clinical outcomes. In this review, we provide a short background on TNBC and immunotherapy and explore the different types of immunotherapy strategies that are currently being evaluated in TNBC. Additionally, we review why combination strategies may be beneficial, provide an overview of the combination strategies, and discuss the novel immunotherapeutic opportunities that may be approved in the near future for TNBC.

Radiation Oncology
Thoidingjam S, **Bhatnagar AR**, **Sriramulu S**, **Siddiqui F**, and **Nyati S**. Optimizing Pancreatic Cancer Therapy: The Promise of Immune Stimulatory Oncolytic Viruses. *Int J Mol Sci* 2024; 25(18). PMID: 39337402. Full Text

Department of Radiation Oncology, Henry Ford Health, Detroit, MI 48202, USA.
Henry Ford Health + Michigan State University Health Sciences, Detroit, MI 48202, USA.
Department of Medicine, Michigan State University, East Lansing, MI 48824, USA.
Department of Radiology, Michigan State University, East Lansing, MI 48824, USA.

Pancreatic cancer presents formidable challenges due to rapid progression and resistance to conventional treatments. Oncolytic viruses (OVs) selectively infect cancer cells and cause cancer cells to lyse, releasing molecules that can be identified by the host's immune system. Moreover, OV can carry immune-stimulatory payloads such as interleukin-12, which when delivered locally can enhance immune system-mediated tumor killing. OVs are very well tolerated by cancer patients due to their ability to

selectively target tumors without affecting surrounding normal tissues. OVs have recently been combined with other therapies, including chemotherapy and immunotherapy, to improve clinical outcomes. Several OVs including adenovirus, herpes simplex viruses (HSVs), vaccinia virus, parvovirus, reovirus, and measles virus have been evaluated in preclinical and clinical settings for the treatment of pancreatic cancer. We evaluated the safety and tolerability of a replication-competent oncolytic adenoviral vector carrying two suicide genes (thymidine kinase, TK; and cytosine deaminase, CD) and human interleukin-12 (hIL12) in metastatic pancreatic cancer patients in a phase 1 trial. This vector was found to be safe and well-tolerated at the highest doses tested without causing any significant adverse events (SAEs). Moreover, long-term follow-up studies indicated an increase in the overall survival (OS) in subjects receiving the highest dose of the OV. Our encouraging long-term survival data provide hope for patients with advanced pancreatic cancer, a disease that has not seen a meaningful increase in OS in the last five decades. In this review article, we highlight several preclinical and clinical studies and discuss future directions for optimizing OV therapy in pancreatic cancer. We envision OV-based gene therapy to be a game changer in the near future with the advent of newer generation OVs that have higher specificity and selectivity combined with personalized treatment plans developed under AI guidance.

Radiation Oncology

Thoidingjam S, **Sriramulu S**, **Hassan O**, **Brown SL**, **Siddiqui F**, **Movsas B**, **Gadgeel S**, and **Nyati S**. BUB1 Inhibition Overcomes Radio- and Chemoradiation Resistance in Lung Cancer. *Cancers (Basel)* 2024; 16(19). PMID: 39409911. Full Text

Department of Radiation Oncology, Henry Ford Health, Detroit, MI 48202, USA.
Department of Surgical Pathology, Henry Ford Cancer Institute, Henry Ford Health, Detroit, MI 48202, USA.
Henry Ford Health + Michigan State University Health Sciences, Detroit, MI 48202, USA.
Department of Radiology, Michigan State University, East Lansing, MI 48824, USA.
Division of Hematology/Oncology, Department of Medicine, Henry Ford Health, Detroit, MI 48202, USA.

Background: Despite advances in targeted therapies and immunotherapies, traditional treatments like microtubule stabilizers (paclitaxel, docetaxel), DNA-intercalating platinum drugs (cisplatin), and radiation therapy remain essential for managing locally advanced and metastatic lung cancer. Identifying novel molecular targets could enhance the efficacy of these treatments. Hypothesis: We hypothesize that BUB1 (Ser/Thr kinase) is overexpressed in lung cancers and its inhibition will sensitize lung cancers to chemoradiation. Methods: BUB1 inhibitor (BAY1816032) was combined with cisplatin, paclitaxel, a PARP inhibitor olaparib, and radiation in cell proliferation and radiation-sensitization assays. Biochemical and molecular assays evaluated the impact on DNA damage signaling and cell death. Results: Immunostaining of lung tumor microarrays (TMAs) confirmed higher BUB1 expression in non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) compared to normal tissues. In NSCLC, BUB1 overexpression correlated directly with the expression of TP53 mutations and poorer overall survival in NSCLC and SCLC patients. BAY1816032 synergistically sensitized lung cancer cell lines to paclitaxel and olaparib and enhanced cell killing by radiation in both NSCLC and SCLC. Molecular analysis indicated a shift towards pro-apoptotic and anti-proliferative states, evidenced by altered BAX, BCL2, PCNA, and Caspases-9 and -3 expressions. Conclusions: Elevated BUB1 expression is associated with poorer survival in lung cancer. Inhibiting BUB1 sensitizes NSCLC and SCLC to chemotherapies (cisplatin, paclitaxel), targeted therapy (olaparib), and radiation. Furthermore, we present the novel finding that BUB1 inhibition sensitized both NSCLC and SCLC to radiotherapy and chemoradiation. Our results demonstrate BUB1 inhibition as a promising strategy to sensitize lung cancers to radiation and chemoradiation therapies.

Radiation Oncology

Yan Y, **Kim JP**, Nejad-Davarani SP, Dong M, Hurst NJ, Jr., Zhao J, and Glide-Hurst CK. Deep Learning-Based Synthetic Computed Tomography for Low-Field Brain Magnetic Resonance-Guided Radiation Therapy. *Int J Radiat Oncol Biol Phys* 2024; Epub ahead of print. PMID: 39357787. Full Text

Department of Human Oncology, University of Wisconsin-Madison, Madison, Wisconsin; Department of Medical Physics, University of Wisconsin-Madison, Madison, Wisconsin.

Department of Radiation Oncology, Henry Ford Health, Detroit, Michigan.
Department of Radiation Oncology, University of Miami, Miami, Florida.
Department of Computer Science, Wayne State University, Detroit, Michigan.
Department of Human Oncology, University of Wisconsin-Madison, Madison, Wisconsin.
Department of Statistics, University of Wisconsin-Madison, Madison, Wisconsin; Department of Biostatistics and Medical Informatics, University of Wisconsin-Madison, Madison, Wisconsin.
Department of Human Oncology, University of Wisconsin-Madison, Madison, Wisconsin; Department of Medical Physics, University of Wisconsin-Madison, Madison, Wisconsin. Electronic address: glidehurst@humonc.wisc.edu.

PURPOSE: Magnetic resonance (MR)-guided radiation therapy enables online adaptation to address intra- and interfractional changes. To address the need of high-fidelity synthetic computed tomography (synCT) required for dose calculation, we developed a conditional generative adversarial network for synCT generation from low-field MR imaging in the brain. METHODS AND MATERIALS: Simulation MR-CT pairs from 12 patients with glioma imaged with a head and neck surface coil and treated on a 0.35T MR-linac were prospectively included to train the model consisting of a 9-block residual network generator and a PatchGAN discriminator. Four-fold cross-validation was implemented. SynCT was quantitatively evaluated against real CT using mean absolute error (MAE), peak signal-to-noise ratio (PSNR), and structural similarity index measure (SSIM). Dose was calculated on synCT applying original treatment plan. Dosimetric performance was evaluated by dose-volume histogram metric comparison and local 3-dimensional gamma analysis. To demonstrate utilization in treatment adaptation, longitudinal synCTs were generated for qualitative evaluation, and 1 offline adaptation case underwent 2 comparative plan evaluations. Secondary validation was conducted with 9 patients on a different MR-linac using a high-resolution brain coil. RESULTS: Our model generated high-quality synCTs with MAE, PSNR, and SSIM of 70.9 ± 10.4 HU, 28.4 ± 1.5 dB, and 0.87 ± 0.02 within the field of view, respectively. Underrepresented postsurgical anomalies challenged model performance. Nevertheless, excellent dosimetric agreement was observed with the mean difference between real and synCT dose-volume histogram metrics of -0.07 ± 0.29 Gy for target D(95) and within [-0.14, 0.02] Gy for organs at risk. Significant differences were only observed in the right lens D(0.01cc) with negligible overall difference (<0.13 Gy). Mean gamma analysis pass rates were 92.2% ± 3.0%, 99.2% ± 0.7%, and 99.9% ± 0.1% at 1%/1 mm, 2%/2 mm, and 3%/3 mm, respectively. Secondary validation yielded no significant differences in synCT performance for whole-brain MAE, PSNR, and SSIM with comparable dosimetric results. CONCLUSIONS: Our conditional generative adversarial network model generated high-fidelity brain synCTs from low-field MR imaging with excellent dosimetric performance. Secondary validation suggests great promise of implementing synCTs to facilitate robust dose calculation for online adaptive brain MR-guided radiation therapy.

Rehabilitation Services/Physical Therapy/Occupational Health

Myszenski AL, **Divine G**, **Gibson J**, Samuel P, **Diffley M**, **Wang A**, and **Siddiqui A**. Risk Categories for Discharge Planning Using AM-PAC "6-Clicks" Basic Mobility Scores in Non-Surgical Hospitalized Adults. *Cureus* 2024; 16(9):e69670. PMID: 39429401. Request Article

Rehabilitation, Henry Ford Health System, Detroit, USA.
Public Health Sciences, Henry Ford Health System, Detroit, USA.
Occupational Therapy, Wayne State University, Detroit, USA.
Plastic and Reconstructive Surgery, Henry Ford Health System, Detroit, USA.
Surgery, Henry Ford Health System, Detroit, USA.

BACKGROUND: Early discharge planning is important for safe, cost-effective, and timely hospital discharges. Patients with deconditioning are at risk for prolonged lengths of stay related to discharge needs. Functional mobility outcome measures are associated with discharge disposition. The purpose of this study is to examine the clinical usefulness of risk categories based on the Activity Measure for Post-Acute Care (AM-PAC) "6-clicks" Basic Mobility (6cBM) scores on predicting discharge destination. METHODS: A retrospective cohort study of 3739 adults admitted to general medical units at an urban, academic hospital between January 1, 2018 and February 29, 2020 who received at least two physical therapy visits and had an AM-PAC 6cBM recorded within 48 hours of admission and before discharge.

The outcome variable was discharge destination dichotomized to post-acute care facilities (PACF); inpatient rehabilitation, skilled nursing facility, or subacute rehabilitation) or home (with or without home care services). The predictor variables were 6cBM near admission and discharge. Logistic regression was used to estimate the odds of being discharged to PACF compared to home, based on the Three-level risk categorization system: (a) low (6cBM score > 20), (b) moderate (6cBM score 15-19), or (c) high (6cBM score < 14) risk. RESULTS: Analysis indicated important differences between the three risk categories in both time periods. Based on 6cBM at admission, patients in the high-risk category were nine times more likely to be discharged to PACF than those in the low-risk category. At discharge, those in the high-risk category were 29 times more likely to go to PACF than those in the low-risk category. Other characteristics differentiating patients who went to PACF were sex (males), age (older) and longer hospitalization. CONCLUSIONS: Predicting risk for discharge to a PACF using risk categories based on AM-PAC 6cBM can be useful for early discharge planning.

Research Administration

Littleton SDR, **Lanfear DE**, Dorsch MP, **Liu B**, and Luzum JA. Equal Treatment, Unequal Outcomes? Debunking the Racial Disparity in Renin Angiotensin Aldosterone System Inhibitor Associated Reduction in Heart Failure Hospitalizations. *J Card Fail* 2024; Epub ahead of print. PMID: 39442611. Full Text

University of Michigan College of Pharmacy, Ann Arbor, MI, USA.
Henry Ford Health System, Detroit, MI, USA.
University of Michigan College of Pharmacy, Ann Arbor, MI, USA. Electronic address: jluzum@med.umich.edu.

BACKGROUND: Renin angiotensin aldosterone system inhibitors (RAASi) are a mainstay treatment in patients with heart failure with reduced ejection fraction (HFrEF) in part to prevent hospitalizations. However, whether RAAS inhibitors reduce the risk of hospitalization in Black patients is not entirely clear because enrollment of Black patients in previous clinical trials was low, and a previous meta-analysis showed a significant racial disparity: reduction in hospitalizations with an RAAS inhibitor in White patients but not Black patients. Previous studies relied on the use of self-identified race instead of genomic ancestry. Therefore, this study aimed to investigate the role of self-identified race and genomic ancestry in the racial disparity in RAAS inhibitor associated reductions in HFrEF hospitalizations. METHODS: The primary outcome was time to first heart failure hospitalization. A (de-identified) heart failure patient registry and data from the GUIDE-IT multi-center randomized control trial were analyzed with Cox proportional hazards models un/adjusted for clinical risk factors, death as a competing risk, and time-varying RAAS inhibitor exposure. The proportion of Yoruba African ancestry was quantified.. Analysis of self - identified race were performed in both the registry and GUIDE-IT. Analysis of genomic ancestry was only performed in the registry since this information was not available in GUIDE-IT. A fixed effect meta-analysis combined results of both the registry and GUIDE-IT for race. RESULTS: The registry had 1010 total HFrEF patients (Black = 509 and White = 501) with 852 having ancestry quantification (>80% Yoruba African Ancestry = 381 and <5% Yoruba African Ancestry = 471). GUIDE-IT had 810 HFrEF patients (Black = 322 and White = 488). There was no significant difference in the association of RAAS inhibitor exposure with heart failure hospitalization by race (meta-analysis p-value for race*RAAS inhibitor exposure interaction = 0.49; Black patients HR [95% CI] for RAAS inhibitor exposure = 0.89 [0.64-1.23)] P = 0.47; White patients = 1.20 (0.83-1.75) P = 0.34). Results were similar when analyzed by ancestry (p-value for ancestry*RAAS inhibitor exposure interaction = 0.57; >80% Yoruba African Ancestry = 0.93 [0.51-1.69] P = 0.80; <5% Yoruba African Ancestry = 1.29 [0.57-2.92] P = 0.54). CONCLUSIONS: In contrast to a previous meta-analysis, this more contemporary analysis of 2 HFrEF patient datasets demonstrates the absence of a racial disparity in RAAS inhibitor associated reductions in heart failure hospitalizations. The difference in this racial disparity over time may be due to improvements in background heart failure therapies, racial differences in healthcare usage, and the use of more advanced statistical approaches.

Research Administration

Selvaraj S, Patel S, Sauer AJ, McGarrah RW, Jones P, Kwee LC, Windsor SL, Ilkayeva O, Muehlbauer MJ, Newgard CB, Borlaug BA, Kitzman DW, Shah SJ, Margulies KB, Husain M, Inzucchi SE, McGuire DK, **Lanfear DE**, Javaheri A, Umpierrez G, Mentz RJ, Sharma K, Kosiborod MN, and Shah SH. Metabolic Effects of the SGLT2 Inhibitor Dapagliflozin in Heart Failure Across the Spectrum of Ejection Fraction. *Circ Heart Fail* 2024; e011980. Epub ahead of print. PMID: 39421941. Full Text

Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, NC (S.S., R.W.M., R.J.M., S.H.S.).
Duke Molecular Physiology Institute, Duke University, Durham, NC (S.S., R.W.M., L.C.K., O.I., M.J.M., C.B.N., S.H.S.).
Saint Luke's Mid America Heart Institute, Kansas City, MO (S.P., A.J.S., P.J., S.L.W., M.N.K.).
University of Missouri-Kansas City (A.J.S., M.N.K.).
Division of Endocrinology, Metabolism, and Nutrition, Department of Medicine, Duke University School of Medicine, Durham, NC (O.I.).
Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN (B.A.B.).
Department of Internal Medicine, Sections on Cardiovascular Medicine and Geriatrics, Wake Forest School of Medicine, Winston-Salem, NC (D.W.K.).
Division of Cardiology, Department of Medicine, Bluhm Cardiovascular Institute, Northwestern University Feinberg School of Medicine, Chicago, IL (S.J.S.).
Division of Cardiology, Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia (K.B.M.).
Ted Rogers Centre for Heart Research, University of Toronto, ON, Canada (M.H.).
Yale University School of Medicine, New Haven, CT (S.E.I.).
University of Texas Southwestern Medical Center and Parkland Health and Hospital System, Dallas (D.K.M.).
Center for Individual and Genomic Medicine Research and Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, MI (D.E.L.).
Washington University School of Medicine, St. Louis, MO (A.J.).
Division of Endocrinology, Emory University School of Medicine, Atlanta, GA (G.U.).
Division of Cardiology, Johns Hopkins University School of Medicine, Baltimore, MD (K.S.).

BACKGROUND: Mechanisms of benefit with SGLT2is (sodium-glucose cotransporter-2 inhibitors) in heart failure (HF) remain incompletely characterized. Dapagliflozin alters ketone and fatty acid metabolism in HF with reduced ejection fraction though similar effects have not been observed in HF with preserved ejection fraction. We explore whether metabolic effects of SGLT2is vary across the left ventricular ejection fraction spectrum and their relationship with cardiometabolic end points in 2 randomized trials of dapagliflozin in HF. METHODS: Metabolomic profiling of 61 metabolites was performed in 527 participants from DEFINE-HF (Dapagliflozin Effects on Biomarkers, Symptoms and Functional Status in Patients With HF With Reduced Ejection Fraction) and PRESERVED-HF (Dapagliflozin in PRESERVED Ejection Fraction HF; 12-week, placebo-controlled trials of dapagliflozin in HF with reduced ejection fraction and HF with preserved ejection fraction, respectively). Linear regression was used to assess changes in principal components analysis-defined metabolite factors with treatment from baseline to 12 weeks, as well as the relationship between changes in metabolite clusters and HF-related end points. RESULTS: The mean age was 66±11 years, 43% were female, and 33% were self-identified as Black. Two principal components analysis-derived metabolite factors (which were comprised of ketone and short-/medium-chain acylcarnitines) increased with dapagliflozin compared with placebo. Ketosis (defined as 3-hydroxybutyrate >500 μM) was achieved in 4.5% with dapagliflozin versus 1.2% with placebo (P=0.03). There were no appreciable treatment effects on amino acids, including branched-chain amino acids. Increases in several acylcarnitines were consistent across LVEF (P(interaction)>0.10), whereas the ketogenic effect diminished at higher LVEF (P(interaction)=0.01 for 3-hydroxybutyrate). Increases in metabolites reflecting mitochondrial dysfunction (particularly long-chain acylcarnitines) and aromatic amino acids and decreases in branched-chain amino acids were associated with worse HF-related outcomes in the overall cohort, with consistency across treatment and LVEF. CONCLUSIONS: SGLT2is demonstrate common (fatty acid) and distinct (ketogenic) metabolic signatures across the LVEF spectrum. Changes in key pathways related to fatty acid and amino acid metabolism are associated with

HF-related end points and may serve as therapeutic targets across HF subtypes. REGISTRATION: URL: https://www.clinicaltrials.gov; Unique Identifiers: NCT03030235 and NCT02653482.

Sleep Medicine
Cheng P, **Jennings MB**, **Kalmbach D**, Johnson DA, **Habash S**, Casement MD, and **Drake C**. Neighborhood social vulnerability as a mediator of racial disparities in insomnia severity. *Sleep Health* 2024; Epub ahead of print. PMID: 39477783. Full Text

Sleep Disorders and Research Center, Henry Ford Health, Detroit, Michigan, USA. Electronic address: pcheng1@hfhs.org.
Sleep Disorders and Research Center, Henry Ford Health, Detroit, Michigan, USA.
Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia, USA.
Department of Psychology, University of Oregon, Eugene, Oregon, USA.

STUDY OBJECTIVES: Recent data has indicated that Black Americans experience more severe insomnia compared to their White counterparts. Although previous studies have identified psychosocial mechanisms driving this disparity, little is known about the structural determinants of insomnia disparities. This study tested neighborhood social vulnerability as a mechanism driving Black-White disparities in insomnia severity in the United States. METHODS: Participants with a previous diagnosis of insomnia (N = 196) reported their race and insomnia severity (Insomnia Severity Index). As a measure of the neighborhood environment Social Vulnerability Index was calculated by geocoding home address at the time of participation to the respective census tract from the 2020 US Census. A mediation analysis tested the indirect effect of the Social Vulnerability Index between race and insomnia severity. RESULTS: Black participants reported worse insomnia severity compared to White participants. Black participants also had 3.3 times the odds of living in neighborhoods with higher social vulnerability compared to White participants, with a group median difference of 0.26 percentile points (scale 0 to 1). As hypothesized, results revealed a significant indirect effect of the Social Vulnerability Index, which accounted for 31.1% of the variance between race and insomnia severity. CONCLUSION: Living in a socially vulnerable neighborhood environment may be a mechanism driving racial disparities in insomnia severity. Interventions that consider structural determinants of health, including community-based and policy-level interventions could have an enhanced impact on addressing insomnia and its public health consequences.

Sleep Medicine
Reffi AN, **Cheng P**, **Kalmbach DA**, **Moore DA**, **Mahr GC**, Seymour GM, **Solway M**, and **Drake CL**. Understanding nightmares after traumatic events in Detroit (UNiTED): prospective associations with interpersonal violence and posttraumatic stress disorder symptoms. *Eur J Psychotraumatol* 2024; 15(1):2409561. PMID: 39376120. Full Text

Sleep Disorders & Research Center, Henry Ford Health, Detroit, MI, USA.
Department of Psychiatry, Michigan State University College of Human Medicine, Grand Rapids, MI, USA.
Department of Surgery, Division of Acute Care Surgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Psychiatry and Behavioral Health, Division of Consultation Liaison Psychiatry, Henry Ford Hospital, Detroit, MI, USA.
Department of Psychology, University of Kentucky, Lexington, Kentucky, USA.
Department of Psychiatry, Henry Ford Hospital, Detroit, MI, USA.

ABSTRACTBackground: Research suggests trauma-related nightmares (TRNs) during the acute aftermath of trauma may contribute to posttraumatic stress disorder (PTSD). However, it is unknown who is most vulnerable to TRNs, which is critical to identify at-risk patients toward whom early nightmare-focused treatments can be targeted to prevent PTSD.Objective: We tested trauma type (interpersonal violence [e.g. assault] vs non-interpersonal trauma [e.g. motor vehicle collision]) as a risk factor for TRNs in a predominantly low-income, Black, urban sample in Detroit, MI, USA.Method: We recruited patients from the intensive care unit following traumatic injury (N = 88; M(age) = 39.53 ± SD 14.31 years, 67.0% male, 67.0% Black, 47.7% annual income ≤ $20,000) and administered surveys at three post trauma

timepoints: one week (T1), one month (T2; n = 61), and two months (T3; n = 59). Trauma type was assessed at T1 via electronic medical records. Participants reported the extent to which their dreams' content was similar to the trauma for which they were hospitalized across T1-T3. Participants then completed the PTSD Checklist for DSM-5 at T3.Results: TRNs were more prevalent over time among patients exposed to interpersonal violence (80%) vs non-interpersonal trauma (48.7%, p = .005). Patients hospitalized for interpersonal violence faced greater odds for TRNs across timepoints relative to non-interpersonal trauma patients (Odds Ratio = 4.95, p = .021). TRNs, in turn, prospectively predicted PTSD symptoms such that TRNs at T2 presaged more severe PTSD at T3 (p = .040, η(p)(2)= .31), above and beyond T1 PTSD status.Conclusions: This prospective study provides first evidence that interpersonal violence exposure is a robust risk factor for TRNs, which prospectively contribute to PTSD symptom development. Early intervention on TRNs after interpersonal violence exposure may decrease PTSD risk. Future studies are encouraged to use ambulatory methods to capture nightmares sooner after they occur. Interpersonal violence exposure is a risk factor for trauma-related nightmaresTrauma-related nightmares predict PTSD symptoms, above and beyond baseline PTSDTreating nightmares early after interpersonal violence may decrease PTSD risk.

Surgery

Bennett FJ, Keilson JM, Turgeon MK, Oppat KM, Warren EAK, Shah SA, Agopian VG, Magliocca JF, Cameron A, Orloff SL, Kubal CA, Cannon RM, Akoad ME, Emamaullee J, Aucejo F, Vagefi PA, Nguyen MH, Dhanireddy K, Kazimi MM, Sonnenday CJ, Foley DP, **Abdouljoud M**, Sudan DL, Humar A, Doyle MBM, Chapman WC, and Maithel SK. Racial Disparities in Liver Transplant for Hepatitis C-Associated Hepatocellular Carcinoma. *Ann Surg Oncol* 2024; Epub ahead of print. PMID: 39414703. Full Text

Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA, USA.
Department of Surgery, University of Cincinnati College of Medicine, Cincinnati, OH, USA.
Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA.
Department of Surgery, Johns Hopkins, Baltimore, MD, USA.
Department of Surgery, Oregon Health and Science University, Portland, OR, USA.
Department of Surgery, Indiana University Health, Indianapolis, IN, USA.
Department of Surgery, University of Alabama at Birmingham, Birmingham, AL, USA.
Department of Surgery, Lahey Hospital and Medical Center, Boston, MA, USA.
Department of Surgery, Keck Hospital of University of Southern California, Los Angeles, CA, USA.
Department of Surgery, Cleveland Clinic, Cleveland, OH, USA.
Department of Surgery, UT Southwestern Medical Center, Dallas, TX, USA.
Department of Medicine, Stanford University Medical Center, Palo Alto, CA, USA.
Department of Surgery, Tampa General Hospital, Tampa, FL, USA.
Department of Surgery, Piedmont Healthcare, Atlanta, GA, USA.
Department of Surgery, University of Michigan, Ann Arbor, MI, USA.
Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA.
Department of Surgery, Henry Ford Health System, Detroit, MI, USA.
Department of Surgery, Duke University School of Medicine, Durham, NC, USA.
Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA.
Department of Surgery, Washington University School of Medicine at St. Louis, St. Louis, MO, USA.
Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA, USA. smaithe@emory.edu.

BACKGROUND: In the United States, hepatitis C virus-associated hepatocellular carcinoma incidence and mortality are highest among minorities. Socioeconomic constraints play a major role in inequitable treatment. We evaluated the association between race/ethnicity and outcomes in a population that overcame treatment barriers. METHODS: We report a retrospective cohort study of 666 patients across 20 institutions in the United States Hepatocellular Carcinoma Liver Transplantation Consortium from 2015 to 2019 with hepatitis C virus-associated hepatocellular carcinoma who completed direct-acting antiviral therapy and underwent liver transplantation. Patients were excluded if they had a prior liver transplantation, hepatocellular carcinoma recurrence, no prior liver-directed therapy, or if race/ethnicity

data were unavailable. Patients were stratified by race/ethnicity. Primary outcomes were recurrence-free survival and overall survival, and secondary outcome was major postoperative complication. RESULTS: Race/ethnicity was not associated with differences in 5-year recurrence-free survival (White 90%, Black 88%, Hispanic 92%, Other 87%; p = 0.85), overall survival (White 85%, Black 84%, Hispanic 84%, Other 93%; p = 0.70), or major postoperative complication. CONCLUSIONS: Race/ethnicity was not associated with worse oncologic or postoperative outcomes among those who completed direct-acting antiviral therapy and underwent liver transplantation, suggesting that overcoming socioeconomic constraints equalizes outcomes across racial/ethnic groups. Eliminating barriers that prohibit care access among minorities must be a priority.

Surgery

Bennett FJ, Keilson JM, Turgeon MK, Oppat KM, Warren EAK, Shah SA, Agopian VG, Magliocca JF, Cameron A, Orloff SL, Kubal CA, Cannon RM, Akoad ME, Emamaullee J, Aucejo F, Vagefi PA, Nguyen MH, Dhanireddy K, Kazimi MM, Sonnenday CJ, Foley DP, **Abdouljoud M**, Sudan DL, Humar A, Doyle MBM, Chapman WC, and Maithel SK. ASO Visual Abstract: Racial Disparities in Liver Transplant for Hepatitis C-Associated Hepatocellular Carcinoma. *Ann Surg Oncol* 2024; Epub ahead of print. PMID: 39470892. Full Text

Winship Cancer Institute, Division of Surgical Oncology, Department of Surgery, Emory University, Atlanta, GA, USA.
Department of Surgery, University of Cincinnati College of Medicine, Cincinnati, OH, USA.
Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA.
Department of Surgery, Johns Hopkins, Baltimore, MD, USA.
Department of Surgery, Oregon Health and Science University, Portland, OR, USA.
Department of Surgery, Indiana University Health, Indianapolis, IN, USA.
Department of Surgery, University of Alabama at Birmingham, Birmingham, AL, USA.
Department of Surgery, Lahey Hospital and Medical Center, Boston, MA, USA.
Department of Surgery, Keck Hospital of University of Southern California, Los Angeles, CA, USA.
Department of Surgery, Cleveland Clinic, Cleveland, OH, USA.
Department of Surgery, UT Southwestern Medical Center, Dallas, TX, USA.
Department of Medicine, Stanford University Medical Center, Palo Alto, CA, USA.
Department of Surgery, Tampa General Hospital, Tampa, FL, USA.
Department of Surgery, Piedmont Healthcare, Atlanta, GA, USA.
Department of Surgery, University of Michigan, Ann Arbor, MI, USA.
Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA.
Department of Surgery, Henry Ford Health System, Detroit, MI, USA.
Department of Surgery, Duke University School of Medicine, Durham, NC, USA.
Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA.
Department of Surgery, Washington University School of Medicine at St. Louis, St. Louis, MO, USA.
Winship Cancer Institute, Division of Surgical Oncology, Department of Surgery, Emory University, Atlanta, GA, USA. smaithe@emory.edu.

Surgery

Chamseddine H, **Kadiyala D**, **Dobesh K**, Natour AK, **Shepard A**, **Nypaver T**, **Weaver M**, **Kavousi Y**, **Onofrey K**, and **Kabbani L**. Quality of Life Predictors in Patients with Acute Lower Limb Ischemia Quality of Life in Acute Limb Ischemia. *Ann Vasc Surg* 2024; 110(Pt A):137-143. PMID: 39343359. Full Text

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI. Electronic address: hchamse1@hfhs.org.
Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI.
Division of Vascular and Endovascular Surgery, Mayo Clinic, Rochester, MN.
Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI. Electronic address: lkabban1@hfhs.org.

BACKGROUND: While existing literature has established factors associated with improved health-related quality of life (HRQOL) in patients with chronic limb-threatening ischemia, similar work has not been done in individuals with acute lower limb ischemia (ALLI). This study aims to identify the factors associated with HRQOL in patients presenting with ALLI. METHODS: Using a prospectively collected registry, all patients who received treatment for ALLI between May 2016 and July 2023 at a quaternary medical center were identified and invited to complete two HRQOL questionnaires: the Vascular Quality of Life Questionnaire-6 (VascuQoL-6) and the EuroQol 5-Dimension 5-Level (EQ-5D-5L). Simple linear regression followed by multivariate analysis using multiple linear regression were used to determine the patient variables independently associated with HRQOL. RESULTS: Of the 216 eligible patients treated for ALLI during the study period, 47 (20%) of patients with a mean age of 58 ± 10 years completed the HRQOL questionnaires. Questionnaires were completed at a median time of 16.5 months after the episode of ALLI. On multiple linear regression, higher age was associated with higher VascuQoL-6 (P = 0.037) and EQ-5D-5L (P = 0.041) scores, while hypertension and nonambulatory status were significant predictors of lower VascuQoL-6 (P = 0.006, P = 0.013) and EQ-5D-5L (P = 0.009, P = 0.026) scores. Any ambulation had a significantly higher HRQOL compared to nonambulatory status, but no significant HRQOL difference was observed between patients with any type of ambulation (unhindered ambulation, ambulation with pain, and ambulation using a prosthesis). CONCLUSIONS: This study demonstrates that the ability to ambulate after ALLI, and not amputation per se, is an important predictor of HRQOL. As such, early rehabilitation strategies should be a focus of post-ALLI care. Further exploration of factors that shape HRQOL after ALLI is needed.

Surgery

Chamseddine H, **Shepard A**, **Nypaver T**, **Weaver M**, **Boules T**, **Kavousi Y**, **Onofrey K**, **Peshkepija A**, Hoballah J, and **Kabbani L**. National Trends and Outcomes of Pedal Bypass Surgery. *J Vasc Surg* 2024; Epub ahead of print. PMID: 39365192. Full Text

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI. Electronic address: hchamse1@hfhs.org.
Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI.
Division of Vascular Surgery, Department of Surgery, American University of Beirut Medical Center, Beirut, Lebanon.

OBJECTIVE: The technical demands associated with pedal bypass (PB) surgery place it at risk of underutilization and may be limiting its widespread adoption as a valuable revascularization modality. This study aims to evaluate trends in PB performance, assess its outcomes, and compare its results between high- and low-volume centers. METHODS: All patients receiving a PB between 2003 and 2023 were identified in the Vascular Quality Initiative (VQI) infrainguinal bypass (IIB) module. The ratio of PB to total IIB performed was calculated for each year and trended over the study period. Centers performing PB were categorized according to their annual PB volume into tertiles of low-volume centers (LVC, <2 PB/year), medium-volume centers (MVC, 2-4 PB/year), and high-volume centers (HVC, >4 PB/year) for comparison. Patient characteristics and outcomes were compared using the $\chi(2)$ or Fisher exact test as appropriate for categorical variables and the analysis of variance test or Kruskal-Wallis test as appropriate for continuous variables. Cox regression analysis was used to study the association between center volume and the primary outcomes of primary patency, primary-assisted patency, secondary patency, reintervention, amputation, and major adverse limb events (MALE), defined as the composite outcome of amputation and/or reintervention. RESULTS: A total of 3466 patients received a PB during the study period. The ratio of PB to IIB dropped from 14% to 4% between 2003 and 2023. Primary, primary-assisted, and secondary patency rates were 65%, 76%, and 80%, respectively, and limb salvage rate was 83% at 1 year. Nineteen percent of centers performing IIBs in the VQI did not perform any PBs during the study period. Of the 246 centers performing PBs, 78% were LVC, 15% were MVC, and only 7% were HVC. On Cox regression analysis, HVCs were associated with a lower risk of primary patency loss (hazard ratio [HR], 0.79; 95% confidence interval [CI], 0.66-0.95; P = .010), reintervention (HR, 0.75; 95% CI, 0.60-0.95; P = .016), amputation (HR, 0.77; 95% CI, 0.61-0.98; P = .034), and MALE (HR, 0.78; 95% CI, 0.66-0.93; P = .005) compared with LVCs. No difference in secondary patency between high- and low-volume centers was observed (P = .680). CONCLUSIONS: The utilization of PB operations experienced a four-fold decrease over the past 20 years, despite

favorable patency and limb salvage outcomes. Centers with a higher operative volume in PB achieve better outcomes than LVCs, and accordingly, patients with extensive tibioperoneal disease may benefit from evaluation at centers with documented expertise in PB before resorting to an alternative revascularization modality or a major limb amputation.

Surgery

Ciria R, **Ivanics T**, Aliseda D, Claasen M, Alconchel F, Gaviria F, Briceño J, Berardi G, Rotellar F, and Sapisochin G. Liver transplantation for primary and secondary liver tumours. patient-level meta-analyses compared to unos conventional indications. *Hepatology* 2024; Epub ahead of print. PMID: 39465987. Full Text

Unit of Hepatobiliary Surgery and Liver Transplantation. University Hospital Reina Sofia. University of Cordoba. IMIBIC. Cordoba. Spain.
Unit of Hepatobiliary Surgery. Hospital Quiron Salud. Cordoba. Spain.
Multi-Organ Transplant Program, University Health Network, Toronto, Ontario, Canada.
Department of Surgery, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Surgical Sciences, Uppsala University, Akademiska Sjukhuset, Uppsala, Sweden.
Hepatobiliary Surgery and Liver Transplant Unit. Clinica Universidad de Navarra. Pamplona. Spain.
Institute of Health Research of Navarra (IdisNA), Pamplona, Spain.
Department of Surgery, Erasmus MC, University Medical Center Rotterdam, the Netherlands.
Unit of Hepatobiliary Surgery and Liver Transplantation. Hospital Clínico Universitario Virgen Arrixaca. University of Medicine. IMIB-Pascual Parrilla. Murcia. Spain.
Division of General Surgery, University of Toronto, Toronto, Ontario, Canada.
General Surgery and Organ Transplantation Unit, San Camillo-Forlanini Hospital, Rome, Italy.

BACKGROUND AIMS: Liver transplant (LT) for Transplant Oncology (TO) indications is being slowly adopted worldwide and has been recommended to be incorporated cautiously due to concerns on mid-long term survival and its impact on waiting list. APPROACH RESULTS: We conducted four systematic reviews of all series on TO indications (intrahepatic (iCC) and perihilar cholangiocarcinoma (phCC)), liver metastases from neuroendocrine tumors (NET) and colorectal cancer (CRLM)) and compared them using patient-level meta-analyses to data obtained from UNOS database considering conventional daily-practice indications. Secondary analyses were done for specific selection criteria (Mayo-like protocols for phCC, SECA-2 for CRLM and Milan criteria for NET). A total of 112.014 LT were analyzed from 2005 to 2020 from the UNOS databases and compared with 345, 721, 494 and 103 patients obtained from meta-analyses on iCC and phCC, and liver metastases from NET and CRLM, respectively. Five-years overall survival was 53,3%, 56,4%, 68,6% and 53,8%, respectively. In Mantel-Cox one-to-one comparisons, survival of TO indications was superior to combined LT, second and third LT and and not statistically significant different to LT in recipients>70 years and high BMI. CONCLUSIONS: Liver transplantation for TO indications has adequate 5-years survival rates, mostly when performed under the selection criteria available in literature (Mayo-like protocols for phCC, SECA-2 for CRLM and Milan for NET). Despite concerns on its impact on waiting list, some other LT indications are being performed with lower survival. These oncological patients should be given the opportunity to have a definitive curative therapy within validated criteria.

Surgery

Diffley M, **Hall JMD**, **Tepper D**, and **Siddiqui A**. The Educational Benefits of Plastic Surgery Rotations for Off-Service Residents. *Adv Med Educ Pract* 2024; 15:999-1004. PMID: 39464207. Full Text

Department of General Surgery, Henry Ford Health, Detroit, MI, USA.
Division of Plastic Surgery, Henry Ford Health, Detroit, MI, USA.
Michigan State University, College of Human Medicine, Henry Ford Hospital, Detroit, MI, USA.

PURPOSE: With increasing specialization among surgical divisions, a well-rounded education during a surgical residency is often accomplished by rotating among different subspecialties. Inclusion of specific rotations in the resident curriculum can be considered as a cost-benefit calculation balancing the value of exposure to a subspecialty versus the opportunity cost of potential learning from another rotation. We find

that often these decisions are based on anecdotal feedback. Our goal is to supplement these reports with a quantifiable metric of learning achieved on the plastic surgery rotation. Our hypothesis in this prospective study was that residents would demonstrate improved performance on a post-rotation test after their 1-month rotation on plastic surgery compared to the pre-rotation test. METHODS: A question bank was developed to reflect institutional curriculum objectives and clinical scenarios commonly seen on the service. The questions were developed, validated and vetted in collaboration with medical educators and attending plastic surgeons yielding 20 questions available for use. Postgraduate year 1 residents were given a 10-question test before and after their plastic surgery rotation. A one-tailed paired t-test was used to assess improvement between the pre-rotation test and the post-rotation test. RESULTS: A total of 378 tests were administered with 228 (60%) pre- and post-rotation tests completed meeting inclusion criteria. Average percentage of correct answers for the pre-rotation test was 29% and 88% for the post-rotation test showing a differential improvement of 58% ($p < 0.001$). CONCLUSION: Surgical trainee time is a limited commodity. Each clinical rotation needs proven consistent benefit for the trainees. We developed a questionnaire that documents the improvement in clinical knowledge after a one-month rotation on plastic surgery relative to before. The test results were consistent even when comparing trainees who did the rotation early versus late in the PGY-1 year. Clinical exposure reinforces and solidifies specialty learning.

Surgery

Gutterman SA, Dinh DN, Bradley SE, Ross RA, Vitous CA, Obeid NR, **Varban OA**, and Suwanabol PA. The Role of Informal Social Support for Patients Undergoing Bariatric Surgery. *Obes Surg* 2024; Epub ahead of print. PMID: 39433605. Full Text

University of Michigan-Ann Arbor, Ann Arbor, USA. gutterman.sophie@gmail.com.
University of Michigan-Ann Arbor, Ann Arbor, USA.
Michigan Bariatric Surgery Collaborative, Ann Arbor, USA.
Henry Ford Health System, Detroit, USA.
University of Michigan-Ann Arbor, Ann Arbor, USA. pasuwan@med.umich.edu.

BACKGROUND: Bariatric surgery is underutilized as a treatment for metabolic disease and its associated comorbidities. While social support is known to play a crucial role in outcomes following bariatric surgery, little is known about the role of social support prior to surgery, which may impact preparedness for and willingness to undergo surgery. The study's objective was to examine the role of informal social support prior to bariatric surgery, the types of support received, and patient attitudes toward different demonstrations of support. METHODS: We conducted semi-structured interviews with patients who had previously undergone bariatric surgery (n = 20) from two high-volume bariatric surgery centers. Interviews focused on patient engagement with and attitudes about social support during the preoperative process. Transcripts from each interview were iteratively analyzed through steps informed by deductive and inductive thematic analysis. RESULTS: Four major themes emerged characterizing social support among patients undergoing bariatric surgery: (1) emotional support, (2) instrumental support, (3) informational support, and (4) self-support. Examples of meaningful support participants received included "cheerleading" (i.e., unconditional encouragement), advice from role models who had previously undergone surgery (e.g., receiving information on the process), shared experiences with loved ones regarding dietary and activity modifications (e.g., exercising with friends), and self-support measures (e.g., seeking therapy). CONCLUSIONS: A comprehensive understanding of how patients receive informal social support can offer valuable insights for individuals considering surgery. Further, such knowledge may enable providers to effectively counsel patients through the decision-making process and to ensure the establishment of support systems both pre- and post-surgery.

Surgery

Hutchings H, **Boyajian H**, and **Okereke I**. Reply: Achieving environmental justice will reduce lung cancer health disparities. *J Thorac Cardiovasc Surg* 2024; Epub ahead of print. PMID: 39387730. Full Text

Department of Surgery, Henry Ford Health, Detroit, Mich.

Surgery

McNamara DA, Albright J, Sukul D, Chetcuti S, Forrest A, Grossman P, **Alnajjar RM**, Patel H, Gurm HS, and Madder RD. Institutional Variation in Patient Radiation Doses During Transcatheter Valve Interventions: A Statewide Experience. *JACC Cardiovasc Interv* 2024; Epub ahead of print. PMID: 39453367. Full Text

Frederik Meijer Heart & Vascular Institute, Corewell Health West, Grand Rapids, Michigan, USA. Electronic address: david.mcnamara@corewellhealth.org.
Department of Internal Medicine, Division of Cardiovascular Medicine, University of Michigan, Ann Arbor, Michigan, USA.
Department of Cardiothoracic Surgery, Henry Ford Macomb, Clinton Township, Michigan, USA.
Frederik Meijer Heart & Vascular Institute, Corewell Health West, Grand Rapids, Michigan, USA.

BACKGROUND: Little is known about institutional radiation doses during transcatheter valve interventions. OBJECTIVES: The authors sought to evaluate institutional variability in radiation doses during transcatheter valve interventions. METHODS: Using a large statewide registry, transcatheter edge-to-edge mitral valve repair, transcatheter mitral valve replacement, and transcatheter aortic valve replacement procedures between January 1, 2020, and December 31, 2022, with an air kerma (AK) recorded were analyzed. Patient and procedural characteristics were compared between cases with AK ≥2 and <2 Gy. Associations of variables with AK ≥2 Gy were investigated using Bayesian random effects modeling and median ORs for the performing hospital. RESULTS: Among 9,446 procedures across 30 hospitals, median (Q1-Q3) procedural AK was 0.592 Gy (0.348-0.989 Gy) with AK ≥2 Gy in 533 cases (5.6%). Wide variation in procedural AK was observed, with an institutional frequency of AK ≥2 Gy ranging from 0.0% to 29.5%. Bayesian modeling identified the performing hospital as more strongly associated with the odds of a procedural AK ≥2 Gy than any patient or procedural factors (hospital median OR: 3.54 [95% credible interval: 2.52-16.66]). CONCLUSIONS: In a large, multicenter state-wide registry, there is wide institutional variability in patient-level radiation doses during transcatheter valve interventions, with the performing hospital having a higher odds of an AK ≥2 Gy than any patient or procedural factors. Future interventions are warranted to reduce procedural-related variation in radiation exposure.

Surgery

Mott NM, Zope M, Reynolds IS, Tadé Y, **Serra GP**, Long JJ, and Oslock WM. AJS virtual research mentor: Tips on writing an abstract for a conference. *Am J Surg* 2024; 116009. Epub ahead of print. PMID: 39419639. Full Text

National Clinician Scholars Program, University of Michigan, Ann Arbor, MI, USA; Veterans Affairs Center for Clinical Management Research, Ann Arbor, MI, USA.
University of Alabama at Birmingham, Department of Surgery, Birmingham, AL, USA.
Mayo Clinic, Department of Surgery, Division of Colon and Rectal Surgery, Rochester, MN, USA.
Creighton University School of Medicine, Omaha, NE, USA.
Henry Ford Health Macomb Hospital, Clinton Township, MI, USA.
Mayo Clinic, Department of Surgery, Rochester, MN, USA.
University of Alabama at Birmingham, Department of Surgery, Birmingham, AL, USA; Birmingham Veterans Affairs Medical Center, Department of Quality, Birmingham, AL, USA.

Surgery

Myszenski AL, **Divine G**, **Gibson J**, Samuel P, **Diffley M**, **Wang A**, and **Siddiqui A**. Risk Categories for Discharge Planning Using AM-PAC "6-Clicks" Basic Mobility Scores in Non-Surgical Hospitalized Adults. *Cureus* 2024; 16(9):e69670. PMID: 39429401. Request Article

Rehabilitation, Henry Ford Health System, Detroit, USA.
Public Health Sciences, Henry Ford Health System, Detroit, USA.
Occupational Therapy, Wayne State University, Detroit, USA.
Plastic and Reconstructive Surgery, Henry Ford Health System, Detroit, USA.
Surgery, Henry Ford Health System, Detroit, USA.

BACKGROUND: Early discharge planning is important for safe, cost-effective, and timely hospital discharges. Patients with deconditioning are at risk for prolonged lengths of stay related to discharge needs. Functional mobility outcome measures are associated with discharge disposition. The purpose of this study is to examine the clinical usefulness of risk categories based on the Activity Measure for Post-Acute Care (AM-PAC) "6-clicks" Basic Mobility (6cBM) scores on predicting discharge destination. METHODS: A retrospective cohort study of 3739 adults admitted to general medical units at an urban, academic hospital between January 1, 2018 and February 29, 2020 who received at least two physical therapy visits and had an AM-PAC 6cBM recorded within 48 hours of admission and before discharge. The outcome variable was discharge destination dichotomized to post-acute care facilities (PACF); inpatient rehabilitation, skilled nursing facility, or subacute rehabilitation) or home (with or without home care services). The predictor variables were 6cBM near admission and discharge. Logistic regression was used to estimate the odds of being discharged to PACF compared to home, based on the Three-level risk categorization system: (a) low (6cBM score > 20), (b) moderate (6cBM score 15-19), or (c) high (6cBM score < 14) risk. RESULTS: Analysis indicated important differences between the three risk categories in both time periods. Based on 6cBM at admission, patients in the high-risk category were nine times more likely to be discharged to PACF than those in the low-risk category. At discharge, those in the high-risk category were 29 times more likely to go to PACF than those in the low-risk category. Other characteristics differentiating patients who went to PACF were sex (males), age (older) and longer hospitalization. CONCLUSIONS: Predicting risk for discharge to a PACF using risk categories based on AM-PAC 6cBM can be useful for early discharge planning.

Surgery

Reffi AN, **Cheng P**, **Kalmbach DA**, **Moore DA**, **Mahr GC**, Seymour GM, **Solway M**, and **Drake CL**. Understanding nightmares after traumatic events in Detroit (UNiTED): prospective associations with interpersonal violence and posttraumatic stress disorder symptoms. *Eur J Psychotraumatol* 2024; 15(1):2409561. PMID: 39376120. Full Text

Sleep Disorders & Research Center, Henry Ford Health, Detroit, MI, USA.
Department of Psychiatry, Michigan State University College of Human Medicine, Grand Rapids, MI, USA.
Department of Surgery, Division of Acute Care Surgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Psychiatry and Behavioral Health, Division of Consultation Liaison Psychiatry, Henry Ford Hospital, Detroit, MI, USA.
Department of Psychology, University of Kentucky, Lexington, Kentucky, USA.
Department of Psychiatry, Henry Ford Hospital, Detroit, MI, USA.

ABSTRACTBackground: Research suggests trauma-related nightmares (TRNs) during the acute aftermath of trauma may contribute to posttraumatic stress disorder (PTSD). However, it is unknown who is most vulnerable to TRNs, which is critical to identify at-risk patients toward whom early nightmare-focused treatments can be targeted to prevent PTSD.Objective: We tested trauma type (interpersonal violence [e.g. assault] vs non-interpersonal trauma [e.g. motor vehicle collision]) as a risk factor for TRNs in a predominantly low-income, Black, urban sample in Detroit, MI, USA.Method: We recruited patients from the intensive care unit following traumatic injury (N = 88; M(age) = 39.53 ± SD 14.31 years, 67.0% male, 67.0% Black, 47.7% annual income ≤ $20,000) and administered surveys at three post trauma timepoints: one week (T1), one month (T2; n = 61), and two months (T3; n = 59). Trauma type was assessed at T1 via electronic medical records. Participants reported the extent to which their dreams' content was similar to the trauma for which they were hospitalized across T1-T3. Participants then completed the PTSD Checklist for DSM-5 at T3.Results: TRNs were more prevalent over time among patients exposed to interpersonal violence (80%) vs non-interpersonal trauma (48.7%, p = .005). Patients hospitalized for interpersonal violence faced greater odds for TRNs across timepoints relative to non-interpersonal trauma patients (Odds Ratio = 4.95, p = .021). TRNs, in turn, prospectively predicted PTSD symptoms such that TRNs at T2 presaged more severe PTSD at T3 (p = .040, η(p)(2)= .31), above and beyond T1 PTSD status.Conclusions: This prospective study provides first evidence that interpersonal violence exposure is a robust risk factor for TRNs, which prospectively contribute to PTSD symptom

development. Early intervention on TRNs after interpersonal violence exposure may decrease PTSD risk. Future studies are encouraged to use ambulatory methods to capture nightmares sooner after they occur. Interpersonal violence exposure is a risk factor for trauma-related nightmaresTrauma-related nightmares predict PTSD symptoms, above and beyond baseline PTSDTreating nightmares early after interpersonal violence may decrease PTSD risk.

Surgery

Simanovski J, Ralph J, and Morrell S. Key Associations Found in the Struggle With Sleep in Lung Transplant Recipients. *Prog Transplant* 2024; 15269248241289149. Epub ahead of print. PMID: 39403772. Full Text

Faculty of Nursing, University of Windsor, Windsor, Canada. RINGGOLD: 8637
Transplant Institute, Henry Ford Hospital, Detroit, MI, USA. RINGGOLD: 2971

INTRODUCTION: Gaps exist in the understanding of the etiology of poor sleep quality after lung transplantation. Research Question: What factors are associated with poor sleep quality in lung transplant recipients? DESIGN: A quantitative, single-site, cross-sectional study used an anonymous survey based on 3 scales. The Pittsburgh Sleep Quality Index scale with scores dichotomized to poor versus good sleepers based on the cutoff score > 8. The Hospital Anxiety and Depression Scale evaluated symptoms of anxiety and depression, and the Short Form-12 measured health-related quality of life using the mental and physical component scores. Additional self-reported data included demographic and transplant-related variables. RESULTS: The response rate was 38.4% (61/158), and 52.5% of the sample (32/61) evidenced a Pittsburgh Sleep Quality Index score > 8, suggestive of poor sleep quality. Bivariate analyses demonstrated that poor sleep was significantly related to symptoms of depression ($P < .01$), anxiety ($P < .01$), stressors of hospitalization ($P < .05$), and treatment of acute rejection ($P < .05$). Multivariate analysis demonstrated that anxiety was significantly associated with poor sleep (odds ratio = 1.34, $P < .05$). CONCLUSION: Poor subjective sleep quality remains prevalent in lung transplant recipients. Individuals with anxiety symptoms were at a greater risk for poor sleep. Guidance for strategies to improve sleep quality requires further in-depth exploration before implementation of interventions.

Urology

Bologna E, Licari LC, Badani KK, Razdan S, Psutka SP, Ditonno F, Ramos-Carpinteyro R, Soputro NA, Jackson JC, **Nelson R**, Rais-Bahrami S, White WM, Djaladat H, Pierorazio PM, Eun DD, Kutikov A, Margulis V, Kovac E, Kim IY, Anele UA, Mehrazin R, Ben-David R, Viers BR, Su LM, **Rogers CG**, **Abdollah F**, Ghazi A, Cherullo EE, Vourganti S, Coogan CL, Raman JD, Sundaram CP, Stifelman M, Link RE, Kaouk J, Crivellaro S, and Autorino R. The impact of single-port robotic surgery: a survey among urology residents and fellows in the United States. *J Robot Surg* 2024; 18(1):369. PMID: 39402405. Full Text

Department of Urology, Rush University Medical Center, 1725 W. Harrison Street, Suite 970, Chicago, IL, 60612, USA.
Department of Maternal-Child and Urological Sciences, Sapienza University Rome, Policlinico Umberto I Hospital, Rome, Italy.
Department of Urology, Icahn School of Medicine at Mount Sinai Hospital, New York, NY, USA.
Department of Urology, Miami Robotic Surgery at the Comprehensive Urologic Surgery Institute, Miami, FL, USA.
Department of Urology, University of Washington, Fred Hutchinson Cancer Center, Seattle, WA, USA.
Department of Urology, University of Verona, Verona, Italy.
Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, OH, USA.
Department of Urology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA.
Department of Urology, Henry Ford Macomb, Clinton Township, MI, USA.
Department of Urology, University of Alabama at Birmingham, Birmingham, AL, USA.
Department of Urology, University of Tennessee Medical Center, Knoxville, TN, USA.
Catherine and Joseph Aresty Department of Urology, Keck School of Medicine, USC, Los Angeles, CA, USA.
Division of Urology, Penn Medicine, University of Pennsylvania Health System, Philadelphia, PA, USA.

Department of Urology, Lewis Katz School of Medicine Temple University, Philadelphia, PA, USA.
Department of Urology, Fox Chase Cancer Center, Philadelphia, PA, USA.
Department of Urology, UT Southwestern Medical Center, Dallas, TX, USA.
Division of Urology, Department of Surgery, Rutgers New Jersey Medical School, Newark, NJ, USA.
Department of Urology, Yale School of Medicine, New Haven, CT, USA.
Department of Urology, University of Louisville Medical Center Louisville, Louisville, KY, USA.
Department of Urology, University of Louisville School of Medicine, Louisville, KY, USA.
Department of Urology, Mayo Clinic, Rochester, MN, USA.
Department of Urology, University of Florida, 1600 SW Archer Road, Room N202B, Gainesville, FL, USA.
Vattikuti Urology Institute, Henry Ford Health, Detroit, MI, USA.
Brady Urological Institute, Johns Hopkins University, Baltimore, MD, USA.
Department of Urology, Penn State Health, Hershey, PA, USA.
Department of Urology, Indiana University, Bloomington, IN, USA.
Department of Urology, Hackensack Meridian School of Medicine, Nutley, NJ, USA.
Scott Department of Urology, Baylor College of Medicine, Houston, TX, USA.
Department of Urology, University of Illinois at Chicago, Chicago, IL, USA.
Department of Urology, Rush University Medical Center, 1725 W. Harrison Street, Suite 970, Chicago, IL, 60612, USA. riccardo_autorino@rush.edu.

Our aim was to investigate the perception and future expectations of Single-Port (SP) surgery among urology trainees in the United States. A 34-item online survey was distributed to urological residency and fellowship programs across the US, covering demographic profiles, SP training opportunities, perceived educational impact, and future perspectives. Descriptive analysis and multivariable linear regression were used to assess predictors of SP adoption. 201 surveys were completed (28.6% completion rate). Among institutions with an SP platform, about 50% have used it regularly for over 2 years, though often in less than 50% of procedures. While robotic simulators are commonly available, only 17% offer both multi-port and SP simulators, and structured pre-clinical SP training is limited. Approximately 30% of respondents expressed concerns over limited hands-on experience and a steeper learning curve with SP. Around 40% felt that their robotic surgery exposure was negatively impacted by SP's introduction. SP surgery's benefits are seen mostly in the immediate post-operative period and a significant number of respondents foresee a major role for SP in urology. However, proficiency in SP surgery is not seen as crucial for career advancement or job opportunities. Academic job aspirations, SP platform availability, and SP surgery workload are predictors of future SP implementation. Trainees increasingly recognize the clinical benefits of SP procedures but express concerns about the potential negative impact on hands-on experience. Training programs should more systematically integrate SP technology into curricula. There is a correlation between training in high-volume SP centers and future SP adoption.

Urology

Cannarella R, Shah R, Ko E, Kavoussi P, **Rambhatla A**, Hamoda TAA, Saleh R, Harraz AM, Calogero AE, Durairajanayagam D, Toprak T, Calik G, Crafa A, Gunes S, Gherabi N, Kuroda S, Kandil H, Gül M, Boitrelle F, Ghayda RA, Kosgi R, Karthikeyan VS, Russo GI, Cayan S, Singh R, Chung E, Giulioni C, Busetto GM, and Agarwal A. Effects of Varicocele Repair on Testicular Endocrine Function: A Systematic Review and Meta-Analysis. *World J Mens Health* 2024; Epub ahead of print. PMID: 39434394. Full Text

Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy.
Glickman Urological & Kidney Institute, Cleveland Clinic Foundation, Cleveland, OH, USA.
Global Andrology Forum, Moreland Hills, OH, USA.
Division of Andrology, Department of Urology, Lilavati Hospital and Research Centre, Mumbai, India.
Department of Urology, Loma Linda University Health, Loma Linda, CA, USA.
Austin Fertility & Reproductive Medicine/Westlake IVF, Austin, TX, USA.
Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI, USA.
Department of Urology, King Abdulaziz University, Jeddah, Saudi Arabia.
Department of Urology, Faculty of Medicine, Minia University, Minia, Egypt.
Department of Dermatology, Venereology and Andrology, Faculty of Medicine, Sohag University, Sohag, Egypt.
Ajyal IVF Center, Ajyal Hospital, Sohag, Egypt.

Mansoura University Urology and Nephrology Center, Mansoura, Egypt.
Department of Surgery, Urology Unit, Farwaniya Hospital, Farwaniya, Kuwait.
Department of Urology, Sabah Al Ahmad Urology Center, Kuwait City, Kuwait.
Department of Physiology, Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh Campus, Selangor, Malaysia.
Department of Urology, University of Health Sciences, Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Türkiye.
Department of Urology, Istanbul Medipol University, Istanbul, Türkiye.
Department of Medical Biology, Medical Faculty, Ondokuz Mayis University, Samsun, Türkiye.
Department of Medicine, University of Algiers 1, Algiers, Algeria.
Fakih IVF Fertility Center, Abu Dhabi, UAE.
Department of Urology, Selçuk University School of Medicine, Konya, Türkiye.
Reproductive Biology, Fertility Preservation, Andrology, CECOS, Poissy Hospital, Poissy, France.
Department of Biology, Reproduction, Epigenetics, Environment and Development, Paris Saclay University, UVSQ, INRAE, BREED, Jouy-en-Josas, France.
Urology Institute, University Hospitals, Case Western Reserve University, Cleveland, OH, USA.
Department of Andrology & Men's Health, Apollo Hospitals, Hyderabad, India.
Andrology Unit, Department of Urology, Apollo Hospitals, Chennai, India.
Urology Section, Department of Surgery, University of Catania, Catania, Italy.
Department of Urology, University of Mersin School of Medicine, Mersin, Türkiye.
Division of Endocrinology, Central Drug Research Institute, Lucknow, India.
Department of Urology, Princess Alexandra Hospital, University of Queensland, Brisbane, Australia.
Department of Urology, Polytechnic University of Marche, Ancona, Italy.
Department of Urology and Organ Transplantation, University of Foggia, Foggia, Italy.
Cleveland Clinic, Cleveland, OH, USA. agarwaa32099@outlook.com.

PURPOSE: The objective of this manuscript is to assess the effect of varicocele repair (VR) in patients with clinical varicoceles on serum total testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and inhibin B serum levels. MATERIALS AND METHODS: The study was performed in compliance with the Meta-Analysis and Systematic Reviews of Observational Studies (MOOSE) guidelines and the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P). All eligible studies were selected following the PICOS (Population, Intervention, Comparison/Comparator, Outcomes, Study design) model. The values of each outcome measured after VR were compared to the before parameters and, when available, to the values on patients with unrepaired varicocele, and to those of healthy controls with no varicocele. For total testosterone, the values were sub-analyzed based on the mean total testosterone levels before VR (<300 ng/dL or >300 ng/dL), the fertility status, the time of follow-up and the technique used for VR. RESULTS: From a total of 460 abstracts retrieved, 48 articles were included in our meta-analysis. Serum total testosterone levels were significantly higher after VR compared to both pre-treatment levels (mean difference [MD] 82.45 ng/dL, 95% confidence interval [CI]: 64.14-100.76; p<0.00001) and to the levels of patients with unrepaired varicocele (MD 91.64 ng/dL, 95% CI: 62.30-120.99; p<0.00001). They did not differ from the levels of healthy controls with no varicocele (MD -22.01 ng/dL, 95% CI: -68.59-24.58; p=0.35). The increase resulted to be independent from the mean total testosterone levels before VR, fertility status, time of follow-up and type of VR. After VR, a trend toward lower serum LH levels was found compared to before values (MD -0.37 IU/L, 95% CI: -0.74-0.01; p=0.06). When compared to the levels of patients with unrepaired VR, LH levels after VR were significantly lower (MD -0.96 IU/L, 95% CI: -1.56 to -0.35; p=0.002). LH levels were not significantly higher than healthy men without varicocele (MD 0.84 IU/L, 95% CI: -0.68-2.36; p=0.28). Patients with VR had significantly lower FSH levels compared to their pre-treatment values (MD -1.43 IU/L, 95% CI: -1.82 to -1.04; p<0.00001), and also to those of patients with non-repaired varicocele (MD -2.35 IU/L, 95% CI: -4.06 to -0.65; p=0.007). When compared to healthy controls with no varicocele, FSH levels were significantly higher (MD 2.71 IU/L, 95% CI: 1.12-4.31; p=0.0009). Lastly, after VR no significant change in inhibin B serum levels was seen compared to pre-treatment levels (MD 11.76 pg/mL, 95% CI: -3.83-27.35; p=0.14). CONCLUSIONS: The present meta-analysis is the largest to date to assess the impact of VR on Leydig cell and Sertoli cell function using a before-after analysis for uncontrolled studies, and using data from patients with unrepaired varicoceles or healthy patients without varicocele as controls. VR was found to increase and restore to normality serum

levels of total testosterone and LH. This evidence could be of value in considering the treatment of varicocele in patients with low testosterone or those who show a progressive decline in testosterone levels.

Urology

Cirulli GO, **Davis M**, **Stephens A**, **Chiarelli G**, **Finati M**, **Chase M**, **Tinsley S**, **Arora S**, Sood A, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Midlife baseline prostate-specific antigen, velocity, and doubling time association with lethal prostate cancer and mortality. *Cancer* 2024; Epub ahead of print. PMID: 39377255. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, Michigan, USA.
Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Public Health Sciences, Henry Ford Health System, Detroit, Michigan, USA.
Department of Urology, IRCCS Humanitas Research Hospital, Humanitas University, Milan, Italy.
Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
Department of Urology, The James Cancer Hospital and Solove Research Institute, The Ohio State University Wexner Medical Center, Columbus, Ohio, US.

BACKGROUND: Midlife baseline prostate-specific antigen (MB PSA), defined as a single PSA value measured between 40-59 years of age, has been proposed as a tool that can limit potential harms of PSA screening. This study aimed to examine the ability of MB PSA versus PSA doubling time (PSADT) and PSA velocity (PSAV) in assessing the likelihood of developing of lethal prostate cancer (PCa) in a diverse and contemporary North American population. METHODS: Men 40-59 years old, who received their first PSA between the years 1995 and 2019, were included. For MB PSA values, the first PSA test result was included. For PSADT, the first two PSA test results were included. For PSAV, the first three PSA test results within 30 months were included. Selection criteria resulted in a total of 77,594 patients with at least two PSA test results and 11,634 patients with at least three PSA test results. Multivariable Fine-Gray regression was used to examine the impact of the value of the PSA testing methods on the development of lethal PCa (defined as death from PCa or development of metastatic disease either at diagnosis or during follow-up). Time-dependent receiver operating characteristic/area under the curve (AUC) at 5, 10, and 15 years were plotted. RESULTS: In the main cohort, patients were most frequently in the 50-54 age category (32.8%), had a Charlson comorbidity index of 0 (70.5%), and were White (63.2%). Of these, 9.3% had the midlife baseline PSA in the top 10th percentile, and 0.4% had a PSADT 0-6 months. Lethal PCa was diagnosed in 593 (0.8%) patients. The median (interquartile range) time to lethal PCa was 8.6 (3.2-14.9) years. In the main cohort, MB PSA and PSADT showed significant associations with the occurrence of lethal PCa, with a hazard ratio (HR) of 6.10 (95% confidence interval [CI], 4.85-7.68) and HR of 2.20 (95% CI, 1.07-4.54) for patients in the top 10th percentile MB PSA group and in the PSADT between 0 to <6 months group, respectively. In patients with three PSA results available, MB PSA and PSAV showed significant associations with the occurrence of lethal PCa, with a HR of 3.95 (95% CI, 2.29-6.79) and 3.57 (95% CI, 2.17-5.86) for patients in the top 10th percentile MB PSA group and in the in the PSAV >0.4 ng/mL/year group, respectively. PSADT and PSAV did not exhibit higher AUCs than MB PSA in assessing the likelihood of lethal PCa. Specifically, they were 0.818 and 0.708 at 10 and 15 years, respectively, for the PSADT; 0.862 and 0.756 at 10 and 15 years, respectively, for the PSAV; and 0.868 and 0.762 at 10 and 15 years, respectively, for the MB PSA (all $p > .05$). CONCLUSIONS: The study findings are that PSAV or PSADT were not superior to midlife baseline in assessing the likelihood of developing lethal PCa. This suggests that these variables may not have practical use in enhancing PSA screening strategies in a clinical setting.

Urology

Etta P, **Chien M**, **Wang Y**, and **Patel A**. Robotic partial nephrectomy: Indications, patient selection, and setup for success. *Urol Oncol* 2024; Epub ahead of print. PMID: 39424432. Full Text

Henry Ford Health, Detroit, MI.
Henry Ford Health, Detroit, MI. Electronic address: apatel28@hfhs.org.

Robot-assisted partial nephrectomy (RAPN) has readily become the benchmark treatment of small renal masses (SRMs). The management of SRMs is focused on preserving renal function and limiting the morbidity of a traditional open operation, thus greatly impacting overall prognosis and long-term survival. Indications and techniques have evolved over the last 2 decades. In this article, we discuss the application of this nephron-sparing technique regarding its indications, surgical considerations, and functional outcomes.

Urology

Finati M, Morrison C, **Stephens A**, **Chiarelli G**, **Cirulli GO**, **Tinsley S**, **Davis M**, Sood A, **Buffi N**, **Lughezzani G**, Salonia A, Briganti A, Montorsi F, Busetto GM, Bettocchi C, **Rogers C**, Carrieri G, and **Abdollah F**. Association of race with incidence, characteristics, and mortality from incidental prostate cancer: Analysis of two North American contemporary cohorts. *Prostate* 2024; e24803. Epub ahead of print. PMID: 39465565. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health, Detroit, Michigan, USA.
Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
Wayne State University School of Medicine, Detroit, Michigan, USA.
Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA.
Department of Biomedical Sciences, Humanitas University, Milan, Italy.
Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Department of Urology, The James Cancer Hospital and Solove Research Institute, The Ohio State University Wexner Medical Center, Columbus, Ohio, USA.
Vattikuti Urology Institute, Henry Ford Health, Detroit, Michigan, USA.

BACKGROUND: Non-Hispanic Black (NHB) men are at higher risk both for incidence and mortality from prostate cancer (PCa) compared to Non-Hispanic White (NHW) men, but these findings arise from biopsy-detected PCa reports. We aimed to compare the incidence, subsequent management and cancer-specific mortality (CSM) of incidental PCa among NHB and NHW men, using two different North American cohorts. METHODS: The Surveillance, Epidemiology and End-Result (SEER: 2004-2017) and our institutional Henry Ford Health (HFH: 1995-2022) databases were queried to identify men diagnosed with incidental PCa. Cumulative incidence estimates were used to calculate CSM differences between NHB and NHW men. Competing-risk multivariable regression analysis tested the impact of race on CSM, after accounting for all available covariates. RESULTS: A total of 418 and 6,124 incidental PCa cases were recorded in HFH and SEER database respectively. No pathological differences were observed between NHB and NHW men in both the cohorts, except for prostate-specific antigen (PSA) value at diagnosis, which was higher in NHB men. At 10-years, the CSM rates were 5.5% vs 7.2% in our cohort and 8.6% vs 10.3% in the SEER cohort for NHW and NHB men, respectively (all Gray's test p-value > 0.05). At multivariable, race was not an independent predictor of CSM in our HFH cohort (HR: 1.46, 95% CI: 0.57-3.71, p = 0.6). In the SEER cohort, NHB men were 34% less likely to die from PCa from 1 year to the next (95% CI: 0.49-0.90, p = 0.008), when compared with NHW men. CONCLUSIONS: In the comparison of incidental PCa findings between NHB and NHW men, both groups had similar pathological characteristic and survival outcomes. These findings are different from the 'conventional' screening-detected PCa and suggest that racial differences have minimal to no adverse effects on PCa-specific mortality after incidental diagnosis.

Urology

Fletcher SA, Pallauf M, Watts EK, Lombardo KA, Campbell JA, Rezaee ME, Rouprêt M, Boorjian SA, Potretzke AM, Roshandel MR, Ploussard G, Djaladat H, Ghoreifi A, Mari A, Campi R, Khene ZE, Raman JD, Kikuchi E, Rink M, **Abdollah F**, Boormans JL, Fujita K, D'Andrea D, Soria F, Breda A, Hoffman-Censits J, McConkey DJ, Shariat SF, Pradere B, and Singla N. Carcinoma Following Neoadjuvant Chemotherapy Oncologic Outcomes in Patients with Residual Upper Tract Urothelial. *Eur Urol Oncol* 2024; 7(5):1061-1068. PMID: Not assigned. Full Text

Background and objective: Growing evidence supports the use of neoadjuvant chemotherapy (NAC) for upper tract urothelial carcinoma (UTUC). However, the implications of residual UTUC at radical nephroureterectomy (RNU) after NAC are not well characterized. Our objective was to compare oncologic outcomes for pathologic risk-matched patients who underwent RNU for UTUC who either received NAC or were chemotherapy-na & iuml;ve. Methods: We retrospectively identified 1993 patients (including 112 NAC recipients) who underwent RNU for nonmetastatic, high-grade UTUC between 1985 and 2022 in a large, international, multicenter cohort. We divided the cohort into low-risk and high-risk groups defined according to pathologic findings of muscle invasion and lymph node involvement at RNU. Recurrence-free survival (RFS), overall survival (OS), and cancer-specific survival (CSS) estimates were calculated using the Kaplan-Meier method. Multivariable analyses were performed to determine clinical and demographic factors associated with these outcomes. Key findings and limitations: Among patients with low-risk pathology at RNU, RFS, OS, and CSS were similar between the NAC and chemotherapy-na & iuml;ve groups. Among patients with high-risk pathology at RNU, the NAC group had poorer RFS (hazard ratio [HR] 3.07, 95% confidence interval [CI] 2.10-4.48), OS (HR 2.06,95% CI 1.33-3.20), and CSS (subdis- tribution HR 2.54, 95% CI 1.37-4.69) in comparison to the pathologic risk-matched, chemotherapy-na & iuml;ve group. Limitations include the lack of centralized pathologic review. Conclusions and clinical implications: Patients with residual invasive disease at RNU after NAC represent a uniquely high-risk population with respect to oncologic outcomes. There is a critical need to determine an optimal adjuvant approach for these patients. Patient summary: We studied a large, international group of patients with cancer of the upper urinary tract who underwent surgery either with or without receiving chemotherapy beforehand. We identified a high-risk subgroup of patients with residual aggressive cancer after chemotherapy and surgery who should be prioritized for clinical trials and drug development.

Urology
Majdalany SE, **Butaney M**, **Tinsley S**, **Corsi N**, **Arora S**, **Rogers CG**, and **Abdollah F**. Challenges of Urologic Oncology in Low-to-Middle-Income Countries. *Soc Int Urol J* 2024; 5(5):303-311. PMID: Not assigned. Full Text

VCORE—Vattikuti Urology Institute Center for Outcomes Research, Analytics and Evaluation, Henry Ford Hospital, Detroit, MI 48202, USA
Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI 48202, USA
School of Medicine, Wayne State University, Detroit, MI 48202, USA

Urology
Rambhatla A, Shah R, Pinggera GM, Mostafa T, Atmoko W, Saleh R, Chung E, Hamoda T, Cayan S, Jun Park H, Kadioglu A, Hubbard L, and Agarwal A. Pharmacological therapies for male infertility. *Pharmacol Rev* 2024; Epub ahead of print. PMID: 39433442. Full Text

Department of Urology,, Henry Ford Health System, United States.
Division of Andrology, Department of Urology,, Lilavati Hospital and Research Centre,, Mexico.
Innsbruck Medical University, Austria.
Faculty of Medicine, Cairo University, Egypt.
Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital, Indonesia.
Faculty of Medicine, Sohag University,, Egypt.
Urology, University of Queensland, Australia.
King Abdulaziz University, Saudi Arabia.
University of Mersin School of Medicine, Turkey.
Medical Research Institute of Pusan National University Hospital, Korea, Democratic People's Republic of.
Istanbul University, Turkey.
Thomas Jefferson University, United States.
Global Andrology Forum, United States agarwaa32099@outlook.com.

Male factor infertility is a multifaceted problem that affects approximately 50% of couples suffering from infertility. Causes of male infertility include endocrine disturbances, gonadotoxins, genetic abnormalities,

varicocele, malignancies, infections, congenital or acquired urogenital abnormalities, iatrogenic factors, immunological factors, and idiopathic reasons. There are a variety of treatment options for male infertility, depending on the underlying cause(s). These can include surgical treatments, medical/hormonal therapies, and assisted reproductive techniques (ART), which can be combined with surgical sperm retrieval (SSR) if necessary. In this review article, the pharmacological therapies for male infertility are grouped by their underlying causes. Some of these therapies are targeted and specific, while others are used empirically to treat idiopathic male infertility. This will include treatments to optimize infertility in patients who have hypogonadism, ejaculatory dysfunction, infections, or idiopathic male infertility. Finally, we will provide an overview of the future directions of pharmacological therapies for male infertility. Significance Statement Male infertility is a significant worldwide problem. Detailed knowledge of the pharmacological therapies available will ensure the prescription of appropriate therapy and avoid the use of unnecessary or harmful treatments.

Urology

Ramos-Carpinteyro R, Soputro N, Pedraza AM, Calvo RS, Raver M, Manfredi C, **Wang Y**, Chavali JS, Okhawere K, Mikesell C, Ferguson E, Stifelman M, Badani KK, Autorino R, **Rogers C**, Ahmed M, Schwen ZR, Crivellaro S, and Kaouk J. Incidental prostate carcinoma after single-port robot-assisted simple prostatectomy: a multi-institutional report (SPARC). *Minerva Urol Nephrol* 2024; 76(5):588-595. PMID: 39320249. Request Article

Department of Urology, Cleveland Clinic, Cleveland, OH, USA.
Department of Urology, University of Illinois, Chicago, IL, USA.
Department of Urology, Hackensack University Medical Center, Hackensack, NJ, USA.
Department of Urology, RUSH University Medical Center, Chicago, IL, USA.
Department of Urology, Henry Ford Health, Detroit, MI, USA.
Department of Urology, The Mount Sinai Hospital, New York, NY, USA.
Department of Urology, Hackensack Meridian School of Medicine Nutley, Nutley, NK, USA.
Department of Urology, Cleveland Clinic, Cleveland, OH, USA - kaoukj@ccf.org.

BACKGROUND: Single-port robot-assisted simple prostatectomy is a minimally invasive alternative for patients with large benign prostatic hyperplasia with severe symptoms and/or failure of medical treatment. In recent literature, the rate of incidental prostate cancer after simple prostatectomy ranges from 1.8% to 13.0%. Our objective is to report the rate of incidental prostate cancer after single-port robot-assisted simple prostatectomy and to compare our findings to other approaches. METHODS: A Single-Port Advanced Research Consortium [SPARC] multi-institutional retrospective analysis of all initial consecutive single-port robot-assisted simple prostatectomy cases performed from 2019 to 2023 by eleven surgeons from six centers. Our primary outcome was the rate of incidental prostate cancer in adenoma specimens. We used descriptive statistics to analyze the data. RESULTS: A total of 235 cases were performed successfully without conversions or additional ports. Eleven patients (4.6%) were found to have incidental prostate cancer on pathological analysis. The median percentage of tissue involved by the tumor was 5%. The overall rate of clinically significant prostate cancer was 2.1%. Most cases were Gleason Grade Group 1 (55%). Those with Grade Group ≤3 were subsequently managed with active surveillance with a median follow-up of 17 months. A patient with Gleason Grade Group 4 underwent an uncomplicated multi-port robot-assisted radical prostatectomy with satisfactory functional and oncological outcomes. CONCLUSIONS: Initial multi-institutional experience with single-port robot-assisted simple prostatectomy showed an incidental prostate cancer rate of 4.6%, comparable to MP, laparoscopic, and open techniques.

Urology

Tuderti G, Mastroianni R, Proietti F, Wu Z, Wang L, Franco A, **Abdollah F**, **Finati M**, Ferro M, Tozzi M, Porpiglia F, Checcucci E, Bhanvadia R, Margulis V, Bronimann S, Singla N, Hakimi K, Derweesh IH, Correa A, Helstrom E, Mendiola DF, Gonzalgo ML, David RB, Mehrazin R, Moon SC, Rais-Bahrami S, Yong C, Sundaram CP, Tufano A, Perdonà S, Ghoreifi A, Moghaddam FS, Djaladat H, Ditonno F, Antonelli A, Autorino R, and Simone G. Role of neoadjuvant chemotherapy in patients with locally advanced and clinically positive nodes Upper Tract Urothelial Carcinoma treated with Nephroureterectomy: real-world data from the ROBUUST 2.0 Registry. *World J Urol* 2024; 42(1):575. PMID: 39395052. Full Text

Department of Urology, IRCCS "Regina Elena" National Cancer Institute, Via Elio, Chianesi 53, Rome, Italy. gabriele.tuderti@gmail.com.
Department of Urology, IRCCS "Regina Elena" National Cancer Institute, Via Elio, Chianesi 53, Rome, Italy.
Department of Urology, Changhai Hospital, Naval Medical University, Shanghai, China.
Department of Urology, Rush University, Chicago, IL, USA.
Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA.
Division of Urology, European Institute of Oncology (IEO)-IRCCS, Milan, Italy.
Division of Urology, University of Turin, San Luigi Gonzaga Hospital, Turin, Italy.
Department of Surgery, Candiolo Cancer Institute, FPO-IRCCS, Candiolo, Italy.
Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX, USA.
The James Buchanan Brady Urological Institute and Department of Urology, Johns Hopkins University School of Medicine, Baltimore, MD, USA.
Department of Urology, UC San Diego School of Medicine, La Jolla, CA, USA.
Department of Surgical Oncology, Division of Urologic Oncology, Fox Chase Cancer Center, Philadelphia, USA.
Desai Sethi Urology Institute, University of Miami Miller School of Medicine, Miami, FL, USA.
Department of Urology, Icahn School of Medicine at Mount Sinai Hospital, New York, NY, USA.
Department of Urology, University of Alabama at Birmingham, Birmingham, AL, USA.
Department of Urology, Indiana University, Indianapolis, IN, USA.
Uro-Gynecological Department, Fondazione "G. Pascale" IRCCS, Naples, Italy.
Norris Comprehensive Cancer Center, Institute of Urology, University of Southern California, Los Angeles, USA.
Department of Urology, University of Verona, Verona, Italy.

PURPOSE: To assess the impact of neoadjuvant and adjuvant chemotherapy on survival outcomes, within a large multicenter cohort of Upper tract urothelial carcinoma patients treated with Nephroureterectomy. METHODS: A multicenter retrospective analysis utilizing the Robotic surgery for Upper Tract Urothelial Cancer Study registry was performed. Baseline, preoperative, perioperative, and pathologic variables of three groups of patients receiving surgery only, neoadjuvant or adjuvant chemotherapy were compared. Categorical and continuous variables among the three subgroups were compared with Chi square and ANOVA tests. The impact of perioperative chemotherapy on survival outcomes was assessed with the Kaplan Meier method. Univariable and multivariable Cox regression analyses were performed to identify predictors of survival. RESULTS: Overall, 1,994 patients were included. Overall and Clavien grade ≥3 complications rates were comparable among the three subgroups ($p = 0.65$ and $p = 0.92$). At Kaplan Meier analysis, neoadjuvant chemotherapy significantly improved cancer-specific survival ($p = 0.03$) and overall survival ($p = 0.03$) probabilities of patients with $cT \geq 3$ tumors and of those with positive cN ($p = 0.03$ and $p = 0.02$). On multivariable analysis, neoadjuvant chemotherapy was independently associated with an improvement of cancer-specific survival in $cT \geq 3$ patients (HR 0.44; $p = 0.04$), and of both cancer-specific survival (HR 0.50; $p = 0.03$) and overall survival (HR 0.53; $p = 0.02$) probabilities in positive cN patients. CONCLUSIONS: This large multicenter retrospective analysis suggests significant survival benefit in Upper tract urothelial carcinoma patients with either locally advanced or clinically positive nodes disease receiving neoadjuvant chemotherapy. These findings can be regarded as "hypothesis generating", stimulating future trials focusing on such advanced stages.

Urology

Vellaichamy G, Poulik J, **Palanisamy N**, **Kis O**, **Fang X**, **Al-Obaidy KI**, **Shwayder TA**, and **Friedman BJ**. Spitz-Type Proliferative Nodules Arising Within a Large Congenital Melanocytic Nevus Harboring a Novel LMNA-RAF1 Fusion. *J Cutan Pathol* 2024; Epub ahead of print. PMID: 39462150. Full Text

Department of Dermatology, Henry Ford Health, Detroit, Michigan, USA.
Detroit Medical Center, Children's Hospital of Michigan, Detroit, Michigan, USA.
Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, Michigan, USA.
Department of Pathology & Laboratory Medicine, Henry Ford Health, Detroit, Michigan, USA.

Urology

Yoshida T, Motoki Y, **Rogers CG**, Raza J, Nakamoto T, Matsuda T, and Kinoshita H. Photodynamic Diagnosis-Guided Ureteroscopic Laser Ablation of Upper Urinary Tract Urothelial Carcinoma: Phase 2, Open-Label, Single-Arm Trial. *Ann Surg Oncol* 2024; Epub ahead of print. PMID: 39402321. Full Text

Department of Urology and Andrology, Kansai Medical University, Osaka, Japan. yoshidtk@takii.kmu.ac.jp.
Graduate School of Engineering, Tottori University, Tottori, Japan. yoshidtk@takii.kmu.ac.jp.
Department of Urology, Osaka Saiseikai-Noe Hospital, Osaka, Japan. yoshidtk@takii.kmu.ac.jp.
Corporate Sponsored Research Programs for Multicellular Interactions in Cancer, Kansai Medical University, Osaka, Japan. yoshidtk@takii.kmu.ac.jp.
Department of Urology and Andrology, Kansai Medical University, Osaka, Japan.
Vattikuti Urology Institute, Henry Ford Health, Detroit, MI, USA.

Urology

Zappia J, Yong C, Slaven J, Wu Z, Wang L, Djaladat H, Wood E, Ghoreifi A, **Abdollah F**, **Davis M**, **Stephens A**, Simone G, Tuderti G, Gonzalgo ML, Mendiola DF, Derweesh IH, Dhanji S, Hakimi K, Margulis V, Taylor J, Ferro M, Tozzi M, Autorino R, Pandolfo SD, Mehrazin R, Eilender B, Porpiglia F, Checcucci E, and Sundaram CP. Survival Outcomes by Race Following Surgical Treatment for Upper Tract Urothelial Carcinoma. *Clin Genitourin Cancer* 2024; 22(6):102220. PMID: 39332082. Full Text

Department of Urology, Indiana University, Indianapolis, IN. Electronic address: jzappia@iu.edu.
Department of Urology, Indiana University, Indianapolis, IN.
Department of Biostatistics and Health Data Science, Indiana University, Indianapolis, IN.
Department of Urology, Changhai Hospital, Naval Medical University, SH, China.
Norris Comprehensive Cancer Center, Institute of Urology, University of Southern California, Los Angeles, CA.
Henry Ford Hospital, Vattikuti Urology Institute, Detroit, MI.
Department of Urology, IRCCS "Regina Elena" National Cancer Institute, Rome, Italy.
Desai Sethi Urology Institute, University of Miami Miller School of Medicine, Miami, FL.
Department of Urology, UC San Diego School of Medicine, La Jolla, CA.
Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX.
Division of Urology, European Institute of Oncology (IEO)-IRCCS, Milan, Italy.
Division of Urology, Rush University, Chicago, IL.
Division of Urology, VCU Health, Richmond, VA.
Department of Urology, Icahn School of Medicine at Mount Sinai Hospital, New York, NY.
Division of Urology, University of Turin, San Luigi Gonzaga Hospital, Turin, Italy.

OBJECTIVE: Discrepancies in survival outcomes of various genitourinary tract malignancies have been documented across different racial and ethnic groups. Here we sought to examine long-term survival outcomes of patients with upper tract urothelial carcinoma (UTUC) following radical nephroureterectomy (RNU) when stratified by race. METHODS: A multicenter retrospective analysis using the ROBUUST (ROBotic surgery for Upper tract Urothelial cancer Study) registry identified patients undergoing RNU for UTUC between 2015 and 2022 at 12 centers across the United States, Europe, and Asia. Patients were stratified by race (white, black, Hispanic, and Asian) and primary outcomes of interest-including recurrence-free survival (RFS), metastasis free survival (MFS) and overall survival (OS) - were assessed

using univariate analysis, multivariate Cox regression modeling, and Kaplan-Meier analysis. RESULTS: 1446 patients (white n = 652, black n = 70, Hispanic n = 87, and Asian n = 637) who underwent RNU for treatment of the UTUC were included in our analysis. Cox regression modeling demonstrated pathologic nodal staging to be a significant predictor of RFS (HR 2.25; P = .0010), MFS (HR 2.50; P = .0028), and OS (HR 5.11; P < .0001). When using whites as the reference group, there were no significant differences in RFS, MFS, or OS across racial groups. CONCLUSIONS: Unlike other genitourinary tract malignancies, our study failed to demonstrate a survival disadvantage among minority racial groups with UTUC who underwent RNU. Furthermore, a significant difference in RFS, MFS, and OS was not identified across whites, blacks, Asians, or Hispanics with UTUC who underwent RNU.

Urology

Zohdy W, Shah R, Ho CCK, Calik G, Malhotra V, Erkan BK, Duran MB, Tsampoukas G, Radion G, Saleh R, Harraz AM, Kavoussi P, Chung E, Ko E, Boeri L, Kumar N, Çayan S, **Rambhatla A**, Rajmil O, Arafa M, Cannarella R, Raheem O, Mostafa T, Atmoko W, Hamoda TAA, Zini A, and Agarwal A. Changes in Testosterone Levels Following Surgical Sperm Retrieval in Men with Non-Obstructive Azoospermia: Systematic Review and Meta-Analysis. *World J Mens Health* 2024; Epub ahead of print. PMID: 39344115. Full Text

Department of Andrology, Sexology & STIs, Faculty of Medicine, Cairo University, Cairo, Egypt.
Global Andrology Forum, Moreland Hills, OH, USA.
Department of Urology, Lilavati Hospital and Research Centre, Mumbai, India.
Department of Surgery, School of Medicine, Taylor's University, Subang Jaya, Selangor, Malaysia.
Department of Urology, Istanbul Medipol University, Istanbul, Türkiye.
Department of Urology, VNA Hospital, New Delhi, India.
Department of Histology and Embryology, Istanbul Medipol University, Istanbul, Türkiye.
Department of Urology, Pamukkale University School of Medicine, Denizli, Türkiye.
Department of Urology, Princess Alexandra Hospital, Harlow, UK.
U-merge Ltd, Urology for Emerging Countries, London, UK.
Department of Urology, University Hospital of Tübingen, Tübingen, Germany.
Department of Dermatology, Venereology and Andrology, Faculty of Medicine, Sohag University, Sohag, Egypt.
Ajyal IVF Center, Ajyal Hospital, Sohag, Egypt.
Mansoura University Urology and Nephrology Center, Mansoura, Egypt.
Department of Surgery, Urology Unit, Farwaniya Hospital, Farwaniya, Kuwait.
Department of Urology, Sabah Al Ahmad Urology Center, Kuwait City, Kuwait.
Austin Fertility & Reproductive Medicine/Westlake IVF, Austin, TX, USA.
Department of Urology, Princess Alexandra Hospital, University of Queensland, Brisbane, Australia.
Department of Urology, Loma Linda University Health, Loma Linda, CA, USA.
Department of Urology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy.
Department of Urology, All India Institute of Medical Sciences, Patna, India.
Department of Urology, University of Mersin School of Medicine, Mersin, Türkiye.
Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI, USA.
Andrology Department, Fundació Puigvert, Barcelona, Spain.
Instituto de Investigaciones Biomédicas Sant Pau, IIB-Sant Pau, Universitat Autò noma de Barcelona, Barcelona, Spain.
Department of Urology, Hamad Medical Corporation, Doha, Qatar.
Department of Urology, Weill Cornell Medical-Qatar, Doha, Qatar.
Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy.
Glickman Urological & Kidney Institute, Cleveland Clinic Foundation, Cleveland, OH, USA.
Department of Urology, The University of Chicago Medical Center, Pritzker School of Medicine, Chicago, IL, USA.
Department of Urology, Cipto Mangunkusumo General Hospital, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia.
Department of Urology, King Abdulaziz University, Jeddah, Saudi Arabia.
Department of Urology, Faculty of Medicine, Minia University, Minia, Egypt.

Division of Urology, Department of Surgery, The Royal Victoria Hospital, McGill University, Montreal, QC, Canada.
Cleveland Clinic Foundation, Cleveland, OH, USA. agarwaa32099@outlook.com.

PURPOSE: Surgical sperm retrieval (SSR) is used to extract spermatozoa for use with intracytoplasmic sperm injection in men with obstructive and non-obstructive azoospermia (NOA). The procedure may lead to segmental devascularization, postoperative fibrosis, and atrophy with a subsequent decrease in testosterone. The aim of the study is to investigate the impact of SSR on serum levels of total testosterone (TT), follicle-stimulating hormone (FSH), luteinizing hormone (LH) testicular volume, and sexual function in infertile azoospermic men. MATERIALS AND METHODS: In this systematic review and meta-analysis (SRMA), we searched articles in "PubMed" and "Scopus" exploring the impact of SSR on TT, FSH, LH, and testicular volume. The full-text articles were screened to assess eligibility before data extraction, quality assessment, and meta-analysis. RESULTS: Seventeen studies meeting the inclusion criteria were finally analyzed and included 1,685 infertile, azoospermic men. Patients underwent SSR and were followed in the postoperative period (one week to 32 months). The analysis showed a significant reduction in TT (mean difference [MD] 3.81 nmol/L, 95% confidence interval [CI] 0.55:7.06; p=0.02) compared to pre-SSR values. We also observed insignificant differences in serum FSH (MD 5.08 IU/L, 95% CI -5.6:15.8; p=0.35), LH (MD -2.96 IU/L, 95% CI -6.31:0.39; p=0.08), and no change in testicular volume (MD 0.07 mL, 95% CI -1.92:2.07; p=0.94) after SSR. Sexual dysfunction was associated with hypogonadism, depression, and anxiety, especially in men with unsuccessful SSR and Klinefelter syndrome. CONCLUSIONS: The results of this SRMA indicate a significant reduction in TT after SSR. Sexual dysfunction after testicular sperm extraction and the potential negative impact of future SSR repeat should be considered during preoperative counseling.

Administration

Speak A, **Hijaz M**, **Singh H**, **Udumula M**, **Miller M**, **Munkarah A**, and **Rattan R**. Inhibiting mitochondria potentiates PARPi-triggered, STING-dependent immune response in pre-clinical models of epithelial ovarian cancer. *Gynecol Oncol* 2024; 190:S233-S234. Full Text

Objectives: In ovarian cancer patients with hereditary or somatic BRCA1/2 mutations, PARP inhibitors (PARPi) have altered the treatment landscape. DNA damage caused by PARPi in conjunction with DNA repair errors due to mutations in BRCA1/2 initiates immunologic signaling via the cGAS/STING pathway. Studies have shown that therapy with a STING agonist can boost the efficacy of olaparib in BRCA-mutated ovarian cancer cells. Current research suggests that the activity of almost all immune cells is regulated by their cellular metabolism, especially energy metabolism. We have previously shown that inhibiting mitochondria by metformin augmented the therapeutic efficacy of PARPi in BRCA-intact pre-clinical ovarian cancer models. This study examined whether mitochondrial inhibition could increase STING pathway activation by olaparib in BRCA1/2-mutated and wild-type ovarian cancer cells and mouse models. Methods: ID8 p53+/+, ID8 p53-/-, ID8 p53-/-, BRCA1-/-, and ID8 p53-/-, BRCA2-/- mouse ovarian cancer cells were treated with olaparib (5mm) or metformin (2.5mM) or a combination of both; 2′,3′-Cyclic GAMP was measured by ELISA. DNA damage (gH2AX) was evaluated by flow cytometry. Mitochondrial function was assessed by an XF seahorse analyzer. Treated cells were co-cultured with naïve CD8 T cells and profiled by flow cytometry. All cell lines were used to validate the response in vivo. Results: Olaparib increased γH2AX ($P < 0.001$) in the ID8 p53-/-, BRCA2-/- cells relative to ID8 p53-/-, BRCA1-/- and wild-types, and metformin further augmented this effect ($P < 0.0001$); while the lowest DNA damage was induced in BRCA and p53 intact ID8 p53+/+ ($P < 0.001$) cells. Increased DNA damage in ID8 p53-/-, BRCA2-/- cells correlated with elevated STING by olaparib, which was further exacerbated by the addition of metformin ($P < 0.0001$). When co-cultured with naïve splenic CD8 T cells, all cell lines activated CD8 effector and cytotoxic function (CD8+IFNg+, $P < 0.0001$; CD8+perforin+, $P < 0.001$; CD8+granzyme B+, $P < 0.001$) and STING response (CD8+STING+, $P < 0.000$; CD8+TBK+, $P < 0.001$). The effector activity and STING were highly elevated in CD8 T cells when co-cultured with olaparib-treated ID8 p53-/-, BRCA2-/- compared to ID8 p53-/-, BRCA1-/- and wild-type ID8 cells; this effect was further enhanced by the addition of metformin. Metabolic phenotyping revealed that CD8 T cells treated with olaparib and metformin exhibited an increase in glycolysis linked with a greater STING response. Similar results were replicated by CPI-613, another mitochondrial inhibitor. Conclusions: Olaparib activates cGAS/STING differently in ovarian cancer cells with BRCA1 and BRCA2 mutations. Mitochondrial inhibition promotes DNA damage and STING pathway activation induced by olaparib. Overall, the combination of metabolic modulators with PARPi may offer a possible therapeutic strategy for boosting the immunomodulatory effect of PARPi.

Anesthesiology

Mumtaz N, **Valliani A**, and **Chopra K**. ID: 330272 Splanchnic nerve block: a safe and effective alternative to celiac block for median arcuate ligament-syndrome. *Neuromodulation* 2024; 27(7):S58. Full Text

Introduction: Celiac artery compression syndrome is defined as chronic, recurrent abdominal pain related to compression of the celiac artery by the median arcuate ligament. Also known as median arcuate ligament syndrome (MALS), it is a rare disorder characterized by a triad of postprandial abdominal pain, weight loss and abdominal bruit. Celiac plexus block is one of the diagnostic testing modalities for MALS alongside imaging. Common treatment for MALS is celiac artery decompression by resection of the median arcuate ligament and nerve fibers. Here we discuss splanchnic nerve block as a diagnostic modality and bridging analgesia till definitive surgical management. Case Presentation: 21-year-old female with history of Ehler's Danlos Syndrome (EDS), Postural orthostatic tachycardia syndrome (POTS), sick sinus syndrome with pacemaker and MALS. She initially presented to pain clinic with abdominal pain for several weeks. Medical management was discussed with a follow-up. A week later, she ended up in ER with severe pain. Imaging showed 95% narrowing of celiac trunk by mass effect from the left hemi-diaphragmatic crus with normal distal branches of celiac axis. Vascular and general surgery were consulted. Due to multiple comorbidities including EDS that made her high risk for wound healing

and hernia, optimization and family discussion was required for robotic release of median arcuate ligament. Pain team was consulted and we performed bilateral splanchnic nerve blocks with steroid giving her near-total relief of pain for 2months. Repeat intervention was performed in 3months while awaiting surgery which showed similar pain relief. Discussion: Celiac plexus is present adjacent to the median arcuate ligament. Pain associated with celiac artery compression syndrome may be mediated by celiac plexus, however this is controversial. Diagnosis of MALS includes imaging studies. Celiac ganglion block can also be used as provocative physiologic test. The rationale for ganglion nerve block is that symptoms of celiac artery compression syndrome may be due to inflammation and compression of nerve fibers of celiac plexus. In our institution, celiac plexus blocks are reserved for chronic cancer pain patients due to associated complications. We performed splanchnic plexus block in our young patient with chronic abdominal pain considering it a safe approach to avoid complications and hoped to achieve similar results. Patient had near-total relief of pain. Conclusion: Splanchnic nerve block is a safer option with similar diagnostic and therapeutic results as celiac plexus block for MALS. Ethanol based neurolysis can also be used if surgery is not an option. Disclosures: Ketan Chopra: None, Narjis Mumtaz, MD: None, Arif Valliani, MD: None

Anesthesiology
Nofar J, **Sitto M**, **Ali A**, and **Sallowm Y**. Occipital Nerve Block Leading to the Discovery of Carcinosarcoma (P10-12.008). *Neurology* 2024; 102(17_supplement_1). Full Text

J. Nofar, Neurology, United States

Objective: NA Background: Occipital nerve blocks are routinely performed for the treatment of various headache disorders. When conventional medications are not sufficient, minimally invasive methods such as occipital nerve blocks become a viable treatment option. The targeted nerves can be reached using anatomical landmarks or imaging. We present a case of an occipital nerve block inadvertently leading to the discovery of a high-grade neoplasm. Design/Methods: 78-year-old female complaining of headache for 2 years. It was moderate to severe intensity, originated from the left > right occipital region, and radiated anteriorly. Quality was sharp/shooting/stabbing. She was previously diagnosed with occipital neuralgia by outside provider and had undergone two occipital nerve blocks, with significant but temporary relief. She was evaluated by neurology at our institution, who concurred with the diagnosis of bilateral occipital neuralgia, and referred her for bilateral occipital nerve blocks. Using standard protocol, a 25-gauge, 1.5-inch needle was advanced 0.5 inches on the left, but no contact was made with the occipital bone. The thickness of the scalp was re-evaluated by palpation and was normal. A lateral X-ray was taken to assess the distance between the needle tip and the periosteum, and demonstrated an abnormal appearance of the occipital bone. The procedure was aborted. Results: Non-contrast CT head demonstrated destructive osseous changes involving the majority of the occipital bone with extraosseous soft tissue extension. MRI brain with and without gadolinium demonstrated an expansile, heterogeneous lesion involving the occipital calvarium without intracranial enhancement. CT-guided biopsy confirmed neoplasm favoring carcinosarcoma. Conclusions: Occipital nerve blocks are commonly performed without prior imaging or image-guidance. This case raises the potential need of pre-intervention screening (e.g. x-ray) or ultrasound guidance, particularly in elderly patients with new-onset occipital neuralgia. This would accommodate varying skull sizes, pathologies, and anatomical variations, which can improve the effectiveness of the block, minimize recurrence, and avoid complications. .

Behavioral Health Services/Psychiatry/Neuropsychology
Gui H, Huang Y, Tao S, **Meng Z**, Liu Y, **Levin A**, **Ahmedani B**, and Wang Q. 15. Genetic Relationships and Biological Pathways Underlying Suicidality and Comorbid Mental Disorders: A Comprehensive Cross-Phenotype Analysis. *Eur Neuropsychopharmacol* 2024; 87:55. Full Text

Background: The co-occurrence of mental disorders and suicidality are frequently seen in epidemiology. One explanation lies in shared genetic liabilities, hence we aimed to investigate the phenotypic and genetic associations between multiple mental disorders and different levels of suicidality. Methods: Using UK Biobank (UKB) European individual data, we first evaluated the phenotypic and polygenic relationships between 12 mental disorders and gradient scales of suicidality (spanning suicidal ideation, suicide attempts, and suicidal death). Second, we used existing genome-wide association study (GWAS)

summary statistics to estimate genetic correlations and to identify pleiotropic genes using a combination of statistical genetics tools. Summary statistics were accessed from: 1) the Psychiatric Genomics Consortium (major depressive disorder [MDD], bipolar disorder [BD], anxiety disorders [ANX], obsessive-compulsive disorder [OCD], anorexia nervosa [AN], autism spectrum disorder [ASD], attention deficit hyperactivity disorder [ADHD], schizophrenia [SCZ], cannabis use disorder [CUD], and post-traumatic stress disorder [PTSD]), 2) the Million Veterans Program (alcohol use disorder [AUD] and opioid use disorder [OUD]), and 3) their joint analysis (suicidality). Third, using shared genetic liabilities as instrument, we evaluated evidence for causal relationship between mental disorders and suicidality by structural equation models and Mendelian randomizations. Last, we accessed the All of Us (AoU) diverse cohort data for replication in non-European populations. Results: For UKB, 150,861 eligible individuals were retained after standard GWAS quality control. Eight out 12 mental disorders (MDD, BD, ANX, AUD, OCD, AN, ASD and ADHD) showed both significant phenotypic and polygenic correlations with gradient suicidality (false discovery rate < 0.05). Among them, the impact of MDD and BD on suicidality were the most obvious (for MDD: OR=5.78 and 1.26 for phenotypic and polygenic level; for BD: OR=12.98 and 1.14 for phenotypic and polygenic level). Using GWAS summary statistics, we also observed positive global genetic correlations between those 8 mental disorders and suicidality (rg ranging from 0·25 to 0·68, $p < 0.001$). Across pairs of suicidality and mental disorders, we identified 23 functional genes (including novel ones like BPTF, NOL11 and CACNG5) shared by five or more pairs. These genes were significantly enriched in two Gene Ontology sets: developmental process and regulation of biological process. We also identified unique genes within each pair which were enriched in different pathways (e.g., glutamatergic synapse for suicidality-MDD, negative regulation of biological process for suicidality-BD, and actin cytoskeleton for suicidality-AUD). Causal models indicated potential causality from genetic diatheses of MDD, BD, AUD, ADHD, and ASD to risk of suicidality. Multiple cross-phenotype associations with suicidality were also replicated in AoU African and Asian populations (e.g., $p < 0.05$ for MDD and BD polygenic associations). Discussion: This study underscores the urgent need to address the shared and distinct genetic architecture of suicidality and related mental conditions. The combination of longitudinal population-level biobanks and disease-ascertained GWAS are warranted to enhance our understanding of their relationships. Our findings will provide insights into future suicide prevention and management among individuals with and without mental disorders. Disclosure: Nothing to disclose.

Behavioral Health Services/Psychiatry/Neuropsychology

Prabhakar D, **Mitchell S**, **MacLean LM**, and Prabhakar A. Wellness: From an Activity to Fostering a Culture of Well-Being. *J Am Acad Child Adolesc Psychiatry* 2024; 63(10):S372. Full Text

Objectives: This Workshop will share and demonstrate multiprong wellness strategies to help address physician burnout. Methods: The attendees will engage in an interactive Workshop highlighting a wellness approach with patient well-being as a central theme. The content and the activities will be organized around 4 specific prongs: 1) healthy work environment; 2) efficient processes; 3) healthy people; and 4) safe teams. Results: Healthy work environment aligns organizational policies with the values of those who work there. In this prong, focusing on “why” we do the work can be very powerful in sustaining professionals during times of stress. Through programming that addresses financial security, diversity and inclusion, psychological safety, and childcare challenges, we can demonstrate to our physician workforce that we respect and trust them. Efficient processes focus on “how” the work is done. In this prong, running listening sessions across the organization to better understand the processes of work and how easy or onerous it is to complete daily work can help elucidate the challenges. This allows leaders to understand the burnout drivers so that targeted interventions can be created. A sense of control and autonomy can reduce the feelings of helplessness that fuel burnout. The healthy people prong focuses on support for clinicians. One must consider the development of well-being programs that focus not only on reacting to stress, but also on prevention strategies. At the core of any programming must be the philosophy that self-care is a fundamental component of professionalism. The final prong is the creation of safe teams. Within this prong, a focus needs to be on how we work as teams with effective communication and promoting psychological safety. There needs to be space for humanness within medicine. We are not perfect. Indeed, we are imperfect people practicing medicine in an imperfect environment. We can build cohesiveness through peer support, especially after critical events, but also as a matter of routine. Conclusions: This Workshop will highlight a comprehensive approach for health systems to drive patient care outcomes while fostering a culture of wellness. WL, PUP, ADMIN

Cardiology/Cardiovascular Research

Abdelhai O, Alhuneafat L, Madanat L, Hanson I, Renard B, Abbas A, and **Villablanca P**. TCT-929 Long-Term Outcomes Balloon-Expandable vs Self-Expandable Valves for Valve-in-Valve TAVR: Insight From Michigan Structural Heart Consortium. *J Am Coll Cardiol* 2024; 84(18):B392. Full Text

Background: Valve-in-valve transcatheter aortic valve replacement (ViV TAVR) addresses issues with previously implanted aortic valves. Its use is growing because of the rise of bioprosthetic valves, high surgical reoperation risks, and expanding transcatheter aortic valve replacement (TAVR) indications. Both balloon-expandable (BE) and self-expandable (SE) valves are used, each with unique features and outcomes. Methods: We analyzed ViV TAVR patients from 2015 to 2022 using data from the Michigan Structural Heart Consortium and linked Medicare claims to extend the analysis of long-term mortality beyond the 1-year follow-up. Results: In our ViV TAVR cohort, 1,394 patients were analyzed comparing 683 BE and 711 SE valves. The cohort was predominantly male (70.3% vs 51.8%; P = 0.001) with lower Society of Thoracic Surgeons scores (4.17% vs 5.1%; P < 0.005). One-year post TAVR mortality was higher in SE valves (7.5% vs 6.4%; P < 0.018). Post-TAVR stroke, readmission, vascular complications, permanent pacemaker, and bleeding were similar between the groups. Severe patient-prosthesis mismatch was significantly higher in the BE cohort (47.9% vs 24.3%; P = 0.001). Three hundred forty cases (24%) were matched to Fee-for-Service Medicare, comprising 172 BE and 168 SE valves. Five-year post-TAVR survival was similar between the groups despite significant baseline differences. After the adjusted Cox regression model, there was no significant difference in survival between the groups (adjusted HR for SE vs BE: 1.03; 95% CI: 0.70-1.53; P = 0.88) (Figure). [Formula presented] Conclusion: In this real-world registry study, our findings showed no significant differences in in-hospital or long-term outcomes between patients with SE and BE valves following ViV TAVR. Categories: STRUCTURAL: Valvular Disease: Aortic.

Cardiology/Cardiovascular Research

Abdelhai O, **Ghoneem A**, **Andrews T**, **Rangavajla G**, and **Maligireddy AR**. TCT-904 Trends and Outcomes of Mechanical Circulatory Support With Transcatheter Valve Intervention From the National Inpatient Sample (2017-2020). *J Am Coll Cardiol* 2024; 84(18):B381. Full Text

Background: The use of mechanical circulatory support (MCS) devices with transcatheter valve interventions (TVIs) is occasionally required; however, data on their use and outcomes are lacking. Methods: We used the Nationwide Inpatient Sample database to identify patients treated with TVI, with or without MCS, between 2017 and 2020. Our analysis included hospital admissions of adults who underwent transcatheter aortic valve replacement (TAVR), MitraClip, transcatheter mitral valve replacement, transcatheter pulmonary valve replacement (PVR), and/or transcatheter tricuspid valve repair. Results: We identified 29,4525 patients undergoing TVI during the study period, with 2,920 in the MCS group and 292,495 in the non-MCS group (Table). Patients in the MCS group were younger; more likely to be males; of Black or other race; or have congestive heart failure, cardiac arrhythmias, or chronic kidney disease. Younger age, nonelective admission, cardiac arrhythmia, myocardial infarction, sudden cardiac arrest, and cardiogenic shock significantly predicted MCS use (P ≤ 0.001 for all). From 2017 to 2020, there was a steady increase in TVI (P for trend = 0.034). Conversely, use of MCS has remained stable (P for trend: total 0.732). The use of any MCS modality was associated with >30-fold increase in mortality (1% vs 30.1%; P <0.05). Length of stay and cost of hospitalization were higher in the MCS group (P <0.05 for both). Mortality remained steadily high with MCS use (P for trend = 0.138), with declining mortality in the non-MCS group showing a trend toward significance (P for trend = 0.058). [Formula presented] Conclusion: The use of MCS in patients undergoing TVI in the United States between 2017 and 2020 was associated with increased mortality, morbidity, and greater use of health care resources. Further research is needed to enhance the safety and cost-effectiveness of MCS in TVI as well as to identify the optimal MCS for these patients. Categories: STRUCTURAL: Congenital and Other Structural Heart Disease.

Cardiology/Cardiovascular Research

Abdelhai O, **Rangavajla G**, **Nguyen F**, **Andrews T**, **O'Neill B**, **Fang J**, **Giustino G**, **Wyman J**, **Gonzalez PE**, **Villablanca P**, **Lee J**, **O'Neill W**, **Zweig B**, **Parikh S**, and **Frisoli T**. TCT-171 Baseline

Invasive Hemodynamics and Clinical Outcomes in Transcatheter Tricuspid Valve Replacement Using the EVOQUE System. *J Am Coll Cardiol* 2024; 84(18):B420. Full Text

Background: Transcatheter tricuspid valve replacement (TTVR) with the Evoque valve represents a newly commercially available non surgical therapy for severe tricuspid regurgitation (TR) in the United States. There is minimal data on the significance of pulmonary hypertension (PH) and right ventricular dysfunction (RVD) in patients undergoing TTVR. Methods: Patients who underwent TTVR at Henry Ford Hospital in Detroit during February-May 2024 (n = 28) were included. We examined how right heart catheterization metrics of PH and RVD—pulmonary vascular resistance (PVR), pulmonary artery pulsatility index (PAPi), and pulmonary capillary wedge pressure (PCWP)—correlated with both procedural success and a composite outcome of death or heart failure hospitalization. Results: The cohort had a median PVR 2.4 (IQR 1.3-2.9), PCWP 10 (IQR 8.8-19.3), and PAPi 2.1 (IQR 1.4-4.0). For those with complete data, 5/20 (25%) had elevated PVR >3.0 and 7/20 (35%) had elevated PCWP >15. There were no associations between PVR (P = 0.42), PCWP (P = 0.23), and PAPi (P = 0.45) with procedural success (n = 22). There was also no association between PVR, PCWP, and PAPi and death or heart failure hospitalization (n = 6, Figure 1) over a median 12-day (IQR 4-30) follow-up. [Formula presented] Conclusion: Although a small study, these are the first data since the commercial launch of TTVR in the United States. TTVR appears similarly safe across a range of baseline PVR, PCWP, and PAPi values. More research in larger cohorts is needed to determine if preprocedural right heart catheterization findings can predict clinical outcomes after TTVR. Categories: STRUCTURAL: Valvular Disease: Tricuspid.

Cardiology/Cardiovascular Research
Al-Abdouh A, Samadi D, Sukhon F, Mhanna M, Madanat L, Alhuneafat L, **Alqarqaz M**, Paul T, and Kundu A. TCT-501 Paclitaxel-Coated Balloon vs Uncoated Balloon Angioplasty for Coronary In-Stent Restenosis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *J Am Coll Cardiol* 2024; 84(18):B166. Full Text

Background: In-stent restenosis (ISR) accounts for 10% of percutaneous coronary intervention (PCI) in the United States. Paclitaxel-coated balloons (PCBs) have been evaluated as a therapy for coronary ISR in multiple randomized controlled trials (RCTs). Methods: We searched PubMed/MEDLINE, Cochrane Library, and ClinicalTrials.gov for RCTs evaluating PCBs vs uncoated/plain old balloon angioplasty (POBA) in patients with coronary ISR. The outcomes of interest were target lesion revascularization (TLR), major adverse cardiovascular events (MACE), all-cause mortality, cardiovascular mortality, myocardial infarction (MI), and stent thrombosis. We pooled the estimates using inverse variance random-effects model. The effect sizes were reported as risk ratio (RR) with 95% CI. Results: A total of 6 RCTs with 1,343 patients were included. At a follow-up ranging from 6-12 months from randomization, use of PCBs was associated with a statistically significant decrease in TLR (RR: 0.28; 95% CI: 0.11 to 0.68), and MACE (RR: 0.35; 95% CI: 0.20 to 0.64) when compared with POBA for coronary ISR. However, there was no significant difference in risk between PCBs and POBA in terms of all-cause mortality (RR: 0.56; 95% CI: 0.14 to 2.31) cardiovascular mortality (RR: 0.61; 95% CI: 0.02 to 16.85), MI (RR: 0.60; 95% CI: 0.27 to 1.31), and stent thrombosis (RR: 0.13; 95% CI: 0.00 to 5.06). [Formula presented] Conclusion: This meta-analysis suggests that PCBs compared with POBA for treatment of coronary ISR was associated with significant decrease in TLR, and MACE without any significant difference in mortality, MI, or stent thrombosis. Categories: CORONARY: Drug-Eluting Balloons and Local Drug Delivery.

Cardiology/Cardiovascular Research
Alexandrou M, Mastrodemos O, Al-Ogaili A, Rangan B, Allana S, Rempakos A, Strepkos D, Carvalho P, Mutlu D, Jalli S, Sandoval Y, Burke MN, Brilakis E, and **Alaswad K**. TCT-754 Native Coronary Artery Instead of Saphenous Vein Graft Intervention for Treatment of Significant Saphenous Vein Graft Lesions (NASA Registry). *J Am Coll Cardiol* 2024; 84(18):B303. Full Text

Background: The outcomes of native coronary artery percutaneous coronary intervention (PCI) in patients with previous coronary artery bypass graft surgery (CABG) presenting with saphenous vein graft (SVG) failure have received limited study. Methods: We examined the outcomes of 76 PCIs of patients with a de

novo SVG lesion causing symptoms and treated with PCI of the corresponding native coronary artery, performed at 2 centers from 2016 to 2024. Results: Mean age of the patients was 72.3 ± 11.1 years; 86.8% were men. The previous SVG graft was more often to the right posterior descending artery (44.9%) or the first obtuse marginal branch (43.6%); 78.2% of the patients had a left internal mammary artery graft. Native vessel chronic total occlusions (CTOs) were treated in 97.4% of the patients. Mean PROGRESS-CTO and J-CTO scores were 1.01 ± 0.95 and 2.84 ± 1.01, respectively. Overall technical success was 98.7%, with 1.3% in-hospital major adverse cardiovascular events (MACE). Follow-up was available for 66 cases (86.84%, median: 359 days; Q1-Q3: 182-366 days). MACE included 12 acute coronary syndrome events, 7 target lesion revascularizations, 2 deaths (of which 1 cardiac). Target vessel failure (TVF) occurred in 10 cases (15.2%). The 1-year Kaplan-Meier estimates were 66.0% (95% CI: 53.5%-81.4%) for MACE-free survival and 79.1% (95% CI: 68.0%-92.0%) for TVF-free survival. Median time to TVF was 163 days (Q1-Q3: 75-220 days). [Formula presented] Conclusions: Native coronary PCI in previous CABG patients with SVG failure is effective with high technical success but patients have high risk of recurrent MACE. Categories: CORONARY: Complex and Higher Risk Procedures for Indicated Patients (CHIP).

Cardiology/Cardiovascular Research
Allen K, Rogers T, Greenbaum A, Kirker E, McCabe J, Cheema M, Logsdon D, **Alnajjar R**, Paone G, Harrington K, Lederman R, and Chhatriwalla A. TCT-891 Transcarotid Versus Transcaval Access for Transcatheter Aortic Valve Replacement Using a Balloon Expandable Valve: Propensity-Matched Analysis From a Real-World Registry. *J Am Coll Cardiol* 2024; 84(18):B375. Full Text

Background: Transcarotid and transcaval access for transcatheter aortic valve replacement (TAVR) have demonstrated superior outcomes to transaxillary/transthoracic access; however, comparisons of transcarotid vs transcaval alternate access are lacking. Methods: The Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry was queried for patients undergoing transcarotid and transcaval TAVR with the SAPIEN 3 (Edwards Lifesciences) valve platform between November 2018 and September 2023. Procedural, in-hospital, 30-day, and 1-year outcomes, including CMS linkage, were evaluated and then compared using 3:1 propensity score matching. Results: The study included 5,712 patients (transcarotid 5,297; transcaval 415) with a well-matched propensity matched cohort of 1,218 transcarotid and 406 transcaval patients. Overall, this high-risk cohort of patients had a high burden of comorbidities. Transcarotid and transcaval patients had similar mortality at 30 days (4.1% vs 5.5%; P = 0.25) and 1-year (19.4% vs 19.2%; P = 0.87) and similar stroke rates at 30-days (5.6% vs 3.8%; P = 0.15) and 1 year (7.8% vs 5.6%; P = 0.13). Transcarotid access was performed more frequently with general anesthesia (94.9% vs 60.1%; P < 0.0001), admitted to the ICU more often (79.7% vs 66.2%; P = 0.002) and had longer mean ICU times (36.2 h vs 26.7 h; P = 0.03). Procedure time (88.0 vs 119.0 min; P < 0.0001), fluoroscopy time (15.8 vs 36.2 min; P < 0.0001), contrast volume (75.8 mL vs 128.9 mL; P < 0.0001), life-threatening bleeding (1.6% vs 3.9%; P = 0.006) and need for blood transfusion (12.2% vs 20.7%; P < 0.0001) were lower with transcarotid access. Most patients in both groups were discharged home after TAVR (>85%) with a similar median LOS of 2.0 days. Transcarotid access was associated with a lower 30-day rate of new PPM/ICD (7.3% vs 10.9%; P = 0.04) and 30-day readmission rate (11.0% vs 14.9%; P = 0.03). Conclusion: Transcarotid and transcaval access for TAVR with the SAPIEN 3 family valves is associated with similar 30-day and 1-year mortality and stroke. Depending on patient anatomy and Heart Team expertise, both are appropriate and the preferred approaches when TAVR requires nonfemoral access. Categories: STRUCTURAL: Valvular Disease: Aortic.

Cardiology/Cardiovascular Research
Andrews T, **McBride P**, **Abdelhai O**, **Fang J**, **Giustino G**, **Gonzalez PE**, **Villablanca P**, **O'Neill B**, **O'Neill W**, **Zweig B**, **Lee J**, and **Frisoli T**. TCT-825 Hemodynamic Valve Deterioration in Under- vs Over-Expanded Balloon Expandable Transcatheter Aortic Valves. *J Am Coll Cardiol* 2024; 84(18):B334. Full Text

Background: Non-nominal deployment of balloon-expandable valves (BEVs) is a common transcatheter aortic valve replacement (TAVR) practice. Effects of under- vs over-expansion of a BEV on hemodynamic valve deterioration (HVD) are not well studied. Methods: We conducted a single-center retrospective

study of 175 patients who underwent TAVR with BEVs deployed at non-nominal and nominal volumes. Criteria of moderate HVD—changes from 1 month to 1 year after TAVR in peak and mean gradients and aortic valve area and dimensionless index (DI) as well as new aortic regurgitation—were studied. Results: There were no significant differences between the over- and under-expanded BEVs for any of the following criteria: 1-year AVA (P = 0.065), Δ AVA (P = 0.256), % Δ AVA (P = 0.156), 1-year peak gradient (P = 0.272) and mean gradient (P = 0.303), Δ mean gradient (P = 0.499), DI (P = 0.434), Δ DI (P = 0.382), % Δ DI (P = 0.379), AI (P = 0.373), and Δ AI (P = 0.416); Figure 1. In a linear regression analysis by actual volume subtracted from or added to nominal, there was no association with Δ AVA or Δ DI at 1-year (P = 0.55 and P = 0.85, respectively). [Formula presented] Conclusion: In this first in vivo analysis of non-nominally expanded BEVs and HVD, over-expanded and under-expanded BEVs appear to perform similarly out to 1 year. Larger studies with longer follow-up are needed. Categories: STRUCTURAL: Valvular Disease: Aortic.

Cardiology/Cardiovascular Research

Aurora L, Bharadwaj A, Todd J, Kaki A, Dupont A, Wohns D, Lemor A, **Gorgis S**, Bentley D, Jortberg E, Jin W, and **O'Neill W**. TCT-278 Clinical Outcomes of Patients Who Experienced Loss of Pulse Pressure During Treatment With Impella for Acute Myocardial Infarction and Cardiogenic Shock. *J Am Coll Cardiol* 2024; 84(18):B57. Full Text

Background: Patients experiencing acute myocardial infarction and cardiogenic shock (AMI-CS) may become transiently dependent on Impella and experience loss of pulse pressure (LOPP). Characteristics and outcomes of such patients are unknown. Methods: Patients enrolled in the National Cardiogenic Shock Initiative with available automated Impella controller logs capturing real-time hemodynamics for the first 24 hours after Impella implantation were included. Loss of pulse pressure (LOPP) was defined as a mean pulse pressure of <10 mm Hg for ≥5 seconds while on Impella support. Patient characteristics, hemodynamics and clinical outcomes were compared between those with no episodes of LOPP vs those who experienced minimal LOPP (defined as experiencing LOPP <4.83% of time within the first 24 hours) and those who experienced sustained LOPP (defined as experiencing LOPP ≥4.83% of time within the first 24 hours). Results: There were no significant differences in baseline patient or procedural characteristics across cohorts. Pulmonary artery pulsatility index was significantly lower in those experiencing sustained LOPP compared with those with no or minimal LOPP after the procedure (P < 0.01). At 12 hours, SBPs and MAPs were lower in the LOPP subgroups (P < 0.01 for both). Those with LOPP were more likely to have an elevated lactate at 12 hours compared with those with without LOPP (P < 0.01). Survival through discharge was 86% in those who did not experience LOPP, 75% in those who experienced minimal LOPP, and 48% in those who experienced sustained LOPP (P < 0.01). Conclusions: Sustained LOPP on Impella for AMI-CS was associated with lower blood pressures, higher lactate, lower pulmonary artery pulsatility index, and lower survival. Sustained LOPP may be a marker for consideration of mechanical circulatory support (MCS) escalation or the need for more prolonged MCS duration. Categories: CORONARY: Hemodynamic Support, Cardiogenic Shock and Cardiac Arrest.

Cardiology/Cardiovascular Research

Basala T, Seth M, Madder R, Wanamaker B, **Fuller B**, Shlofmitz E, Daher E, Tucciarone M, Alraies C, Kaki A, Rao S, Gurm H, and Sukul D. TCT-56 Effectiveness of Image-Guided Percutaneous Coronary Intervention in Contemporary Practice: Insights From BMC2. *J Am Coll Cardiol* 2024; 84(18):B175. Full Text

Background: Studies show that intracoronary imaging (ICI)-guided percutaneous coronary intervention (PCI) results in larger stent/balloon diameters and longer stent length. Whether these findings are seen in real-world practice is poorly understood. Methods: Between July 2019 and June 2022, there were 74,621 lesions treated at 48 non-federal hospitals in Michigan. Associations between ICI use for de novo lesion PCI optimization with maximum balloon/stent diameters and total stent length were evaluated using regression models controlling for patient and procedural factors. A sensitivity analysis controlling for the operator was performed. Results: ICI was used in 16,777 (22.5%) PCI-treated lesions. Compared with angiography alone, ICI use was associated with larger stent diameters (median 3.50 mm [3.00, 3.50] vs 3.00 mm [2.50, 3.50]), larger maximum balloon diameters (3.50 mm [3.00, 4.50] vs 3.00 mm [2.50, 3.50]), and longer stent lengths (32.00 mm [22.00, 48.00] vs 24.00 mm [18.00, 38.00]) (p<0.001 for all) (Figure

1). Average patient/procedural adjusted treatment effects included: +0.19-mm stent diameter (95% CI: +0.16-0.22), +0.45-mm maximum balloon diameter (95% CI: +0.40-0.51), and +3.51-mm stent length (95% CI: +2.54-4.48). These findings persisted when controlling for the operator (Figure 1). [Formula presented] Conclusion: In real-world practice, ICI-guided PCI was associated with larger stent/balloon diameters and longer stents. Categories: IMAGING AND PHYSIOLOGY: Imaging: Intravascular.

Cardiology/Cardiovascular Research
Basala T, Seth M, Madder R, Wanamaker B, **Fuller B**, Shlofmitz E, Daher E, Tucciarone M, Alraies C, Kaki A, Rao S, Gurm H, and Sukul D. TCT-55 Safety of Image-Guided Percutaneous Coronary Intervention in Contemporary Practice: Insights From BMC2. *J Am Coll Cardiol* 2024; 84(18):B174-B175. Full Text

Background: Studies show that intracoronary imaging (ICI)-guided percutaneous coronary intervention (PCI) results in larger stent/balloon diameters and better patient outcomes. However, the association between ICI use and risks of dissection and perforation in real-world practice is poorly understood. Methods: Between July 2019 and June 2022, there were 74,621 lesions treated at 48 non-federal hospitals in Michigan. We evaluated associations between ICI use for de novo lesion PCI with dissections/perforations using regression models controlling for patient and procedural factors. We assessed temporal trends in ICI use, stent/balloon sizes, and rates of dissection/perforation. Results: ICI was used in 16,777 (22.5%) PCI-treated lesions and increased from 11.2% of cases in July 2019 to 32.1% in June 2022. ICI use was associated with a higher risk for dissections (aOR: 2.55; 95% CI: 2.05-3.16) and perforations (aOR: 2.25; 95% CI: 1.74-2.91). However, increased use of ICI and larger average maximal stent/balloon diameters over the study period ($P < 0.001$ for trend for both) was not associated with a concomitant increase in rates of dissection or perforation ($P = 0.78$ and $P = 0.33$ for trend, respectively) (Figure 1), suggesting that at least some of the ICI use was in response to the complication. [Formula presented] Conclusion: In real-world practice, although ICI use was associated with dissections and perforations, there was no significant increase in these complications despite significant increases in ICI use during the study period. Categories: IMAGING AND PHYSIOLOGY: Imaging: Intravascular.

Cardiology/Cardiovascular Research
Batchelor W, Kirtane A, Shlofmitz R, Moses J, Bachinsky W, Dohad S, Rudick S, Stoler R, Jefferson B, Nicholson W, Altman J, Bateman C, Krishnaswamy A, **Alaswad K**, Kimmelstiel C, Dixon W, Reitman A, Bhatt P, Song S, and Yeh R. TCT-492 One-Year Clinical Outcomes After PCI With Agent Paclitaxel-Coated Balloon Among Underrepresented Racial and Ethnic Subgroups With In-Stent Restenosis: Analysis of the AGENT IDE Trial. *J Am Coll Cardiol* 2024; 84(18):B162. Full Text

Background: Minorities bear a higher risk of adverse ischemic events following coronary stenting. The efficacy of drug-coated balloon (DCB) angioplasty for in-stent restenosis (ISR) has not been studied in this underrepresented population. Methods: AGENT IDE is a prospective multicenter trial that randomized ISR patients (2:1) with reference vessel diameter [RVD] >2.0 to ≤4.0 mm and lesion length <26 mm to receive treatment with AGENT (n = 406) or conventional balloon angioplasty (BA; n = 194). A prespecified analysis comparing outcomes of underrepresented racial and ethnic minorities (non-White race/Hispanic ethnicity) with those of White patients was performed using Cox regression. Results: Mean age was 68 years and 27% of patients were women. A total of 148 patients from underrepresented minorities were available for analysis, including 15 Asian, 33 Hispanic or Latino, and 41 Black patients. More minority than White patients were diabetic (61% vs 48%; $P = 0.006$). Single and multiple layer ISR occurred in 57% and 43% patients, respectively. Angiographic core lab reported mean RVD was 2.7 mm in both groups, and lesion length was 12.4 mm vs 12.5 mm ($P = 0.84$). One-year outcomes are shown in Table 1. Compared with Whites, minority patients had similar restenosis rates and relative risk reductions in ischemic events with AGENT. TLR rates were significantly reduced with AGENT vs BA in minority patients (11.3% vs 26.7%; $P = 0.01$), consistent with results observed in White patients (P interaction = 0.38). There was no definite/probable ST with AGENT. Additional data on risk adjusted outcomes and interactions between race/ethnicity and treatment will be available at the time of presentation. [Formula presented] Conclusions: In the only DCB study evaluating underrepresented minorities, AGENT paclitaxel-coated balloon appeared safe and was associated with similar relative risk reductions in 1-year

ischemic events vs BA as noted for White patients within the trial. Categories: CORONARY: Drug-Eluting Balloons and Local Drug Delivery.

Cardiology/Cardiovascular Research
Boukhris M, Mutlu D, Rempakos A, Aboyans V, Rouchaud A, Alexandrou M, Strepkos D, Carvalho P, Quadros A, Dens J, Rafeh NA, Agostoni P, **Alaswad K**, Avran A, Belli K, Carlino M, Choi J, El Guindy A, Jaffer F, Khatri J, Khelimskii D, Knaapen P, la Manna A, Krestyaninov O, Piccaro de Oliveira P, Ojeda S, Padilla L, Pan M, Spratt J, Harada M, Tanabe M, Walsh S, Sandoval Y, Rangan B, Brilakis E, and Azzalini L. TCT-400 In-Hospital Outcome of Antegrade Dissection Reentry in Left Anterior Descending Artery Chronic Total Occlusions: Patient Data Pooled Analysis of 4 Multicenter Registries. *J Am Coll Cardiol* 2024; 84(18):B114. Full Text

Background: The outcomes of chronic total occlusion (CTO) percutaneous coronary intervention (PCI) depend on the target vessel. The left anterior descending (LAD) subtends the largest myocardial territory and gives several branches that could be compromised by extraplaque tracking during antegrade dissection/reentry (ADR). We compared the success and safety of ADR in LAD vs non-LAD CTO PCI. Methods: We analyzed the data of 20,431 CTO PCIs enrolled in 4 multicenter registries: the PROGRESS-CTO registry, the LATAM CTO registry, the RECHARGE registry, and an international 7-center registry. CTO PCIs were subdivided into LAD (n = 5,560) and non-LAD (n = 14,871). Technical success was defined as successful CTO revascularization with achievement of <30% residual diameter stenosis within the treated segment and restoration of grade 3 TIMI flow. Procedural success was defined as the achievement of technical success without any in-hospital major adverse cardiac events (MACE). Results: ADR was used in 4,945 procedures (24.2%) (LAD: n = 1,183 [21.3%], non-LAD: n = 3,762 [25.3%]). ADR was attempted in more complex CTOs in both LAD (J-CTO score: ADR 2.46 ± 1.14 vs non-ADR 1.91 ± 1.16; P < 0.001) and non-LAD CTO PCI (ADR 2.82 ± 1.15 vs non-ADR 2.26 ± 1.27; P < 0.001). In 81.8% of cases, ADR was used as a bail-out strategy, particularly in LAD (85.8% vs 80.4% non-LAD; P < 0.001). Stingray-based reentry was attempted in 31.5% of ADR cases (LAD 30.6% vs non-LAD 31.8%; P = 0.473). ADR was the final successful crossing strategy in 50.5% of ADR cases (LAD 49.6% vs non-LAD 50.8%; P = 0.489). Overall, technical and procedural success rates were higher in LAD than non-LAD cases ([88.4% vs 85.6%; P < 0.001] and [85.7% vs 82.8%; P < 0.001], respectively). Among ADR cases, LAD CTO PCI was associated with higher technical (81.1% vs 77.5%: P = 0.009) and procedural (76.5% vs 73.4%; P = 0.042) success, and similar in-hospital MACE (7.3% vs 6.0%; P = 0.114) than non-LAD CTO PCI. In LAD ADR cases, Stingray use was associated with higher technical (86.3% vs 78.7%; P = 0.004) and procedural (81.2% vs 74.6%; P = 0.022) success rates. Conclusions: ADR was used in almost one-fourth of CTO PCIs, especially in more complex CTOs and was associated with high success and acceptable MACE. Categories: CORONARY: Complex and Higher Risk Procedures for Indicated Patients (CHIP).

Cardiology/Cardiovascular Research
Cantey E, Seth M, Wanamaker B, Daher E, **Basir B**, Kaki A, Madder R, Sukul D, and Gurm H. TCT-270 Contemporary Use of Mechanical Circulatory Support for the Treatment of Acute Myocardial Infarction Cardiogenic Shock (AMI-CS): Insights From the BMC2 Registry. *J Am Coll Cardiol* 2024; 84(18):B53. Full Text

Background: Recent randomized controlled trial evidence suggest a mortality benefit of microaxial flow pump (mAFP) in AMI-CS. We investigated the contemporary prevalence of MCS use in the treatment of AMI-CS in Michigan. Methods: We included all primary PCIs for STEMI complicated by CS performed at 48 Michigan hospitals between April 1, 2018, and December 31, 2023. We excluded patients with persistent neurologic deficit after cardiac arrest (CA) and the use of right ventricular MCS. The analysis cohort was divided into 4 groups: no-MCS, mAFP, IABP, and other MCS. Site-specific utilization of MCS was compared between the 4 groups. Results: AMI-CS was present in 9.3% (n = 1,989) of STEMIs; 38.3% were excluded from the analysis due to neurological injury post-CA. Of the study cohort, 52.4% of patients with AMI-CS were treated without MCS, 23.1% with IABP, 23.0% with mAFP, and 1.5% with other MCS devices. There was significant heterogeneity in the baseline comorbidities, procedural characteristics, and outcomes across MCS groups. Over the study period, each individual site treated a median of 17 patients (Q1, Q3: 12.3-34.8 patients) with AMI-CS with a median usage of mAFP of 21.6%

(Q1, Q3: 10.1%, 33.3%). AMI-CS volume did not correlate with mAFP utilization (Pearson rho 0.092; P = 0.5) (Figure 1). [Formula presented] Conclusion: Hospitals in Michigan have low annual case volumes and significant heterogeneity in the treatment of AMI-CS. Future efforts are needed to enhance early recognition of AMI-CS, implement protocol-based care to optimize evidence-based use of mAFP, and streamline “hub and spoke models” to facilitate delivery of contemporary AMI-CS therapies including mAFP. Categories: CORONARY: Hemodynamic Support, Cardiogenic Shock and Cardiac Arrest.

Cardiology/Cardiovascular Research
Fadel R, **Mshelbwala F**, **Alrayes H**, **Aurora L**, **Gorgis S**, **Grafton G**, **Villablanca P**, **Tanaka D**, **Aronow H**, **Cowger J**, **O’Neill W**, **Basir B**, **Kim H**, **Frisoli T**, **Fuller B**, **Koenig G**, **Alqarqaz M**, **O’Neill B**, **Alaswad K**, **Williams C**, and **Gonzalez PE**. TCT-469 A Prospective Registry of Complications Associated With Temporary Mechanical Circulatory Support (The PROCTOR MCS Registry). *J Am Coll Cardiol* 2024; 84(18):B152. Full Text

Background: Mechanical circulatory support (MCS) devices are increasingly used in the management of cardiogenic shock (CS) and are associated with high complications rates. There are no prospective studies quantifying the rates of complications across MCS devices and nursing burden of such complications. Methods: We compiled a prospective registry of patients in CS, requiring MCS, who were admitted to our quaternary care institution. Patients were enrolled in consecutive fashion for the entirety of their hospital stay, with 30-day postdischarge follow-up. A comprehensive log of patient care was maintained daily by the patient’s nursing team. Results: One hundred eighty-three patients were enrolled in the study. The median age was 64 years (Q1-Q3: 54-71 years), 62.3% were White, and 72.7% were male. The most common cause of CS was acute myocardial infarction (67.2%). The majority of patients were in stage D shock (44.3%). MCS devices used included intra-aortic balloon pump (38%), Impella CP/5.5 (Abiomed, 22.4%), venoarterial extracorporeal membrane oxygenation (22.4%), venovenous extracorporeal membrane oxygenation (8.2%), RP Impella (Abiomed, 4.9%), and EcPella (Abiomed, 3.8%). Nursing logs were completed for a median of 84% (Q1-Q3: 65%-95%) of patient care days; 26.2% of patients had Doppler loss of pulses, 5.5% required cath lab activation for acute limb ischemia, 72.7% of patients required 1 to 2 dressing changes per shift, 55.2% required 1 to 2 phone calls related to the MCS device per shift, 33.9% required 1 to 2 calls related to bleeding, 26.2% required 1 to 2 calls related to device adjustment, and 30.1% required 1 to 2 transfers out of the cardiac intensive care unit per shift. Major complications included blood transfusion (63.4%), acute kidney injury (61.2%), hemolysis (48.1%), major bleeding (27.9%), sepsis requiring antibiotics (15.8%), and stroke (10.4%). Rates of complications and phone calls per shift were all more likely in patients with large-bore MCS compared to intra-aortic balloon pump ($P < 0.05$). Overall in-hospital mortality was 36.6%, and 30-day mortality was 32.2%. Conclusion: This prospective registry of patients with CS treated with MCS demonstrates that the use of MCS devices is associated with high rates of complications and nursing care requirements, which are driven primarily by large-bore MCS devices. Categories: CORONARY: Hemodynamic Support, Cardiogenic Shock and Cardiac Arrest.

Cardiology/Cardiovascular Research
Fadel R, **Villablanca P**, **Giustino G**, **Gonzalez PE**, **O’Neill B**, **Frisoli T**, **Basir B**, **Cowger J**, **Shelters R**, **Lee J**, **Aurora L**, **Michaels A**, **Alaswad K**, and **O’Neill W**. TCT-460 Left Atrial Venoarterial Extra-Corporeal Membrane Oxygenation (LAVA-ECMO) Compared to Combination VA-ECMO and Impella (ECPELLA) in the Management of Acute Myocardial Infarction Cardiogenic Shock (AMI-CS). *J Am Coll Cardiol* 2024; 84(18):B145. Full Text

Background: Left ventricular (LV) unloading is associated with improved mortality among patients with cardiogenic shock on venoarterial extracorporeal membrane oxygenation (VA-ECMO). There is a paucity of data comparing mechanical support devices, particularly percutaneous cannulation strategies. Methods: We performed a retrospective analysis of patients with acute myocardial infarction–related cardiogenic shock (AMI-CS) on VA-ECMO from 2018 to 2023 at a quarternary care center. Patients were divided based on index cannulation strategy. Complications related to extracorporeal membrane oxygenation (ECMO) and mortality outcomes were analyzed. Results: Seventy patients were analyzed; 20 (29%) were treated with left atrial venoarterial ECMO, and 50 (71%) were treated with combination VA-ECMO plus Impella (Abiomed) (ECPELLA). Baseline demographics including age, sex, race, body

mass index, and medical history as well as baseline lactate levels and Society of Cardiovascular Angiography and Interventions shock stage at the time of cannulation were similar. Hemodynamic effects of both strategies (Figure) were similar. Patients treated with ECPELLA experienced more access site bleeding (34.0% vs 10.0%; P = 0.042) and received more blood transfusions (90.0% vs 60.0%; P = 0.003). Incidence of limb ischemia and stroke were higher among patients with ECPELLA but did not meet statistical significance. Thirty-day survival from cannulation was similar between the 2 groups. [Formula presented] Conclusion: Left atrial venoarterial ECMO demonstrates a similar hemodynamic profile compared to ECPELLA among patients with AMI-CS, with lower rates of access site bleeding and blood transfusions. Future studies comparing these treatment modalities are warranted. Categories: CORONARY: Hemodynamic Support, Cardiogenic Shock and Cardiac Arrest.

Cardiology/Cardiovascular Research
Falah B, Thompson J, **Basir B**, Moses J, Redfors B, Schonning M, **O'Neill W**, and Wollmuth J. TCT-407 Clinical Characteristics and Outcomes of Impella-Supported High-Risk Percutaneous Coronary Intervention in Patients With Chronic Total Occlusion: Insights From the cVAD PROTECT III Registry. *J Am Coll Cardiol* 2024; 84(18):B118. Full Text

Background: Patients (pts) with chronic coronary total occlusion (CTO) have high-risk features and greater procedural risk. Little is known about CTO pts receiving Impella-supported high-risk percutaneous coronary intervention (HRPCI). Methods: Baseline clinical and angiographic characteristics, procedural complications, and outcomes in pts with and without coronary CTOs who received Impella-supported HRPCI in the cVAD PROTECT III study (NCT04136392) were evaluated. CTO was defined as at least 1 coronary lesion with Thrombolysis In Myocardial Infarction (TIMI) grade 0 flow by independent angiographic core lab assessment. Major adverse cardiovascular and cerebrovascular events (MACCE: composite of all-cause death, myocardial infarction, stroke/transient ischemic attack, and repeat revascularization) were assessed by a clinical events committee at 30 and 90 days. Results: Of 1,237 pts enrolled in the cVAD PROTECT III study, 1,019 had angiographic core lab TIMI flow assessment; 12.6% had CTO, of which 58.5% were successfully revascularized. Patients with CTOs had longer procedures (2.4 vs 2.0 h, P = 0.0002), higher pre-PCI SYNTAX scores (31.2 vs 27.5, p = 0.004), longer lesions (18.5 vs 13.7 mm, P < 0.0001), and more lesions treated (2.7 vs 2.5, P = 0.04). There was no significant difference in PCI-related intraprocedural complications between groups. MACCE rates at 30 and 90 days were comparable between groups (P = 0.23 and P = 0.36, respectively). [Formula presented] Conclusion: Results from PROTECT III indicate that pts with a CTO undergoing Impella-supported HRPCI have higher anatomical complexity, but comparable periprocedural and acute outcomes as those without CTO. Categories: CORONARY: Complex and Higher Risk Procedures for Indicated Patients (CHIP).

Cardiology/Cardiovascular Research
Falah B, Zhao D, Thompson J, **Basir B**, Moses J, Redfors B, Schonning M, **O'Neill W**, and Wollmuth J. TCT-576 The Impact of Atherectomy in Severely Calcified Lesions in Patients With Impella-Supported High-Risk Percutaneous Coronary Intervention: Insights From the cVAD PROTECT III Study. *J Am Coll Cardiol* 2024; 84(18):B210-B211. Full Text

Background: Severely calcified coronary lesions lead to worse patient outcomes. Atherectomy is often used to treat these lesions, but there are limited data on outcomes for patients receiving Impella (Abiomed)-supported high-risk percutaneous coronary intervention (HRPCI). Methods: Patients in the cVAD PROTECT III study (NCT04136392) were stratified into groups: severe calcification who underwent atherectomy, severe calcification who did not undergo atherectomy, and nonsevere calcification. Calcification severity was dictated by an independent quantitative coronary angiography core lab based on angiographic radiopacities. Major adverse cardiovascular and cerebrovascular events (composite of all-cause death, myocardial infarction, stroke/transient ischemic attack, and repeat revascularization) were assessed at 30 and 90 days (Figure). Results: Of 1,015 patients, 28.5% had severe calcification without atherectomy, 32.1% had severe calcification with atherectomy, and 39.4% had nonsevere calcification. Intravascular imaging was used in 54.6% of cases with severe calcification undergoing atherectomy. At 90 days, severe calcification without atherectomy had higher major adverse cardiovascular and cerebrovascular event rates compared to the other groups. However, adjusted multivariable analysis found no significant difference at 90 days in severe calcification with atherectomy

vs severe calcification without atherectomy (HR: 0.76; 95% CI: 0.48-1.22; P = 0.25) or nonsevere calcification vs severe calcification without atherectomy (HR: 0.62; 95% CI: 0.38-1.00; P = 0.051). [Formula presented] Conclusion: Impella-supported HRPCI with atherectomy for severe calcification has comparable short-term safety and efficacy as Impella-supported HRPCI without atherectomy. Categories: CORONARY: Complex and Higher Risk Procedures for Indicated Patients (CHIP).

Cardiology/Cardiovascular Research
Fang J, **O'Neill B**, **Frisoli T**, **Nguyen F**, **Lee J**, **Gonzalez PE**, **Giustino G**, **Alrayes H**, Lok Lai LK, **O'Neill W**, and **Villablanca P**. TCT-168 Predictors of Procedural Abortion and Failure From Right Femoral Access in Transcatheter Tricuspid Valve Replacement With Edwards Evoque System in a Real-World Population. *J Am Coll Cardiol* 2024; 84(18):B418-B419. Full Text

Background: The Evoque system (Edwards Lifesciences) is the only commercially available transcatheter tricuspid valve replacement (TTVR) in the United States for severe tricuspid regurgitation (TR). We examine the determinants of transfemoral Evoque TTVR in a real-world population. Methods: Thirty-four consecutive patients underwent commercial transcatheter tricuspid valve replacement (TTVR) at a tertiary center in the United States in February through June, 2024. We perform retrospective analysis for the factors associated with unsuccessful right transfemoral attempts, including those requiring switching over to left femoral approach and those with abortion. Results: Overall success rate was 79.4% (27/34), including 22 patients from right femoral vein (RFV) access, 4 patients with success after switching from right to left femoral vein (LFV) access, and 1 patient with upfront left femoral access, all of which were switched due to a too ventricular delivery system position from right femoral access with concerns of inability to capture the tricuspid annulus. Abortion rate was 20.6% (7/34), including 4 cases due to overly ventricular system, 1 due to discrepant annular size too large for a 52-m valve on procedure day, and 1 due to venous tortuosity. Right atrial height: the distance from tricuspid annulus to top of right atrium, was larger in patients with initial RFV success group: 72.8 mm (67.4-79.7) compared LFV/aborted group: 65.7 mm (57.9-72.6), rank-sum P = 0.04. Median RA height 72.8 in RFV group, 68.5 in LFV group, and 65.5 in aborted group. TR was more likely to be primary (14%) and functional (77%) in RFV group; and more likely to be pacing-lead induced (33%) or mixed (17%) in LFV/abortion group, chi-square P = 0.033. Atrial fibrillation was less common in LFV/abortion group. No other significant difference was found. Conclusion: Abortion in commercial Evoque TTVR is considerable. Low RA height and TR due to mixed etiology or pacing-leads factors are associated major determinants. Of note, the median values of RA height for switching to LFV access and case abortion are numerically higher than suggested by industry. Preprocedural diuresis to avoid larger-than-expected annular size and awareness of venous tortuosity are also important. Categories: STRUCTURAL: Valvular Disease: Tricuspid.

Cardiology/Cardiovascular Research
Fang J, **Villablanca P**, **Frisoli T**, **Lee J**, **Gonzalez PE**, **Giustino G**, **Alrayes H**, Kamel-Abusalha L, **Ellauzi R**, Lok Lai LK, **O'Neill W**, and **O'Neill B**. TCT-896 Comparative Effectiveness of Balloon Aortic Valvuloplasty From Radial and Femoral Approach as Temporalizing Procedure. *J Am Coll Cardiol* 2024; 84(18):B377-B378. Full Text

Background: Balloon aortic valvuloplasty (BAV) is traditionally done over large bore femoral arterial access. We examine the comparative effectiveness of BAV via transfemoral and transradial/transulnar approach. Methods: From 2020-2024, 150 patients with severe aortic stenosis had BAV either via transradial/transulnar access (TR) (n = 100) or transfemoral (TF) (n = 50) approach at a tertiary center in the USA. TR approach was performed using an 8-Fr short sheath when deemed feasible on ultrasound and with 18- to 22-mm balloons sized 1:1 to the left ventricular outflow tract from echocardiogram. Hemodynamic effects, periprocedural outcomes, and transcatheter aortic valve replacement (TAVR) was recorded. Results: TR approach was feasible in 90.4% of patients. Switch-over to femoral approach due to spasm or calcium occurred in 2% patients. Vessel patency was preserved in 95.9%. End-stage kidney disease, female sex, and low body weight were independent predictors of unfeasible TR approach on multivariate analysis. Compared with TF, TR approach had shorter procedure time (59 vs 83 min), lower contrast volume (16 vs 31 mL), shorter time to discharge (2 vs 5 days), less bleeding: VARC-II major bleed 3% vs 12%; and less vascular complication: VARC-II major 1% vs 10%, all P < 0.05 after multivariate adjustment. Hemodynamic success was comparable 87% TR 84% TF. Twenty-two percent of

TF and 27% of TR group required more than 2 balloon inflation and pacing runs. Intraprocedural hypotension, stroke, and increased aortic insufficiency rates were not statistically different: 12% TF vs 4% TR for hypotension; 2% TF 1 % TR for stroke. Thirty percent TF 35% TR for increased AI (none severe) (all P>=0.05). There was no statistically significant difference in time-to-event for a composite of heart failure/unplanned hospitalization and all-cause mortality at 90 days, 27% TR, 36% TF, log-rank P = 0.56. Kaplan-Meier showed a trend toward earlier TAVR in TR group at 90 days, log-rank P = 0.0554; 44% TF vs 60.2%. Conclusion: BAV via TR approach is feasible in most patients and associated with quicker procedure and discharge, less vascular and bleeding complication, similar hemodynamic result compared with TF, and possible trend toward quicker transition to TAVR. Categories: STRUCTURAL: Valvular Disease: Aortic.

Cardiology/Cardiovascular Research
Frisoli T, Eleid M, Krishnaswamy A, Kapadia S, Yadav P, Rajagopal V, Makkar R, Stinis C, Chetcuti S, Morse M, Frangieh A, Abbas A, Whisenant B, Guerrero M, Rodriguez E, Ailawadi G, and **O'Neill W**. TCT-86 Real-World 30-Day Outcomes for the SAPIEN 3 Ultra Resilia Transcatheter Heart Valve in the Treatment of Failed Bioprosthetic Mitral Valves: A Propensity-Matched Analysis. *J Am Coll Cardiol* 2024; 84(18):B234. Full Text

Background: Mitral valve in valve (VIV) is safe and effective for severe bioprosthetic mitral degeneration, and associated with high one year survival rates. Little is known about the hemodynamic performance of the newest-generation Resilia SAPIEN 3 Ultra valve when used for mitral VIV. Methods: Retrospective analysis of patients undergoing transseptal mitral VIV with SAPIEN 3 valve family for failed surgical bioprostheses from 2021 through 2023 in the TVT Registry database with CMS data linkage was performed. 1,004 patients were studied in a 1:1 propensity matched analysis comparing Resilia vs non-Resilia valves with adjustment done for various covariates, including balloon valve fracture, predilatation and postdilatation. The primary outcome was echocardiographic mean gradient (MG) at 30 days. Results: Of the 1,004 patients studied, 48, 354, and 602 received 23-, 26-, and 29-mm valves, respectively. The mean age was 70.7 years, mean STS was 8.5, and 56.7% were women. Thirty-day mortality was similar for Resilia vs non-Resilia valves regardless of valve size (3.4% vs 3.8% for the overall cohort; P = 0.8, 4.2% vs 0%; P = 0.3 for 23 mm, 3.0% vs 3.5%; P = 0.8 for 26 mm, and 3.5% vs 4.2%; P = 0.0.7 for 29 mm). Kansas City Cardiomyopathy Questionnaire score at 30 days was also similar between groups regardless of valve size. Echocardiographic MG at 30 days was lower for Resilia vs non-Resilia for all valve sizes (Figure 1) [Formula presented] Conclusion: Resilia valves were associated with similar clinical outcomes following MVIV compared with non-Resilia valves, but with lower echo-derived gradients at 30 days. Categories: STRUCTURAL: Valvular Disease: Mitral.

Cardiology/Cardiovascular Research
Giustino G, **Fang J**, **Frisoli T**, **Lee J**, **Nguyen F**, **Gonzalez PE**, **Villablanca P**, **O'Neill W**, and **O'Neill B**. TCT-167 Transjugular Transcatheter Tricuspid Valve Replacement With the Evoque System. *J Am Coll Cardiol* 2024; 84(18):B418. Full Text

Background: The transcatheter tricuspid valve replacement (TTVR) Evoque system is designed to be delivered to the right ventricle via right or left transfemoral (TF) access. However, certain patients may not be a candidate for TF access. We report our experience of TTVR with Evoque via right internal jugular (RIJ) access in patients who were not suitable for TF-TTVR. Methods: From February 2024, a total of 36 patients were screened for TF-TTVR with the Evoque valve at a tertiary center (Henry Ford Health System, Detroit, Michigan). Among these, 29 underwent successful TTVR and in 7 cases the procedure was aborted. Among the aborted cases, 4 were reevaluated and underwent attempted TTVR via RIJ. In 4/5 patients referred for RIJ-TTVR after failed TF-TTVR, the reason for aborting TF-TTVR was the inability to achieve sufficient right atrial height leading to excessive RV implant depth. Results: Clinical and procedural characteristics of the 5 patients who underwent RIJ-TTVR are reported in Table 1. All cases were performed with the patient under general anesthesia and with TEE guidance. There were no periprocedural adverse events, and all cases were technically successful. [Formula presented] Conclusions: In the largest case series of nontransfemoral TTVR with Evoque reported to date, the RIJ appeared to be a feasible, safe, and effective alternative vascular access that overcomes some of the anatomic constraints encountered from the transfemoral route. Further insights into pre-procedural

anatomic analysis are necessary to identify patients who may benefit from an upfront RIJ-TTVR approach. Categories: STRUCTURAL: Valvular Disease: Tricuspid.

Cardiology/Cardiovascular Research
Gregerson S, **Frisoli T**, **O'Neill B**, **Lee J**, **Villablanca P**, **O'Neill W**, and **Gonzalez PE**. TCT-842 Transcatheter Aortic Valve Replacement in ESRD: Short- and Long-Term Outcomes, Valve Degeneration, and Reintervention Rates in Propensity-Matched Analysis. *J Am Coll Cardiol* 2024; 84(18):B346. Full Text

Background: Transcatheter aortic valve replacement (TAVR) has shown a clear benefit in patients with symptomatic, severe aortic stenosis (AS), yet there is a paucity of data on end-stage renal disease (ESRD) patients. Methods: This retrospective single-center study at a quaternary valve center evaluated the outcomes of ESRD patients undergoing TAVR from 2012-present. We first analyzed rates of major adverse cardiac event (MACE) outcomes, structural valve degeneration (SVD), and structural valve reintervention (SVR) for all ESRD patients (unadjusted cohort). We then performed propensity matching to compare a subset of ESRD patients (adjusted cohort) with non-ESRD chronic kidney disease (CKD) patients. Preoperative risk was determined using the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM). Results: The unadjusted ESRD cohort of 95 patients demonstrated high preoperative risk (9.67%) with correlating high MACE outcome rates during the index hospitalization. At long-term follow-up, the SVD and SVR rates were 26.3% and 3.2%, respectively. There was no correlation between preoperative risk and time to SVD. After propensity matching the adjusted cohorts for preoperative risk (ESRD 7.63% and non-ESRD CKD 7.67%), a total of 54 patients were included in this subanalysis. These ESRD patients demonstrated a nonsignificant trend toward higher death rates during the index hospitalization ($P = 0.09$), as well as significantly higher MACE outcomes ($P < 0.01$) and bleeding events ($P = 0.02$). At the 1-year follow-up period, death ($P = 0.03$), MACE ($P < 0.01$), and SVD rates (0.04) were significantly higher in the ESRD cohort. No SVR was reported in either matched cohort. [Formula presented] Conclusion: In those undergoing TAVR, ESRD patients are at higher risk of MACE outcomes and SVD than non-ESRD CKD patients. Despite this, rates of SVR are low. This study helps risk stratify ESRD patients considered for TAVR and prognosticate post-TAVR valve outcomes in both the short-term and long-term follow-up period. Categories: STRUCTURAL: Valvular Disease: Aortic.

Cardiology/Cardiovascular Research
Halboni A, **Fram G**, **Giustino G**, **Sturla N**, **Gonzalez PE**, **Villablanca P**, **Lee J**, **Frisoli T**, **Alnajjar R**, Wang DD, **O'Neill W**, and **O'Neill B**. TCT-944 Left Ventricular Outflow Tract Impact on Transcatheter Mitral Valve Interventions. *J Am Coll Cardiol* 2024; 84(18):B402. Full Text

Background: In patients planned for transcatheter mitral valve (MV) interventions, left ventricular outflow tract (LVOT) significantly impacts choice of therapy and outcomes. Among patients with MV disease, we studied the patterns of treatment and outcomes based on LVOT. Methods: We conducted a single-center study including all patients with severe MV disease who were evaluated by a multidisciplinary heart team for MV therapies between 2018 and 2023. All patients underwent preprocedural cardiac computed tomography as part of screening. Results: A total of 432 patients were included. One hundred fifty-seven patients (36.3%) had a predicted neo-LVOT <150 mm2, whereas 275 patients (63.7%) had a predicted neo-LVOT ≥150 mm2. The overall median predicted neo-LVOT was 304.5 mm2 (58.3-621.8). Baseline characteristics are shown in the Table. Treatment allocations are demonstrated in the Figure. Median follow-up time was 290 days (83.5-656.5). All-cause mortality in patients with a neo-LVOT <150 mm2 was 26.1% compared to 32.4% in patients with a neo LVOT ≥150 mm2 ($P = 0.17$). [Formula presented] [Formula presented] Conclusion: Patients with a predicted neo-LVOT <150 mm2 were older, mostly female, more likely to have severe mitral stenosis, and had fewer definitive treatment options. Strategies to address the risk of a small LVOT or innovative transcatheter MV therapies are warranted in these patients. Categories: STRUCTURAL: Valvular Disease: Mitral.

Cardiology/Cardiovascular Research
Jebaje Za, **Fadel R**, and **Alaswad K**. TCT-79 Unprotected Left Main PCI in Focus: Procedural Insights, Clinical Outcomes, and Predictors of Mortality in a High-Volume Quaternary Care Center. *J Am Coll Cardiol* 2024; 84(18):B202. Full Text

Background: Unprotected left main coronary artery percutaneous coronary intervention (ULMCA-PCI) presents a unique therapeutic challenge, with conflicting data on short and long-term outcomes. Coronary artery bypass grafting (CABG) remains the guideline-preferred treatment approach. Methods: We performed a retrospective cohort review of patients undergoing ULMCA-PCI at a quaternary care institute in Metropolitan Detroit from 2019 to 2023. Complication rates and outcomes including in-hospital, 30-day, 90-day, and 1-year all-cause mortality were assessed. Subgroup analysis was performed on patients with high Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) scores, defined as ≥33. Results: 626 patients were analyzed, the majority of whom were male (67.6%) and white (63.3%), with a median (Q1-Q3) age of 73 (65-80). LMCA-PCI indications included stable angina (41.9%), unstable angina (17.1%), non–ST-segment myocardial infarction (NSTEMI, 32.1%), STEMI (4.5%), and acute MI–related cardiogenic shock (AMI-CS, 4.5%). Median SYNTAX score was 27.0 (25.0-31.0), with 130 (20.7%) patients having a score ≥33. Mechanical circulatory support (MCS) was utilized electively in 84 (13.4%) of cases. Successful revascularization was achieved in 623 (99.5%) of cases. Complications occurred in 125 (19.9%) of cases when assessed as a composite. 120 subjects (19.2%) required emergency escalation of MCS intraoperatively, and 74 (10.1%) required continuation of MCS postoperatively. All-cause in-hospital mortality rate was 6.1%. 30-day, 90-day, and 1-year survival rates were 91.9%, 90.7%, and 84.3%, respectively. Patients with a high SYNTAX score (≥33) experienced similar complication rates overall but had notably higher rates of perforations (P = 0.02) and higher MCS use (P = 0.041). Despite this, a higher SYNTAX score correlated with greater left ventricular ejection fraction improvement at 1 year (R = 0.201; P = 0.006). Conclusions: Our study results, in conjunction with the evolving data on the viability of ULMCA-PCI, provide a foundation for future research aimed at a more in-depth comparison between PCI and CABG within this high-risk patient cohort. Categories: CORONARY: Complex and Higher Risk Procedures for Indicated Patients (CHIP).

Cardiology/Cardiovascular Research

Madanat L, Alhuneafat L, Hanson I, Abbas A, Al-Abdouh A, Ayyad M, **Obeidat L**, Mhanna M, **Frisoli T**, **Alqarqaz M**, and **Villablanca P**. TCT-884 Transcatheter Aortic Valve Replacement Outcomes in Patients With Cardiogenic Shock: A Systematic Review and Meta-Analysis. *J Am Coll Cardiol* 2024; 84(18):B370. Full Text

Background: While transcatheter aortic valve replacement (TAVR) has broadened treatment options for critically ill patients, outcomes among those with concomitant cardiogenic shock (CS) are not well-explored. Methods: We conducted a comprehensive search of major databases for studies comparing outcomes of TAVR in patients with and without CS since inception up to October 31, 2023. Dichotomous outcomes were assessed using the Mantel-Haenszel method (risk ratio, 95% CI), and continuous outcomes were evaluated using mean difference and 95% CI with the inverse variance method. Results: Five studies were included in the final analysis with a total of 26,283 patients. Among the 7,267 (27.6%) patients with CS, 30-day mortality (OR: 3.41; 95% CI: 2.01-5.76; P < 0.01) and 30-day major vascular complications (OR: 1.72; 95% CI: 1.54-1.92; P < 0.01) were higher compared with those without CS. Conversely, 1-year mortality was not significantly different (OR: 2.68; 95% CI: 0.53-13.46, P = 0.12). No significant differences were observed in the likelihood of 30-day aortic valve reintervention (OR: 3.20; 95% CI: 0.63-16.22, P = 0.09) or post-TAVR aortic insufficiency (OR: 0.91; 95% CI: 0.33-2.51, P = 0.73) between both groups. Furthermore, 30-day stroke, pacemaker implantation, and in-hospital major bleeding were similar between both cohorts (Figure 1). Conclusion: Among TAVR patients, short-term mortality is higher in patients with CS. There was no significant difference in 1-year mortality, need for AV reintervention, in-hospital bleeding or 30-day stroke and pacemaker implantation in patients with CS shock compared with patients not in CS. Categories: STRUCTURAL: Valvular Disease: Aortic

Cardiology/Cardiovascular Research

Madanat L, Ayyad M, Al-Abdouh A, Mhanna M, Alhuneafat L, **Obeidat L**, **Alqarqaz M**, Hanson I, Abbas A, **Frisoli T**, and **Villablanca P**. TCT-144 Comparative Safety and Effectiveness of Transcatheter Aortic Valve Replacement and Surgical Aortic Valve Replacement in Patients With a Small Aortic Annulus: A Systematic Review and Meta-Analysis. *J Am Coll Cardiol* 2024; 84(18):B365-B366. Full Text

Background: Patients with a small aortic annulus (SAA) undergoing aortic valve replacement are at increased risk of patient-prosthesis mismatch (PPM), which adversely affects outcomes. Transcatheter aortic valve replacement (TAVR) has shown promise in mitigating PPM compared with surgical aortic valve replacement (SAVR). Methods: We conducted a systematic review and meta-analysis following PRISMA guidelines to compare clinical outcomes, mortality, and PPM between SAA patients undergoing TAVR and SAVR. Results: Nine studies were included with a total of 2,476 patients (1,259 patients in the TAVR group and 1,217 in the SAVR group). TAVR demonstrated similar 30-day (OR: 0.65; 95% CI: 0.09-4.61; P = 0.22) and 2-year mortality (OR: 0.82; 95% CI: 0.53-1.27: P = 0.24), myocardial infarction (OR: 0.73; 95% CI: 0.1-5.18; P = 0.56), and stroke rates (OR: 1.1; 95% CI: 0.23-5.2; P = 0.86) compared with SAVR. However, TAVR showed significant advantages in reducing severe PPM (OR: 0.53; 95% CI: 0.39-0.72; P < 0.0001) and major bleeding at both 30 days (OR: 0.44; 95% CI: 0.31-0.64; P < 0.01) and 2 years (OR: 0.4; 95% CI: 0.21-0.77; P = 0.03) post procedure. Conversely, TAVR had worse outcomes in 30-day permanent pacemaker implantation rates (OR: 2.76; 95% CI: 1.13-6.75; P =0.04) (Figure 1). Conclusion: Our findings suggest that both TAVR and SAVR are viable options for treating severe AS in patients with small aortic annuli. TAVR offers advantages in reducing PPM and major bleeding, whereas SAVR performs better in terms of pacemaker implantation rates. Consideration of patient characteristics is crucial in selecting the optimal treatment approach for severe AS. Categories: STRUCTURAL: Valvular Disease: Aortic.

Cardiology/Cardiovascular Research

Mahmood S, Madanat L, Renard B, Hanson I, Palomo A, Schwann T, Vivacqua A, Kindzelski B, **Villablanca P**, Khalili H, Chhabra K, Alakhras H, Ahmad E, and Abbas A. TCT-164 Immediate and Pre-Discharge Post-TAVR Invasive and Echocardiographic Hemodynamics of Sapien 3 Resilia, Sapien 3 Ultra and Self-Expanding Valves. *J Am Coll Cardiol* 2024; 84(18):B397. Full Text

Background: Studies suggest similar immediate post transcatheter aortic valve replacement (TAVR) invasive and echocardiographic gradients across TAVR platforms, despite lower discharge echocardiographic gradients in self-expanding valves (SEV) vs balloon-expandable valves (BEV) Sapien 3 Ultra (S3U). Lower discharge echocardiographic gradients have been reported with BEV Sapien 3 Resilia (S3R) vs S3U. We compared immediate post-TAVR invasive and echocardiographic gradients and discharge echocardiographic gradients in BEV S3U, BEV S3R, and SEV. Methods: Consecutive patients who underwent TAVR were included. Immediate post-TAVR invasive gradients were compared with concomitant and discharge echocardiographic gradients across BEV S3U, BEV S3R, and SEV. Results: A total of 166 patients were analyzed (77 S3U, 61 S3R, 28 SEV). Post-TAVR, invasive gradients were lower than echocardiographic gradients in all valves (P value < 0.001 for all). Across all valves, immediate post-TAVR invasive (S3U; 0.21 ± 0.9 mm Hg, S3R; 0.1 ± 0.5 mm Hg, SEV; 0.21 ± 0.70 mm Hg, P = 0.81) and echocardiographic gradients (S3U; 5.0 ± 2.4 mm Hg, S3R; 5.0 ± 2.7 mm Hg, SEV; 6.0 ± 2.3 mm Hg, P = 0.40) were similar. Discharge echocardiographic gradients were highest in S3U valves (12 ± 4.8 mm Hg) vs S3R (10 ± 4.5 mm Hg) and SEV (9 ± 4.4 mm Hg) with P value = 0.002 (Figure 1A and B). [Formula presented] Conclusion: Lower discharge echocardiographic gradients in BEV S3R and SEV vs BEV S3U were noted despite similar immediate post-TAVR invasive and echocardiographic gradients. Valve design and flow states impact discharge echocardiographic gradients but not post-TAVR invasive and echocardiographic gradients. Categories: STRUCTURAL: Valvular Disease: Aortic.

Cardiology/Cardiovascular Research

Mandava S, **Ghazzal A**, Torres C, Vedantam K, Igyarto Z, Martinsen B, Kirtane A, Leon M, and Beohar N. TCT-384 Sex-Based Analysis of Acute Outcomes Post-Orbital Atherectomy for Severely Calcified Coronary Lesions. *J Am Coll Cardiol* 2024; 84(18):B105. Full Text

Background: Limited research exists on the safety and effectiveness of coronary orbital atherectomy (OA) in women vs men, with prior studies suggesting higher rates of complications in women. This single-center analysis aimed to provide a sex-based comparison using real-world data. Methods: Retrospective analysis was conducted on consecutive patients treated with coronary OA for severely calcified lesions at the Mount Sinai Medical Center, Miami Beach, Florida, from January 2014 to September 2020. Severe angiographic complications, bleeding events, in-hospital heart failure, cardiogenic shock, and major adverse and cardiac cerebrovascular events (MACCE) comprised of cardiac death, myocardial infarction

(MI), ischemic cerebrovascular accident (CVA), and hemorrhagic CVA were assessed. Results: Among 609 patients undergoing percutaneous coronary intervention (PCI) with OA, 36% were women and 64% were men, with median ages of 77 and 73 years, respectively. Women exhibited a significantly higher prevalence of Hispanic, Black, or Indigenous ethnicity all with $P < 0.05$, as well as more frequent right coronary artery target vessels (32.6% vs 19.3%; $P < 0.001$). They also had significantly lower rates of smoking, MI, and coronary artery bypass grafting all with $P < 0.05$. No significant sex differences were observed in severe angiographic complications, bleeding events, or in-hospital MACCE. However, heart failure post-PCI was significantly more common among women (1.4% vs 0%; $P = 0.048$). Conclusion: Contrary to previous clinical trial findings, this real-world analysis suggests that women undergoing OA have similar rates of severe angiographic complications and in-hospital MACCE as men. The higher incidence of post-PCI heart failure in women warrants further investigation. Categories: CORONARY: Coronary Atherectomy, Plaque Modification, Lithotripsy, Thrombectomy, Cutting/Scoring Balloons.

Cardiology/Cardiovascular Research
Mutlu D, Alexandrou M, Strepkos D, Carvalho P, Jalli S, Goktekin O, Jaffer F, Frizzell J, Elbarouni B, Khatri J, **Alaswad K**, Davies R, Ozdemir R, Uluganyan M, Ahmed Y, Choi J, Young L, Raj L, Azzalini L, Ybarra L, Riley R, Rangan B, Mastrodemos O, Sandoval Y, Burke MN, and Brilakis E. TCT-404 Trends of Drug Coated Balloon Use in Chronic Total Occlusion Percutaneous Coronary Intervention: Insights From the PROGRESS-CTO Registry. *J Am Coll Cardiol* 2024; 84(18):B116-B117. Full Text

Background: There is limited information on the use of drug-coated balloons (DCBs) in chronic total occlusion (CTO) percutaneous coronary artery intervention (PCI). Methods: We evaluated the frequency of DCB use in an international registry (PROGRESS-CTO [Prospective Global Registry for the Study of Chronic Total Occlusion Intervention]). Results: Among 7,893 patients, DCBs were used in 200 cases (2.5%; paclitaxel coated in 91.8%, sirolimus coated in 8.2%) with increasing frequency over time (Figure). Mean patient age was 64 ± 10 years, 80.1% were men, and 24.5% had prior coronary artery bypass graft surgery. CTOs requiring the use of DCBs were less complex with a lower J-CTO score (Multicenter CTO Registry of Japan) (2.1 ± 1.2 vs 2.3 ± 1.2; $P = 0.008$), higher prevalence of in-stent restenosis (34.2% vs 15.5%; $P < 0.001$), and less moderate to severe calcification (32.3% vs 41.7%; $P = 0.010$) and tortuosity (19.3% vs 25.9%; $P = 0.045$). Lesions requiring DCBs were more frequently located in the right coronary artery (47.9%) and left anterior descending artery (34.0%). The mean number of DCBs was 1.3 ± 0.6 per PCI, with a mean diameter of 3.3 ± 2.4 mm, and mean length of 34.4 ± 18.0 mm. A hybrid strategy was more frequently used (59.0%) than a DCB-only strategy. The primary reason for DCB use was in-stent restenosis (53.8%) followed by investment procedure (33.9%) and side branch treatment (12.3%). The most common successful CTO crossing technique was antegrade wiring (71.7%) followed by retrograde (16.2%) and antegrade dissection and re-entry (8.1%). Technical and procedural success and the incidence of major cardiac adverse events were similar in both groups. [Formula presented] Conclusion: DCB are increasingly being used in CTO PCI and are associated with high success and low complication rates. Categories: CORONARY: Drug-Eluting Balloons and Local Drug Delivery.

Cardiology/Cardiovascular Research
Nguyen F, **Gandolfo C**, **Rangavajla G**, **Giustino G**, **Fang J**, **Ilg K**, **Wyman J**, **O'Neill W**, **Gonzalez PE**, **Villablanca P**, **Lee J**, **Frisoli T**, and **O'Neill B**. TCT-169 Safety of Transcatheter Tricuspid Valve Replacement in Patients With Pacemaker Leads. *J Am Coll Cardiol* 2024; 84(18):B419. Full Text

Background: With recent approval of the EVOQUE valve, transcatheter tricuspid valve replacement (TTVR) has emerged as an effective therapy for severe tricuspid regurgitation (TR). Many patients undergoing TTVR have existing permanent pacemaker (PPM) or implantable cardiac defibrillator (ICD) leads. The impact of TTVR on impedance and thresholds in these patients is unknown. Methods: Patients with PPM/ICDs undergoing TTVR with the commercial EVOQUE valve at Henry Ford Hospital from February-June 2024 were included. Device interrogations were performed before EVOQUE implant, 24 h after, and at 30 days. Lead position pre- and post-EVOQUE was evaluated by review of cine images. Results: Twelve patients with devices who underwent EVOQUE were included. Mean age was 84 years old. Mean New York Heart Association functional class was 2.8 ± 0.5. 9 patients (75%) had atrial fibrillation, and all had severe TR. Eleven patients had PPMs and 1 had an ICD. All 12 had RV leads (100%), 11 had right atrial leads (92%), 5 had coronary sinus leads (42%), and 1 had a His lead (8%).

Average change in lead impedance post-procedure was −5.9% ± 4.9% at 24 h, all <15% (Figure 1). Seven patients had 30-day follow-up with average impedance change of −3.2% ± 4.8%. Average change in RV capture was threshold −3.5% ± 18%. There were no lead dislodgements or need for lead extraction. Mild TR or better post-TTVR was achieved in 9 patients (75%). [Formula presented] Conclusion: TTVR with the EVOQUE appears to be safe in patients with preexisting PPM/ICD leads, with minimal short-term impact on lead parameters. Follow-up beyond 30 days will be necessary to evaluate the long-term effects in these patients. Categories: STRUCTURAL: Valvular Disease: Tricuspid.

Cardiology/Cardiovascular Research
Rangavajla G, **Abdelhai O**, **Nguyen F**, **Giustino G**, **Fang J**, **Dawdy J**, **Gonzalez PE**, **Villablanca P**, **Lee J**, **Parikh S**, **Zweig B**, and **O'Neill B**. TCT-170 Conduction System Disorders After Transcatheter Tricuspid Valve Replacement. *J Am Coll Cardiol* 2024; 84(18):B419-B420. Full Text

Background: Transcatheter tricuspid valve replacement with the Evoque valve was recently approved by the U.S. Food and Drug Administration as a transcatheter therapy for severe tricuspid regurgitation, but initial data suggest a high rate of conduction system disorders (CSDs). As real-world data are limited, we aimed to characterize predictors of post-TTVR CSD and associations with clinical outcomes. Methods: Patients undergoing Evoque at Henry Ford Hospital February-May 2024 were included; those with aborted procedures, prior bundle branch blocks (BBB), or prior pacemakers (PPM) were excluded. Predictors of new CSD, defined as new BBB or complete heart block (CHB) were assessed, and we analyzed the association between CSD and a composite of death or heart failure hospitalization. Results: Of 28 total Evoque patients, 18 were excluded (aborted procedure: 6, prior BBB: 3, prior PPM: 12). Of the 10 studied patients, 5 developed new CSD: 4 with RBBB and 1 with CHB requiring new PPM. Percent oversizing of the valve relative to the native annulus was not associated with CSD; however, greater baseline LVEF was associated (Figure 1A, P <0.05). New CSD post-Evoque was not associated with death or heart failure hospitalization over a median 11-day (IQR 3-32) follow-up (Figure 1B). [Formula presented] Conclusion: Although sample size and follow-up time were limited, we report early real-world data of post-Evoque CSD. Baseline LVEF, but not percent oversizing, was associated with new CSD. We aim to conduct further studies to better inform patient selection by identifying reliable predictors and clinical outcomes of post-Evoque CSD. Categories: STRUCTURAL: Valvular Disease: Tricuspid.

Cardiology/Cardiovascular Research
Richardson LA, **Berry R**, Harding AW, Nustad J, Ozemek C, Savage PD, Walker A, and **Brawner CA**. Clinical Exercise Physiologist: Importance Of Clinical Education. *Med Sci Sports Exerc* 2024; 56(10):668-669. Full Text

[Richardson, Laura A.] Univ Michigan, Ann Arbor, MI 48109 USA. [Berry, Robert; Brawner, Clinton A.] Henry Ford Hosp, Detroit, MI 48202 USA. [Harding, Aaron W.] PeaceHealth, Springfield, OR USA. [Nustad, Jill] Univ Mary, Bismarck, ND USA. [Ozemek, Cemal] Univ Illinois, Chicago, IL USA. [Savage, Patrick D.] Univ Vermont, Med Ctr, Burlington, VT USA. [Walker, Ash] Univ N Carolina, Pembroke, NC USA. System; Henry Ford Hospital; University of Mary; University of Illinois System; University of Illinois Chicago; University of Illinois Chicago Hospital; University of Vermont; University of Vermont Medical Center; University of North Carolina; University of North Carolina at Pembroke
laurari@umich.edu

Cardiology/Cardiovascular Research
Shah T, Holy C, Moses J, Parise H, Lemor A, **O'Neill W**, and Lansky A. TCT-573 Illness Severity Among Patients Undergoing Percutaneous Ventricular Assist Device Versus Intra-Aortic Balloon Pump Supported High-Risk Percutaneous Coronary Intervention (HRPCI). *J Am Coll Cardiol* 2024; 84(18):B209. Full Text

Background: This study was conducted to identify differences between Impella percutaneous ventricular assist device (PVAD) vs intra-aortic balloon pump (IABP)-supported HRPCI cohorts that may confound observational studies comparing the safety and efficacy of these devices. Methods: Patients undergoing HRPCI supported by PVAD or IABP between 2018 and 2024 were identified in the Premier Healthcare Database. Patients were excluded if they had cardiogenic shock or STEMI on admission, required

emergent procedures, had multiple mechanical circulatory support devices used, or underwent coronary artery bypass grafting within the same admission. Variable rate propensity score matching was performed using logistic regression analysis with 87 preprocedural variables (identified by statistical importance) including patient demographics, comorbidities, prior procedures, prior complications and provider/hospital factors. Measured covariates among unmatched patients were compared using standard mean difference (SMD) (with values >0.1 suggesting imbalance). Results: In total, we identified 4,879 patients (3,925 PVAD and 954 IABP) who met inclusion criteria. After matching, 1,414 PVAD and 75 IABP patients were excluded. Among excluded patients, PVAD-supported patients were considerably sicker than IABP-supported patients with more pulmonary disease (20.9% vs 10.7%, SMD = 0.283), peripheral vascular disease (35.9% vs 18.7%, SMD = 0.393), valvular disease (43.1% vs 18.7%, SMD = 0.549), and chronic kidney disease (28.2% vs 13.3%, SMD = 0.373). Excluded PVAD patients were also more likely to undergo more complex procedures with higher rates of 3-vessel percutaneous coronary intervention (16.1% vs 5.3%, SMD = 0.352) and atherectomy. Conclusion: Patients undergoing PVAD- vs IABP-assisted HRPCI are substantially sicker, leading to poor overlap in the propensity scores among these populations. This study demonstrates an inherent limitation of propensity matching in observational studies in this population that may bias any potential benefit of PVAD to the null given that a substantial portion of the sickest patients who receive PVAD, who are the most likely to derive benefit, are excluded and less sick patients who may do equally well with IABP are disproportionately included. Categories: CORONARY: Complex and Higher Risk Procedures for Indicated Patients (CHIP).

Cardiology/Cardiovascular Research
Shah T, Holy C, Moses J, Parise H, Lemor A, **O'Neill W**, and Lansky A. TCT-574 Safety and Efficacy of Percutaneous Ventricular Assist Device Versus Intra-Aortic Balloon Pump Supported High-Risk Percutaneous Coronary Intervention (HRPCI). *J Am Coll Cardiol* 2024; 84(18):B210. Full Text

Background: We compare outcomes between Impella percutaneous ventricular assist device (PVAD) vs intra-aortic balloon pump (IABP)-supported high-risk percutaneous coronary intervention (HRPCI) in a large-scale, contemporary claims dataset. Methods: Patients undergoing HRPCI supported by PVAD or IABP between January 2018 and April 2024 were identified in the Premier Healthcare Database. Patients were excluded if they had cardiogenic shock or STEMI on admission, required emergent procedures, had multiple mechanical circulatory support devices used, or underwent coronary artery bypass graft surgery within the same admission. Variable rate propensity score matching was performed using logistic regression of 87 preprocedural variables (identified by statistical importance) including patient demographics, comorbidities, prior procedures, prior complications, and provider/hospital factors. The primary endpoint was 90-day mortality while secondary endpoints included MACE (defined as myocardial infarction [MI], stroke, or death), new cardiogenic shock, acute kidney injury, cardiovascular-related bleeding, in-hospital bleeding requiring transfusions, length of stay, and discharge disposition. Results: A total of 4,879 patients (3,925 PVAD and 954 IABP) met inclusion criteria. Among these, 2,511 PVAD patients and 879 IABP patients undergoing HRPCI were matched. Mortality and MACE at 90 days and postprocedural cardiogenic shock and 30-day acute kidney injury were lower with PVAD compared with IABP support (Table 1). PVAD patients had shorter lengths of stay and were more likely to be discharged to home. There were no significant differences in rates of bleeding in either group. [Formula presented] Conclusion: This observational study suggests that PVAD-assisted HRPCI is associated with improved postprocedural hemodynamics and 90-day clinical outcomes without a significant increased risk of bleeding compared with IABP support. Categories: CORONARY: Complex and Higher Risk Procedures for Indicated Patients (CHIP).

Cardiology/Cardiovascular Research
Shah T, Holy C, Moses J, Parise H, Lemor A, **O'Neill W**, and Lansky A. TCT-575 Cost-Effectiveness Analysis of Percutaneous Ventricular Assist Devices vs Intra-Aortic Balloon Pump for High-Risk Percutaneous Coronary Intervention (HRPCI). *J Am Coll Cardiol* 2024; 84(18):B210. Full Text

Background: Health care resource utilization and costs are important when considering Impella percutaneous ventricular assist device (PVAD) supported HRPCI. A prior cost-effectiveness comparison of PVAD vs intra-aortic balloon pump (IABP) for HRPCI from the 2012 PROTECT II trial estimated an incremental cost-effectiveness ratio of $39,389/quality-adjusted life year (QALY) for pVAD. Our study

provides an up-to-date cost-effectiveness analysis. Methods: Patients undergoing PVAD vs IABP-supported HRPCI between 2018 and 2024 were identified from the Premier Healthcare Database (PHD) and propensity matched to balance baseline factors. Major adverse cardiovascular events (MACE) including myocardial infarction (MI), stroke, and death up to 2 years were collected. Costs reported in the PHD were used to estimate quality-adjusted life years (QALY) based on age and expected disutility from MI or stroke using previously published assumptions. Markov models were used to calculate incremental cost-effectiveness ratio (ICER) for PVAD vs IABP and evaluate the probability of cost-effectiveness based on willingness to pay thresholds. Results: The cost of index hospitalization was higher for PVAD compared with IABP; however, PVAD was associated with reduced rates of MACE and subsequent reductions in QALYs resulting in an ICER of $26,450/QALY (Figure 1). [Formula presented] Conclusion: The ICER for PVAD vs IABP-supported HRPCI appears to have decreased over the past decade to $26,450/QALY, and based on contemporary US thresholds, is considered cost-effective. Categories: CORONARY: Complex and Higher Risk Procedures for Indicated Patients (CHIP).

Cardiology/Cardiovascular Research
Thakker R, Khalif A, Xu Y, Bilazarian S, Bentley D, Iannaccone M, Wollmuth J, **O'Neill W**, Truesdell A, and Lichaa H. TCT-1005 Optimal PCI Sheath for Low Profile Single-Access PCI With Impella CP Hemodynamic Support. *J Am Coll Cardiol* 2024; 84(18):B430. Full Text

Background: Impella CP (Abiomed) is a percutaneous left ventricular assist device introduced via a 14-F sheath in the femoral artery. Challenges may arise when both percutaneous coronary intervention (PCI) and Impella CP placement must be performed in patients with complex vascular access, leading to development of the single-access technique. A limitation with the single-access technique is optimal PCI sheath diameter resulting in reduced torqueability within the Impella CP sheath. The aim of our study was to characterize the optimal 7-F PCI sheath for the 14-F Low low-profile single-access procedure. Methods: The outer diameter measurement of the PCI sheaths were performed using Keyence 2-axis laser micrometer. Torqueability was assessed using the Mark-10 MFI advances digital force/torque indicator on a simulated single-access setting in a simulated skin pad. The 7-F PCI sheath and guide catheter samples were selected based on physician feedback. Results: The Cordis Brite Tip 11 cm, Cordis Brite Tip 35 cm, and Terumo Destination had the largest outer diameters (Figure A). The Merit Prelude and Terumo Glidesheath were the easiest to insert/remove because of their smaller outer diameters and hydrophilic coating (Figure B). The ABMD LP Companion sheath had the best torqueability (Figure C). The longer ABMD LP Companion sheath did not impact torqueability, but removal force increased by 50%. [Formula presented] Conclusion: The Merit Prelude and Terumo Glidesheath are optimal PCI sheaths for single access Impella-supported PCI because of smaller outer diameters and hydrophilic coating. The ABMD LP Companion demonstrated the best torqueability and the least effort to advance. Categories: OTHER: Vascular Access: Coronary.

Cardiology/Cardiovascular Research
Zordok M, Etiwy M, Abdelazeem M, Dani S, Lichaa H, Kerrigan J, **Basir B**, **Alaswad K**, Brilakis E, and Megaly M. TCT-682 Gender Difference in the Outcomes of Patients With Spontaneous Coronary Artery Dissection Presenting With ST-Elevation Myocardial Infarction and Developing Cardiogenic Shock. *J Am Coll Cardiol* 2024; 84(18):B262. Full Text

Background: There are limited data on gender differences among patients with spontaneous coronary artery dissection (SCAD) who present as ST-elevation myocardial infarction (STEMI) and develop cardiogenic shock (CS). We aim to describe outcomes of SCAD patients presenting with STEMI and CS and outline the differences between men and women. Methods: We queried the US Nationwide Readmissions Database (NRD) from January 2016 to December 2020 to identify patients with SCAD presenting with STEMI who developed CS. We compared the characteristics, trends, and outcomes between men and women in this cohort. Results: Of 582,633 hospitalizations with STEMI, 0.2% (1,176 patients) had SCAD, of whom 346 (29.4%) had CS. There was no difference in median age between men and women (64 years [IQR 57-71] vs 63 years [IQR 49-72], P = 0.181). Men had a higher prevalence of prior myocardial infarction (MI) (14.2% vs 6.2%, P = 0.021). The overall mortality rate of SCAD patients with AMI-CS was 26.3%, with no difference between men and women. Patients with SCAD who had CS and underwent CABG had a mortality of 20%. Extracorporeal membrane oxygenation (ECMO) was used

in 5.4% of SCAD patients presenting with STEMI, and CS received ECMO with a survival rate of 54.5%. Conclusion: There were no differences in the baseline characteristics, rates of revascularization, or in-hospital mortality between men and women who had SCAD complicated by CS (SCAD-CS). Patients with SCAD-CS patients who underwent CABG had 80% in-hospital survival. CABG should be considered as a method of revascularization in this patient cohort. Categories: CORONARY: Hemodynamic Support, Cardiogenic Shock and Cardiac Arrest.

Center for Health Policy and Health Services Research

Gui H, Huang Y, Tao S, **Meng Z**, Liu Y, **Levin A**, **Ahmedani B**, and Wang Q. 15. Genetic Relationships and Biological Pathways Underlying Suicidality and Comorbid Mental Disorders: A Comprehensive Cross-Phenotype Analysis. *Eur Neuropsychopharmacol* 2024; 87:55. Full Text

Background: The co-occurrence of mental disorders and suicidality are frequently seen in epidemiology. One explanation lies in shared genetic liabilities, hence we aimed to investigate the phenotypic and genetic associations between multiple mental disorders and different levels of suicidality. Methods: Using UK Biobank (UKB) European individual data, we first evaluated the phenotypic and polygenic relationships between 12 mental disorders and gradient scales of suicidality (spanning suicidal ideation, suicide attempts, and suicidal death). Second, we used existing genome-wide association study (GWAS) summary statistics to estimate genetic correlations and to identify pleiotropic genes using a combination of statistical genetics tools. Summary statistics were accessed from: 1) the Psychiatric Genomics Consortium (major depressive disorder [MDD], bipolar disorder [BD], anxiety disorders [ANX], obsessive-compulsive disorder [OCD], anorexia nervosa [AN], autism spectrum disorder [ASD], attention deficit hyperactivity disorder [ADHD], schizophrenia [SCZ], cannabis use disorder [CUD], and post-traumatic stress disorder [PTSD]), 2) the Million Veterans Program (alcohol use disorder [AUD] and opioid use disorder [OUD]), and 3) their joint analysis (suicidality). Third, using shared genetic liabilities as instrument, we evaluated evidence for causal relationship between mental disorders and suicidality by structural equation models and Mendelian randomizations. Last, we accessed the All of Us (AoU) diverse cohort data for replication in non-European populations. Results: For UKB, 150,861 eligible individuals were retained after standard GWAS quality control. Eight out 12 mental disorders (MDD, BD, ANX, AUD, OCD, AN, ASD and ADHD) showed both significant phenotypic and polygenic correlations with gradient suicidality (false discovery rate < 0.05). Among them, the impact of MDD and BD on suicidality were the most obvious (for MDD: OR=5.78 and 1.26 for phenotypic and polygenic level; for BD: OR=12.98 and 1.14 for phenotypic and polygenic level). Using GWAS summary statistics, we also observed positive global genetic correlations between those 8 mental disorders and suicidality (rg ranging from 0·25 to 0·68, $p < 0.001$). Across pairs of suicidality and mental disorders, we identified 23 functional genes (including novel ones like BPTF, NOL11 and CACNG5) shared by five or more pairs. These genes were significantly enriched in two Gene Ontology sets: developmental process and regulation of biological process. We also identified unique genes within each pair which were enriched in different pathways (e.g., glutamatergic synapse for suicidality-MDD, negative regulation of biological process for suicidality-BD, and actin cytoskeleton for suicidality-AUD). Causal models indicated potential causality from genetic diatheses of MDD, BD, AUD, ADHD, and ASD to risk of suicidality. Multiple cross-phenotype associations with suicidality were also replicated in AoU African and Asian populations (e.g., $p < 0.05$ for MDD and BD polygenic associations). Discussion: This study underscores the urgent need to address the shared and distinct genetic architecture of suicidality and related mental conditions. The combination of longitudinal population-level biobanks and disease-ascertained GWAS are warranted to enhance our understanding of their relationships. Our findings will provide insights into future suicide prevention and management among individuals with and without mental disorders. Disclosure: Nothing to disclose.

Emergency Medicine

Cook B, **Jaehne AK**, Naiman M, **Wilson I**, **Veryser D**, **Kelly W**, **Ghosh S**, and **Rivers E**. Value Of Monocyte Distribution Width In Bacteremia Assessment In Emergency Department Patients. *Clin Chem* 2024; 70:1. Full Text

[Cook, B.; Jaehne, A. K.; Wilson, I.; Veryser, D.; Kelly, W.; Ghosh, S.; Rivers, E.] Henry Ford Hosp, Detroit, MI USA. [Naiman, M.] Beckman Coulter, Brea, CA USA.

Emergency Medicine
Patel M, **Bender D**, **Zahul S**, **Payne S**, **Hagerman T**, **Rammal JA**, **Klausner H**, **Miller J**, **Brar**, and **Manteuffel J**. Prevalence of People With HIV Visiting the Emergency Department and Linkage to Care Status. *Ann Emerg Med* 2024; 84(4):S104-S104. Full Text

[Patel, M.; Bender, D.; Zahul, S.; Payne, S.; Hagerman, T.; Rammal, J-A; Klausner, H.; Miller, J.; Brar, I; Manteuffel, J.] Henry Ford Hosp, Detroit, MI USA.

Emergency Medicine
Patel M, **Vajda P**, **Klausner H**, **Wanis N**, and **Betham B**. Does Emergency Department Treatment Daily Census Correlate With Patient-Hours of Care Provided: A Comparison of Data from Pre-COVID-19 (2018) to Post-COVID-19 (2022). *Ann Emerg Med* 2024; 84(4):S164-S164. Full Text

[Patel, M.; Vajda, P.; Klausner, H.; Wanis, N.; Betham, B.] Henry Ford Hosp, Detroit, MI USA.

Emergency Medicine
Shih D, **Hawatian K**, **Page B**, **Rammal JA**, **Miller J**, **Klausner H**, and **Stokes-Buzzelli S**. Comparative Analysis of Emergency Department Utilization Patterns During the COVID-19 International Pandemic: Frequent Users vs General Population. *Ann Emerg Med* 2024; 84(4):S28-S29. Full Text.

[Shih, D.; Hawatian, K.; Page, B.; Rammal, J-A; Miller, J.; Klausner, H.; Stokes-Buzzelli, S.] Henry Ford Hosp, Detroit, MI USA.

Emergency Medicine
Van Der Pol B, Arcenas R, Boraas C, Chavoustie S, Crane LL, d'Empaire N, Ermel AC, Harnett G, Hinestrosa F, House S, Lillis R, **Miller J**, Mills A, Poblete R, and Young SA. Clinical Performance Evaluation of the Polymerase Chain Reaction (PCR)-Based cobas CT/NG/MG Test for Use on the cobas liat System in a Clinical Laboratory Setting and Point-of-Care (POC) Location. *Clin Chem* 2024; 70:I136-I136. Full Text

[Van Der Pol, B.] Univ Alabama Birmingham, Heersink Sch Med, Birmingham, AL USA. [Arcenas, R.] Roche Diagnost Ltd, Pleasanton, CA USA. [Boraas, C.] Planned Parenthood North Cent States, St Paul, MN USA. [Chavoustie, S.] Segal Trials North Miami Off, North Miami, FL USA. [Crane, L. L.] Planned Parenthood Gulf Coast, Houston, TX USA. [d'Empaire, N.] BioCollect Worldwide Inc, Miami, FL USA. [Ermel, A. C.] Indiana Univ Sch Med, Indianapolis, IN USA. [Harnett, G.] No Resistance Consulting Grp LLC, Birmingham, AL USA. [Hinestrosa, F.] Orlando Immunol Ctr, Orlando, FL USA. [House, S.] Washington Univ, Sch Med, St Louis, MO USA. [Lillis, R.] Louisiana State Univ, Hlth Sci Ctr, New Orleans, LA USA. [Miller, J.] Henry Ford Hosp, Detroit, MI USA. [Mills, A.] Mills Clin Res, Los Angeles, CA USA. [Poblete, R.] North Jersey Community Res Initiat, Newark, NJ USA. [Young, S. A.] TriCore Reference Labs, Albuquerque, NM USA. University System; Indiana University Bloomington; Orlando Immunology Center; Washington University (WUSTL); Louisiana State University System; Louisiana State University Health Sciences Center New Orleans; Henry Ford Health System; Henry Ford Hospital

Hematology-Oncology
Bachler J, **Wang A**, **Poisson L**, **Adjei Boakye E**, **Tam S**, **Gadgeel S**, **Movsas B**, and **Potugari B**. EP.17B.03 Impact of Social Economic Status on Patient Reported Outcomes (PROs) In Non-Small Cell Lung Cancer (NSCLC). *J Thorac Oncol* 2024; 19(10):S716-S716. Full Text

Henry Ford Health, Detroit/MI/USA

Hematology-Oncology
Burger R, Hamilton E, Adams S, Han H, Spira A, Giordano A, Chaudhry A, Parajuli R, Wang J, **Weise A**, Abuhadra N, McNamara P, and Kalinsky K. XMT-1660: A phase I, first-in-human trial of a B7-H4-directed dolasynthen antibody-drug conjugate in ovarian, endometrial, and breast cancers. *Gynecol Oncol* 2024; 190:S282. Full Text

Objectives: Ovarian (OC), endometrial (EC), and breast cancers (BC) are some of the leading causes of cancer death among women. Despite therapeutic advances, many patients develop resistance to available standard of care (SOC) therapies. B7-H4 is a poor prognostic factor and is overexpressed in several cancers, including OC, EC, and BC, with limited expression in normal healthy tissue. As a cell surface protein, member of the CD28/B7 immune checkpoint family, B7-H4 promotes tumorigenesis by suppressing antitumor immunity. XMT-1660 is a B7-H4-directed dolasynthen antibody-drug conjugate (ADC) designed with a precise, optimized drug-to-antibody ratio (DAR 6) and a proprietary microtubule inhibitor payload with controlled bystander effect. In the pre-clinical setting, XMT-1660 has demonstrated antitumor activity in OC, EC, and BC PDX models. The FDA has granted fast track designation to XMT-1660 for the treatment of adult patients with advanced or metastatic triple-negative breast cancer. Methods: The phase I trial includes a first-in-human dose escalation (DES) evaluating XMT-1660 among patients with solid tumors, including OC, EC, and BC, following progression on SOC. In the DES, a BOIN design will be used to determine the maximum tolerated dose (MTD) and the recommended phase II dose (RP2D). The DES and backfill cohorts will assess safety and preliminary efficacy. Patients are not selected by B7-H4 status, but baseline tumor samples are collected for retrospective analysis. The primary endpoints in the expansion portion (EXP) are safety and tolerability, overall response rate, disease control rate, and duration of response. The trial is currently enrolling patients. NCT05377996

Hematology-Oncology

Czarnecki E, **Bhatnagar AR**, **Mattour A**, **Chang S**, **Kwon D**, **Ulreich C**, **Movsas B**, and **Siddiqui F**. The Impact of an Outpatient Urgent Care Clinic in Patients Treated for Head and Neck Cancer. *Int J Radiat Oncol Biol Phys* 2024; 120(2):S149-S149. Full Text

Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI
Henry Ford Health System, Detroit, MI
Department of Otolaryngology, Henry Ford Cancer Institute, Detroit, MI
Department of Surgical Oncology, Henry Ford Cancer Institute, Detroit, MI
Department of Radiation Oncology, Henry Ford Health, Detroit, MI

Hematology-Oncology

Doi T, Patel MR, Koyama T, Falchook GS, Friedman C, Piha-Paul SA, Gutierrez M, Awad M, **Mattour A**, Satoh T, Takahashi S, Tsunoda T, Kadowaki S, Watanabe Y, Okamoto N, Goto H, Yoshizuka N, Qian M, Qian X, and Johnson M. PS3-3 Clinical and biomarker data from a phase 1/2 trial of ifinatamab deruxtecan (I-DXd; DS-7300) in advanced solid tumors. *Ann Oncol* 2024; 35:S1315. Full Text

Background: I-DXd, a novel B7 homolog 3 (B7-H3)–directed antibody–drug conjugate, leverages the clinically validated deruxtecan (DXd) technology with a plasma-stable linker and a potent topoisomerase I inhibitor payload. This analysis of an ongoing global first-in-human phase 1/2 trial (NCT04145622) includes tumor type subset data in small cell lung cancer (SCLC), esophageal squamous cell carcinoma (ESCC), castration-resistant prostate cancer (CRPC), and squamous non-small cell lung cancer (sqNSCLC) in addition to Japanese subset data. Methods: Efficacy was analyzed in patients treated with I-DXd at doses of 4.8–16.0 mg/kg, and safety was analyzed in all patients dosed. Response was evaluated per RECIST v1.1 in patients with ≥2 post-baseline scans or discontinuation for any reason. B7-H3 level was evaluated retrospectively, as patients were not pre-selected by baseline expression. Results: As of Jan 31, 2023, 8/144 patients remained on treatment. Safety data (N=174) were consistent with previous reports. I-DXd showed a promising objective response rate (SCLC: 11/21 [52%]; ESCC: 6/28 [21%]; CRPC: 15/59 [25%]; sqNSCLC: 4/13 [31%]) and durable response (median duration of response [95% CI] in months (SCLC: 5.9 [2.8–7.5]; ESCC: 3.5 [2.4–not estimable (NE)]; CRPC: 6.4 [3.0–10.0]; sqNSCLC: 4.1 [2.8–NE]). Median overall survival to date is encouraging (in months, SCLC: 12.2 [95% CI: 6.4–NE; n=21]; ESCC: 7.0 [95% CI: 4.8–12.2; n=28]; CRPC: 13.0 [95% CI: 10.3–16.0; n=73]; sqNSCLC: not reported). B7-H3 expression was moderate to high in most patients; correlation between response and B7-H3 level will be presented for SCLC and mCRPC cohorts. Analysis of a subset of Japanese patients will also be presented. Conclusions: I-DXd continues to demonstrate a manageable safety profile and promising antitumor activity in these heavily pretreated patients, which warrants further clinical evaluation. Clinical trial identification: NCT04145622.

Hematology-Oncology

Gadgeel S, Rahman A, Osaghae U, Fernando TM, Lin MT, Koli K, Meyenberg C, Mathisen M, and Skoulidis F. P3.12D.07 Divarasib Versus Adagrasib or Sotorasib in Pretreated KRAS G12C+ Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC). *J Thorac Oncol* 2024; 19(10):S349. Full Text

Introduction: KRAS G12C mutations occur in approximately 12% of patients with NSCLC. Patients with advanced/metastatic KRAS G12C+ NSCLC who have previously received standard-of-care therapies (platinum-based chemotherapy, immunotherapy, or a combination of both) have a poor prognosis. Adagrasib and sotorasib are oral, selective KRAS G12C inhibitors with accelerated FDA and conditional EMA approvals for the treatment of patients with previously treated advanced/metastatic KRAS G12C+ NSCLC. However, an unmet need remains for more effective treatments with acceptable safety and tolerability profiles to improve patient outcomes. Divarasib is an oral, selective, KRAS G12C inhibitor previously shown to be 5-20 times as potent and ≤50 times as selective for KRAS G12C in vitro as adagrasib and sotorasib. Divarasib monotherapy (≤400mg once daily [QD]) previously demonstrated encouraging antitumor activity and an acceptable safety profile in patients with advanced/metastatic KRAS G12C+ solid tumors, including NSCLC (confirmed objective response rate [ORR]: 56.4%, 95% CI 39.6-72.2; progression-free survival [PFS]: 13.7 months, 95% CI 8.1-not estimable, in patients with NSCLC; 400mg dose). The observed adverse events were mostly low grade, manageable, and reversible. The phase 3 trial presented here will evaluate the efficacy and safety of divarasib versus adagrasib or sotorasib in patients with previously treated KRAS G12C+ advanced/metastatic NSCLC. Methods: This phase 3, randomized, active control, open-label multicenter study (EudraCT: 2024-510908-37-00) will enroll patients aged ≥18 years with histologically/cytologically confirmed, unresectable, advanced/metastatic (stage IIIC or IV) NSCLC harboring a KRAS G12C mutation (Figure). Patients must have experienced disease progression on ≥1 prior systemic therapy in the metastatic setting, have measurable disease per RECIST v1.1, and Eastern Cooperative Oncology Group performance status (ECOG PS) 0/1. Prior KRAS inhibitor therapy is not permitted. Patients will be randomized 1:1 to receive divarasib or either adagrasib or sotorasib (based on local approval status and investigator's choice) until disease progression, intolerable adverse events, consent withdrawal, death, or study termination. Tumor assessments will occur at screening, every six weeks for the initial 48 weeks, and every nine weeks thereafter. The primary endpoint is PFS per RECIST v1.1. Secondary endpoints include: overall survival; patient-reported outcomes (time to confirmed deterioration of cough [EORTC QLQ-LC13], dyspnea, or physical functioning [both EORTC QLQ-C30]); ORR and duration of response per RECIST v1.1; and safety. [Formula presented] Keywords: Advanced NSCLC, Divarasib, KRAS G12C+ NSCLC

Hematology-Oncology

Godbole MM, **Abu Rous F**, **Ghosh S**, **Chitale D**, and **Gadgeel S**. EP.13E.04 Racial Disparities in Genomic Subtypes of Small Cell Lung Cancer Patients. *J Thorac Oncol* 2024; 19(10):S682. Full Text

Introduction: Recent studies have identified 4 distinct subtypes of small cell lung cancer (SCLC) defined by the expression of several transcription factors. Immunohistochemistry (IHC) based analysis can help define these genomic subtypes. Previous analyses included very few samples from Black patients with SCLC. We present the initial results of IHC expression of relevant transcription factors in tumor samples from Black and White SCLC patients. Methods: SCLC patients diagnosed between January 2018 and January 2023 at Henry Ford Health were included. Demographics, including self-defined race, clinical characteristics and therapeutic details were retrieved from electronic medical record. A tissue microarray (TMA) was constructed using standard published protocols (1.0 mm cores in triplicate). The constructed TMA and an additional subset of whole sections were used for IHC staining for ASCL1, NEUROD1, POU2F3 and YAP1. IHC scoring was performed using H-score (score ≥10 was considered positive). Chi-square statistics and independent t-test was used for statistical analysis in the SPSS 28 software. Results: Of 258 patients with SCLC, adequate tissue for IHC scoring of all transcriptional factors was obtained for 58 patients (32 on TMA; 26 on whole sections). Of these, 28 were male and 30 female, mean age was 68 years (range: 52-86). 98% of patients were current or former smokers. Nine patients were Black and 49 were White. No statistical differences were observed for demographics, stage at diagnosis and presence of brain metastases between Black and White patients. YAP1 expression was more common in tumors of Black patients compared to tumors of White patients (33% vs 12%, p=0.136), while the expression of POU2F3 (0 vs 13%, p=0.575) and NEUROD1 (22% vs 45%, p=0.282) were more

common in White patients. Positivity for more than one marker was noted in 22% of Black vs 8% of White patients (p=0.231). POU2F3 negative patients had significantly better overall survival than positive patients (p=0.034). Other markers did not show a statistically significant difference in survival. Survival analysis stratified by race was not conducted due to limited sample size. Conclusions: The initial results of our study show that the prevalence of genomic subsets of SCLC defined by IHC expression of relevant transcription factors differs between self-defined Black and White patients. We are evaluating more samples to confirm our initial results. If these differences persist with further analysis, this data could suggest differences in SCLC biology among different racial groups and may have therapeutic implications. [Formula presented] Keywords: Small cell lung cancer, Genomic subtypes, IHC

Hematology-Oncology
Le X, Yu Y, Zhao Y, Planchard D, Cheng Y, Li X, **Gadgeel S**, Zhang J, Spira A, Hayashi H, Riess J, Kitazono S, Leighl N, Gao B, Juan-Vidal O, de Langen AJ, Mazieres J, Pérol M, Jiang Y, and Hu T. PL04.07 FURTHER: A Global, Randomized Study of Firmonertinib at Two Dose Levels in TKI-Naive, Advanced NSCLC with EGFR PACC Mutations. *J Thorac Oncol* 2024; 19(10):S5-S6. Full Text

University of Texas MD Anderson Cancer Center, Houston/TX/USA
Harbin Medical University Cancer Hospital, Harbin/CN
Henan Cancer Hospital, Zhengzhou/CN
Gustave Roussy, Villejuif/FR
Jilin Cancer Hospital, Changchun/CN
The First Affiliated Hospital of Zhengzhou University, Zhengzhou/CN
Henry Ford Cancer Institute, Detroit/MI/USA
Anhui Provincial Hospital, Hefei/CN
Virginia Cancer Specialists Research Institute and Next Oncology, Fairfax/VA/USA
Kindai University Hospital, Osaka/JP
UC Davis Comprehensive Cancer Center, Sacramento/CA/USA
Cancer Institute Hospital of JFCR, Tokyo/JP
University Health Network – Princess Margaret Hospital, Toronto/ON/CA
Blacktown Cancer and Haematology Centre, Blacktown/AU
La Fe University and Polytechnic Hospital, Valencia/ES
Netherlands Cancer Institute, Amsterdam/NL
Cancer Universitary Institute, Toulouse/FR
Léon Bérard Center, Lyon/FR
Shanghai Allist Pharmaceuticals Co, Shanghai/CN
ArriVent Biopharma, Burlingame/CA/USA

Hematology-Oncology
Nguyen D, Besse B, Cho BC, Lee SH, Lee KH, Lu S, Cheng Y, Yao Y, Girard N, Lin CC, Felip E, Aguilar A, Charoentum C, Cruz FJSM, Majem M, Lim CS, Akamatsu H, Hayashi H, Yang JCH, Kowalyszyn R, Tiscoski K, Franke F, Ponomarenko D, Arslan C, Forster M, Urban D, Misch D, Delmonte A, Montes LVG, **Gadgeel SM**, Cruz-Correa M, Peguero J, Rousey S, Gaffar Y, Owen S, Schuchard J, Diels J, Sermon J, Sun T, Ennis M, Fennema E, Daksh M, Sethi S, Bauml JM, and Campelo MRG. MA12.07 Amivantamab Plus Lazertinib vs Osimertinib in First-Line, EGFR-Mutant Advanced NSCLC: Patient-relevant Outcomes from MARIPOSA. *J Thorac Oncol* 2024; 19(10):S103-S104. Full Text

Introduction: Amivantamab is an epidermal growth factor receptor (EGFR)-MET bispecific antibody with immune cell-directing activity. Lazertinib is a highly selective, CNS-penetrant, EGFR tyrosine kinase inhibitor (EGFR-TKI). In MARIPOSA (NCT04487080), amivantamab plus lazertinib (amivantamab-lazertinib) significantly prolonged progression-free survival (PFS) vs osimertinib (hazard ratio [HR], 0.70; P<0.001) in patients with treatment-naïve, EGFR-mutant advanced non-small cell lung cancer (NSCLC; Cho Ann Oncol 2023;34:S1306;LBA14). We evaluated time to symptomatic progression (TTSP) and patient-reported outcomes (PROs) from MARIPOSA. Methods: Analyses included the 429 patients randomized to receive amivantamab-lazertinib and the 429 to osimertinib. TTSP was defined as time from randomization to onset of new/worsening lung cancer symptoms requiring change in anticancer therapy, another clinical intervention, or death, whichever occurred first. PROs were measured using EORTC-

QLQ-C30 and NSCLC-SAQ; all P-values are nominal. The threshold for a meaningful improvement was a 10-point increase on EORTC-QLQ-C30 functioning scales. Results: At a median follow-up of 22.0 months, amivantamab-lazertinib demonstrated a significant improvement in TTSP versus osimertinib (HR, 0.72; 95% confidence interval, 0.57-0.91; P=0.005). As median treatment duration was 18.5 months for amivantamab-lazertinib versus 18 months for osimertinib, PROs at 18 months are reported to evaluate the long term impact of treatment on quality of life. Based on the EORTC-QLQ-C30 functioning scales at 18 months, the percentage of randomized patients on treatment with improved or stable functioning relative to baseline in the amivantamab-lazertinib versus osimertinib arms was significantly higher for emotional functioning (38% versus 31%; P<0.05) and cognitive functioning (38% versus 31%; P<0.05). For other functioning scales, no statistically significant differences between amivantamab-lazertinib and osimertinib were observed. Functioning was maintained over time in both treatment arms as most changes over time were less than the defined threshold for clinically meaningful differences. At 18 months, no statistical differences were observed between the amivantamab-lazertinib and osimertinib arms for the absence of key symptoms from the EORTC-QLQ-C30 including dyspnea (34% versus 31%), pain (27% versus 26%), and fatigue (15% versus 16%). There were no significant differences in symptoms between arms based on the NSCLC-SAQ (Figure). Conclusions: For patients with treatment-naïve, EGFR-mutant advanced NSCLC, amivantamab-lazertinib significantly delayed symptomatic progression versus osimertinib indicating greater control of disease and related symptoms, while maintaining functioning as observed by PRO scales. PROs were comparable across treatment arms at the 18-month landmark, and treatment did not lead to meaningful decrements in patient quality of life. [Formula presented] Keywords: Amivantamab, EGFR TKI, NSCLC

Hematology-Oncology
Ohri N, Jolly S, Cooper B, Kabarriti R, Bodner Iii WR, Guha C, Viswanathan S, Shum E, Sabari JK, Cheng H, Gucalp R, Castellucci E, Qin A, **Gadgeel SM**, and Halmos B. The Selective Personalized Radioimmunotherapy for Locally Advanced NSCLC Trial (SPRINT): Patient-Reported Outcomes. *Int J Radiat Oncol Biol Phys* 2024; 120(2):S59-S59. Full Text

Montefiore Einstein Comprehensive Cancer Center, Bronx, NY
University of Michigan Rogel Cancer Center, Ann Arbor, MI
Perlmutter Cancer Center, NYU Grossman School of Medicine, New York, NY
Henry Ford Cancer Institute/Henry Ford Health System, Detroit, MI

Hematology-Oncology
Owonikoko T, Burns TF, Chiappori AA, Drapkin B, Gentzler RD, Goldschmidt J, Hakimian D, Jotte R, Liu SV, Onitilo AA, Pennell NA, **Potugari B**, Rios J, Sands J, Spira A, Wang B, Waterhouse DM, Lowenthal B, Bebchuk J, and Eli LD. P1.13A.13 ALISertib in Patients with Extensive-Stage Small-Cell Lung Cancer: The Phase 2 ALISCA-Lung1 Study. *J Thorac Oncol* 2024; 19(10):S212-S213. Full Text

University of Maryland, Baltimore/MD/USA
UPMC Hillman Cancer Center, Pittsburgh/PA/USA
Moffitt Cancer Center, Tampa/FL/USA
University of Texas Southwestern Medical Center, Dallas/TX/USA
University of Virginia, Charlottesville/VA/USA
US Oncology, Blue Ridge Cancer Center, Blacksburg/VA/USA
US Oncology, Illinois Cancer Specialists, Niles/IL/USA
Rocky Mountain Cancer Centers, Lone Tree/CO/USA
Georgetown University, Washington/DC/USA
Marshfield Clinic Wisconsin, Rapids/WI/USA
Cleveland Clinic, Cleveland/OH/USA
Henry Ford Hospital, Detroit/MI/USA
Sarah Cannon Zangmeister Cancer Center Columbus, Columbus/OH/USA
Dana-Faber Cancer Institute, Boston/MA/USA
Virginia Cancer Specialists Research Institute, Fairfax/VA/USA
Willamette Valley Cancer Institute and Research Center, Eugene/OR/USA
OHC (Oncology Hematology Care), Cincinnati/OH/USA

Puma Biotechnology, Los Angeles/CA/USA

Hematology-Oncology
Potugari B, **Abu Rous F**, **Gutta R**, Teslow E, Chao C, Jaeger E, and **Gadgeel S**. P3.06D.12 Racial Differences in ALK Gene Alterations Detected by Tissue and Liquid Biopsy Across Patients with Lung Cancer. *J Thorac Oncol* 2024; 19(10):S327. Full Text

Introduction: Racial and ethnic differences in incidence are well-reported in lung cancer associated with Tobacco smoking. ALK gene alterations as driver genetic alterations occur in 2-4% of lung cancer patients. Racial differences in ALK gene-altered lung cancer are not well defined. The objective of this study was to assess the frequency and type of ALK alterations observed in lung cancers across races. Methods: Patients with a primary lung cancer diagnosis (histology and stage agnostic) that underwent testing with the Tempus xT/xR (tissue) or xF (liquid biopsy) assays (n=27,991) and had a confirmed pathogenic ALK gene alteration (SNVs, CNAs, or fusions) were retrospectively identified within the Tempus database (n=377). Race was determined based on abstracted clinical records, and patients were stratified as either white, Black or African American (BAA), Asian Pacific Islander (API), unknown or other. Somatic pathogenic co-mutations were compared across races using Chi-squared/Fisher's Exact tests with FDR correction. Results: Among tissue-tested lung cancer patients (n=17,482), ALK alterations occurred in 1.4% (n=135) white, 1% (n=13) BAA, 3.4% (n=15) API, 3.1% (n=16) other, and 2% (n=108) unknown, which differed across race ($p<0.001$). The most common ALK alterations were fusions, as detected by DNA or RNA-seq, which also differed across race ($p<0.001$), with the lowest frequency in BAA patients (0.9%, n=12). EML4-ALK fusions were most common, occurring in 86% (n=116) of white patients with an ALK alteration, 62% (n=8) BAA, 87% (n=13) API, 100% (n=16) other, and 93% (n=100) unknown race ($p=0.013$). Atypical gene fusion partners ACYP2, RMND5A, BABAM2, MYT1L, and TPR were observed only in BAA, and SOS1, KLC, NPM1, PRKAR1A were observed only in white patients. Interestingly, a subset of patients with ALK fusions also harbored ALK amplifications (n=28), SNVs (n=11), or both (n=2). Similar results were observed in the smaller cohort of patients harboring ALK gene alterations as detected by liquid biopsy (n=90). There were no significant differences in co-mutated genes across races in ALK-altered tumors, including TP53, CDKN2A, or SETD, as detected by liquid or tissue testing. Conclusions: In this large cohort of lung cancer patients, ALK fusions were more commonly observed in API and "other" groups compared to white or BAA patients, with the lowest frequency in BAA. Some atypical fusion partners were observed in white and BAA that were not observed in other races. These data emphasize the importance of testing lung cancer patients with assays that allow for unbiased fusion detection and identification of novel fusion partners across racially diverse populations to better understand racial and ethnic differences in ALK-rearranged lung cancers. Keywords: Racial Differences, ALK Gene Alterations, co-mutations

Hematology-Oncology
Potugari B, **Abu Rous F**, **Gutta R**, Teslow E, Chao C, Jaeger E, and **Gadgeel S**. P3.06D.12 Racial Differences in ALK Gene Alterations Detected by Tissue and Liquid Biopsy Across Patients with Lung Cancer. *J Thorac Oncol* 2024; 19(10):S327-S327. Full Text

Henry Ford Health System, Detroit/MI/USA
Tempus Labs, Inc., Chicago/IL/USA

Hematology-Oncology
Sacher A, Addeo A, Doi T, Chu Q, El Helali A, Villaruz L, Prenen H, Vokes N, Rodon J, Durm G, Lebellec L, O'Neil B, Dy G, Eggert T, Keyvanjah K, and **Gadgeel S**. P3.12D.11 Phase 1/2, Dose-expansion Study of AMG 193, an MTA-cooperative PRMT5 Inhibitor, In MTAP-deleted NSCLC. *J Thorac Oncol* 2024; 19(10):S350-S351. Full Text

Princess Margaret Cancer Centre, Toronto/ON/CA
Hopitaux Universitaires de Geneve, Geneva/CH
National Cancer Center Hospital East, Chiba/JP
Cross Cancer Institute, University of Alberta, Edmonton/AB/CA
Queen Mary Hospital, Hong Kong/CN

UPMC Hillman Cancer Center, Pittsburgh/PA/USA
University Hospital Antwerp, Edegem/BE
MD Anderson Cancer Center, Houston/TX/USA
Indiana University Health Medical Center, Indianapolis/IN/USA
Centre Oscar Lambret, Lille/FR
Community-Health Network of Indianapolis, Indianapolis/IN/USA
Roswell Park Comprehensive Center Institute, Buffalo/NY/USA
Amgen, Thousand Oaks/CA/USA
Henry Ford Health System, Detroit/MI/USA

Hematology-Oncology
Sacher A, Addeo A, Doi T, Chu Q, El Helali A, Villaruz L, Prenen H, Vokes N, Rodon J, Durm G, Lebellec L, O'Neil B, Dy G, Eggert T, Keyvanjah K, and **Gadgeel S**. P3.12D.11 Phase 1/2, Dose-expansion Study of AMG 193, an MTA-cooperative PRMT5 Inhibitor, In MTAP-deleted NSCLC. *J Thorac Oncol* 2024; 19(10):S350-S351. Full Text

Introduction: AMG 193 is an oral S-methyl-5'-thioadenosine (MTA)-cooperative protein arginine methyltransferase 5 (PRMT5) inhibitor being evaluated for the treatment of methylthioadenosine phosphorylase (MTAP)-deleted cancers. MTAP deletion occurs in 16-20% of squamous and 12-16% of non-squamous non-small cell lung cancer (NSCLC). Deletion of MTAP leads to the accumulation of MTA, which binds to and inhibits PRMT5, an enzyme responsible for methylation and gene silencing of cell-essential proteins. Thus, in the context of MTAP-deleted cancers, MTA accumulation creates an additional vulnerability to further inhibit PRMT5 activity. AMG 193 preferentially targets and inhibits the MTA-bound state of PRMT5. In preclinical models, AMG 193 demonstrated selective antitumor activity in in vitro and in vivo MTAP-deleted compared to MTAP-wild type NSCLC cell line assays and NSCLC cell line-derived xenograft mouse models (Belmontes, 2023 AACR-NCI-EORTC). AMG 193 also demonstrated central nervous system penetrance with pharmacokinetic models. In the ongoing first-in-human (FIH) study with AMG 193 monotherapy, RECIST responses have been observed in a variety of MTAP-deleted tumors without dose-limiting myelosuppression and a favorable safety profile (Rodon, 2023 AACR-NCI-EORTC), demonstrating differentiated safety from the first generation indiscriminate PRMT5 inhibitors. This study will enroll up to 40 previously treated NSCLC patients in dose expansion (Part 1c), currently open for enrolment. Methods: This is a FIH, open-label, phase 1/2, dose escalation and expansion study of AMG 193 administered continuously in 28-day cycles in patients with advanced MTAP-deleted tumors (FIGURE). Up to 40 previously treated patients with NSCLC (squamous and non-squamous histology) will be enrolled in Part 1c. Central prescreening NGS will be offered to all participating sites. One interim futility will be conducted by using Simon's minimax two-stage design. The primary objectives are safety and tolerability; secondary objectives include antitumor activity by investigator-assessed RECIST, pharmacokinetics, and pharmacodynamics. Key eligibility criteria for patients with NSCLC (Part 1c) include adult patients (≥ 18 years of age) with MTAP-deleted advanced tumors (determined by NGS or evidence of MTAP depletion determined by IHC); treatment with 1-3 prior lines of systemic therapy in the advanced/metastatic setting including platinum-based chemotherapy. Additionally, patients without actionable mutations must have received treatment with a PD(L)-1 inhibitor (unless contraindicated or PD-L1 < 1%), and patients whose tumors harbor actionable genomic aberrations (i.e. EGFR, ALK, MET, RET, ROS1, KRASG12C) should have disease progression on approved systemic therapies for these aberrations. [Formula presented] Keywords: AMG 193, MTA-cooperative PRMT5 inhibitor, MTAP-deleted NSCLC

Hematology-Oncology
Spigel DR, Ahn MJ, Majem M, Medina Rodríguez L, Lee KH, Carcereny E, Hernández AA, Insa A, Cho EK, Besse B, Rha SY, Weiss J, D'Arcangelo M, Im SA, Kim SW, Carneiro BA, **Gadgeel SM**, Mitchell P, Asare JM, and Gainer SD. OA11.04 Volrustomig + platinum doublet chemotherapy (CTx) in first-line non-small cell lung cancer (NSCLC): Phase 1b trial update. *J Thorac Oncol* 2024; 19(10):S33-S34. Full Text

Sarah Cannon Research Institute, Nashville/TN/USA
Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul/KR
Hospital de la Santa Creu I Sant Pau, Barcelona/ES

Unidad de Gestión Clínica Intercentros de Oncología Médica, Hospitales Universitarios Regional y Virgen de la Victoria, Instituto de Investigación Biomédica de Málaga (IBIMA), Malaga/ES
Chungbuk National University, Cheongju/KR
Catalan Institute of Oncology–Badalona, B-ARGO Group, Barcelona/ES
Instituto Oncológico Dr Rosell, Quirón Dexeus University Hospital, Barcelona/ES
Fundación INCLIVA, Hospital Clínico Universitario de Valencia, Valencia/ES
Gachon University Gil Medical Center, Gachon University College of Medicine, Incheon/KR
Paris-Saclay University, Institut Gustave Roussy, Villejuif/FR
Yonsei Cancer Center, Yonsei University Health System, Seoul/KR
Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill/NC/USA
AUSL della Romagna, Ravenna/IT
Seoul National University College of Medicine, Seoul/KR
Asan Medical Center, University of Ulsan College of Medicine, Seoul/KR
Legorreta Cancer Center at Brown University, The Warren Alpert Medical School, Lifespan Cancer Institute, Providence/RI/USA
Henry Ford Health System, Detroit/MI/USA
AstraZeneca, Waltham/MA/USA
AstraZeneca, Gaithersburg/MD/USA

Hematology-Oncology

Spigel DR, Ahn MJ, Majem M, Medina Rodríguez L, Lee KH, Carcereny E, Hernández AA, Insa A, Cho EK, Besse B, Rha SY, Weiss J, D'Arcangelo M, Im SA, Kim SW, Carneiro BA, **Gadgeel SM**, Mitchell P, Asare JM, Gainer SD, Achour I, Subramaniam DS, and Felip E. OA11.04 Volrustomig + platinum doublet chemotherapy (CTx) in first-line non-small cell lung cancer (NSCLC): Phase 1b trial update. *J Thorac Oncol* 2024; 19(10):S33-S34. Full Text

Introduction: Volrustomig, a novel PD-1/CTLA-4 bispecific antibody, has shown robust pharmacodynamic effect and clinical promise in multiple advanced solid tumors (Tran, AACR 2022; Albiges, ASCO 2022; Voss, ESMO 2023), and especially in PD-L1-negative first-line (1L) NSCLC (Ahn, ESMO 2022). PD-L1-negative NSCLC is a disease segment of key unmet need, with limited benefit gained from addition of anti-PD-(L)1 therapy alone to CTx, and where anti-PD-(L)1/anti-CTLA-4 therapy + CTx has previously shown clinical potential (Paz-Ares, Lancet Oncol 2021; Johnson, JCO 2023). Here we report updated results from patients with 1L advanced NSCLC treated with volrustomig 750mg + CTx in a global Phase 1b study. Methods: Patients with 1L advanced NSCLC were treated with volrustomig 750mg + CTx Q3W based on histology: 120 nonsquamous (Nsq) NSCLC patients enrolled over two different time periods (Cohort 1A: n=66; Cohort 1B: n=54) and 20 squamous (Sq) NSCLC patients (Cohort 2). The primary endpoint was objective response rate (ORR) in the Nsq cohorts and safety in the Sq cohort. Secondary endpoints included safety, tolerability, and disease control rate (DCR). Exploratory endpoints included receptor occupancy and pharmacodynamic biomarkers of CTLA-4 blockade. Results: Among 140 patients enrolled, 89 had PD-L1 tumor cell expression (TC) <1% NSCLC (63.6%), reflecting the unmet need and previously seen benefit of CTLA-4 inhibition in this population; median age was 68.0 years, 73.6% were males, 67.9% with ECOG performance status 1, 15.7% with liver metastases, and 15% with brain metastases. Efficacy outcomes are shown in the Table. Nearly all patients achieved disease control. Among evaluable patients with PD-L1 TC <1%, ORR in the Nsq (n=78) and Sq (n=10) cohorts was 42.3% and 50.0%, respectively. Median number of cycles was 6 (range 1-39); 97.1% and 75.7% of patients experienced all-grade and grade 3/4 treatment-related adverse events (AE), respectively. Seven treatment-related deaths occurred (two of which were volrustomig-related immune-related AEs): 6 in Cohort 1A, 0 in Cohort 1B, 1 in Cohort 2. Clinical peripheral T cell flow cytometry, TCR sequencing, and single-cell sequencing demonstrated greater T cell proliferation and memory T cell activation with volrustomig 750mg + CTx versus anti-PD1 + CTx. Conclusions: Volrustomig 750mg + CTx demonstrates robust PD-1/CTLA-4 blockade, manageable safety, and promising efficacy in 1L advanced NSCLC, especially in patients with PD-L1 TC <1%. The ongoing phase 3 EVOLVE-Lung02 trial (NCT05984277) is evaluating volrustomig + CTx for metastatic NSCLC with PD-L1 TC <50%. [Formula presented]
Keywords: NSCLC, immunotherapy, chemotherapy

Hematology-Oncology

Tsakiridis T, Hu C, Skinner H, Santana-Davila R, Lu B, Erasmus JJ, **Doemer AJ**, Videtic GM, Wang F, Hesselle M, Lee RY, Werner-Wasik M, Schaner PE, McCormack SE, Esparaz BT, McGarry RC, Brownstein J, Struve T, Lyness JA, and Bradley JD. MA01.07 Long-Term Analysis of NRG-LU001, Randomized Phase II Trial of Concurrent Chemoradiotherapy (ccrt) -/+ Metformin in Locally Advanced NSCLC. *J Thorac Oncol* 2024; 19(10):S53-S54. Full Text

Introduction: The highly active glycolytic metabolism of non-small cell lung cancer (NSCLC) is an attractive target for metabolic therapies. NRG-LU001 (NCT02186847) was a phase II trial that found that the addition of anti-diabetic agent metformin, a mitochondrial inhibitor, to the standard of care cCRT did not improve 1-year progression-free survival (PFS) in locally advanced (LA)-NSCLC. Here, we present the long-term analysis with 5-year follow-up. Methods: Stage IIIA/B NSCLC, unresected, non-diabetic, patients were randomized (1:1) to either carboplatin-paclitaxel chemotherapy concurrent with chest RT (60Gy), followed by consolidation carboplatin-paclitaxel chemotherapy (Control Arm) or the same and oral metformin (2000mg daily) during cytotoxic therapy (Experimental Arm). The primary endpoint of this trial was 1-year PFS. Secondary outcomes included overall survival (OS), rates of local-regional and distant failure, and rates of adverse events. PFS and OS were estimated with the Kaplan-Meier method; local-regional progression and distant metastasis were estimated using the cumulative incidence method. Adverse events (AEs) were graded with CTCAE v.4.0. Exploratory landmark analysis was conducted to mitigate immortal bias when evaluating outcomes among patients compliant with metformin. Results: A total of 170 patients were accrued and randomized between Aug. 2014 and Dec. 2016. As of Sep. 2023, minimal additional toxicity was reported and no significant difference was detected in the rates or grade of toxicity between the two arms.1- 2- and 5-year PFS was 60.4%, 40.3% and 29.2% in Control [(95%CI: 48.5, 70.4); (95%CI: 29.2, 51.1); (95%CI: 19.3, 39.7)] vs 51.3%,34.5% and 24.3% in the Metformin arm [(95%CI: 39.8, 61.7), (95%CI: 24.2, 45.1) and (95%CI: 15.5, 34.3)], respectively, (multivariable Cox proportional HR=1.21(95%CI: 0.84, 1.75), p=0.152). OS at 2- and 5-years was 65.3% and 38.1% for Control [(95% CI:53.6, 74.7); (95%CI: 27.1, 49.0)] vs 65.3% and 41.2% for the Metformin arm [(95%CI: 53.1, 74.5); (95%CI: 30.1, 52.0)], respectively, (HR=1.04 (95%CI:0.71, 1.53) p=0.828. Deaths due to disease were 76.5% vs 63.0%, respectively. No significant differences were found in the rates of local-regional and distant failures. In a posthoc analysis investigating the role of metformin compliance, a landmark analysis was conducted among those who survived 3 months or longer. 74 patients received no metformin, 46 patients received ≥95%of the protocol-recommended drug dose, and 31 received <95% of the recommended dose. 2- and 5-year OS rates in those three groups were 68.1%and 39.7% [(95%CI: 56.0, 77.5), (95%CI:28.3, 50.8)], 75.9% and 55.2% [(95%CI:60.7, 85.9), (95%CI:39.4, 68.4)] and 51.6% and 22.6% [(95%CI:33.0,67.4), (95%CI:10.0, 38.3)], respectively. No formal statistical comparison was made given the exploratory nature of this analysis. Conclusions: NRG-LU001 long-term outcomes show that oral daily metformin was well-tolerated in combination with cCRT treatment for LA-NSCLC. In the per-protocol analysis, metformin did not improve PFS and OS and did not alter the rates of local-regional failure or distant metastasis. Nevertheless, long-term OS outcomes in this trial compare favorably to those of control and interventional arms of recently reported trials. The impressive OS rates detected in patients of the metformin arm who adhered to the protocol-recommended drug dose warrant further investigation in future studies. Keywords: Unresected LA-NSCLC, Chemo-radiotherapy, Metformin

Infectious Diseases

Patel M, **Bender D**, **Zahul S**, **Payne S**, **Hagerman T**, **Rammal JA**, **Klausner H**, **Miller J**, **Brar**, and **Manteuffel J**. Prevalence of People With HIV Visiting the Emergency Department and Linkage to Care Status. *Ann Emerg Med* 2024; 84(4):S104-S104. Full Text

[Patel, M.; Bender, D.; Zahul, S.; Payne, S.; Hagerman, T.; Rammal, J-A; Klausner, H.; Miller, J.; Brar, I; Manteuffel, J.] Henry Ford Hosp, Detroit, MI USA.

Internal Medicine

Abdelhai O, **Ghoneem A**, **Andrews T**, **Rangavajla G**, and **Maligireddy AR**. TCT-904 Trends and Outcomes of Mechanical Circulatory Support With Transcatheter Valve Intervention From the National Inpatient Sample (2017-2020). *J Am Coll Cardiol* 2024; 84(18):B381. Full Text

Background: The use of mechanical circulatory support (MCS) devices with transcatheter valve interventions (TVIs) is occasionally required; however, data on their use and outcomes are lacking. Methods: We used the Nationwide Inpatient Sample database to identify patients treated with TVI, with or without MCS, between 2017 and 2020. Our analysis included hospital admissions of adults who underwent transcatheter aortic valve replacement (TAVR), MitraClip, transcatheter mitral valve replacement, transcatheter pulmonary valve replacement (PVR), and/or transcatheter tricuspid valve repair. Results: We identified 29,4525 patients undergoing TVI during the study period, with 2,920 in the MCS group and 292,495 in the non-MCS group (Table). Patients in the MCS group were younger; more likely to be males; of Black or other race; or have congestive heart failure, cardiac arrhythmias, or chronic kidney disease. Younger age, nonelective admission, cardiac arrhythmia, myocardial infarction, sudden cardiac arrest, and cardiogenic shock significantly predicted MCS use ($P \leq 0.001$ for all). From 2017 to 2020, there was a steady increase in TVI (P for trend = 0.034). Conversely, use of MCS has remained stable (P for trend: total 0.732). The use of any MCS modality was associated with >30-fold increase in mortality (1% vs 30.1%; $P < 0.05$). Length of stay and cost of hospitalization were higher in the MCS group ($P < 0.05$ for both). Mortality remained steadily high with MCS use (P for trend = 0.138), with declining mortality in the non-MCS group showing a trend toward significance (P for trend = 0.058). [Formula presented] Conclusion: The use of MCS in patients undergoing TVI in the United States between 2017 and 2020 was associated with increased mortality, morbidity, and greater use of health care resources. Further research is needed to enhance the safety and cost-effectiveness of MCS in TVI as well as to identify the optimal MCS for these patients. Categories: STRUCTURAL: Congenital and Other Structural Heart Disease.

Internal Medicine

Abdelhai O, **Rangavajla G**, **Nguyen F**, **Andrews T**, **O'Neill B**, **Fang J**, **Giustino G**, **Wyman J**, **Gonzalez PE**, **Villablanca P**, **Lee J**, **O'Neill W**, **Zweig B**, **Parikh S**, and **Frisoli T**. TCT-171 Baseline Invasive Hemodynamics and Clinical Outcomes in Transcatheter Tricuspid Valve Replacement Using the EVOQUE System. *J Am Coll Cardiol* 2024; 84(18):B420. Full Text

Background: Transcatheter tricuspid valve replacement (TTVR) with the Evoque valve represents a newly commercially available non surgical therapy for severe tricuspid regurgitation (TR) in the United States. There is minimal data on the significance of pulmonary hypertension (PH) and right ventricular dysfunction (RVD) in patients undergoing TTVR. Methods: Patients who underwent TTVR at Henry Ford Hospital in Detroit during February-May 2024 (n = 28) were included. We examined how right heart catheterization metrics of PH and RVD—pulmonary vascular resistance (PVR), pulmonary artery pulsatility index (PAPi), and pulmonary capillary wedge pressure (PCWP)—correlated with both procedural success and a composite outcome of death or heart failure hospitalization. Results: The cohort had a median PVR 2.4 (IQR 1.3-2.9), PCWP 10 (IQR 8.8-19.3), and PAPi 2.1 (IQR 1.4-4.0). For those with complete data, 5/20 (25%) had elevated PVR >3.0 and 7/20 (35%) had elevated PCWP >15. There were no associations between PVR (P = 0.42), PCWP (P = 0.23), and PAPi (P = 0.45) with procedural success (n = 22). There was also no association between PVR, PCWP, and PAPi and death or heart failure hospitalization (n = 6, Figure 1) over a median 12-day (IQR 4-30) follow-up. [Formula presented] Conclusion: Although a small study, these are the first data since the commercial launch of TTVR in the United States. TTVR appears similarly safe across a range of baseline PVR, PCWP, and PAPi values. More research in larger cohorts is needed to determine if preprocedural right heart catheterization findings can predict clinical outcomes after TTVR. Categories: STRUCTURAL: Valvular Disease: Tricuspid.

Internal Medicine

Andrews T, **McBride P**, **Abdelhai O**, **Fang J**, **Giustino G**, **Gonzalez PE**, **Villablanca P**, **O'Neill B**, **O'Neill W**, **Zweig B**, **Lee J**, and **Frisoli T**. TCT-825 Hemodynamic Valve Deterioration in Under- vs Over-Expanded Balloon Expandable Transcatheter Aortic Valves. *J Am Coll Cardiol* 2024; 84(18):B334. Full Text

Background: Non-nominal deployment of balloon-expandable valves (BEVs) is a common transcatheter aortic valve replacement (TAVR) practice. Effects of under- vs over-expansion of a BEV on hemodynamic valve deterioration (HVD) are not well studied. Methods: We conducted a single-center retrospective

study of 175 patients who underwent TAVR with BEVs deployed at non-nominal and nominal volumes. Criteria of moderate HVD—changes from 1 month to 1 year after TAVR in peak and mean gradients and aortic valve area and dimensionless index (DI) as well as new aortic regurgitation—were studied. Results: There were no significant differences between the over- and under-expanded BEVs for any of the following criteria: 1-year AVA (P = 0.065), Δ AVA (P = 0.256), % Δ AVA (P = 0.156), 1-year peak gradient (P = 0.272) and mean gradient (P = 0.303), Δ mean gradient (P = 0.499), DI (P = 0.434), Δ DI (P = 0.382), % Δ DI (P = 0.379), AI (P = 0.373), and Δ AI (P = 0.416); Figure 1. In a linear regression analysis by actual volume subtracted from or added to nominal, there was no association with Δ AVA or Δ DI at 1-year (P = 0.55 and P = 0.85, respectively). [Formula presented] Conclusion: In this first in vivo analysis of non-nominally expanded BEVs and HVD, over-expanded and under-expanded BEVs appear to perform similarly out to 1 year. Larger studies with longer follow-up are needed. Categories: STRUCTURAL: Valvular Disease: Aortic.

Internal Medicine

Gregerson S, **Frisoli T**, **O'Neill B**, **Lee J**, **Villablanca P**, **O'Neill W**, and **Gonzalez PE**. TCT-842 Transcatheter Aortic Valve Replacement in ESRD: Short- and Long-Term Outcomes, Valve Degeneration, and Reintervention Rates in Propensity-Matched Analysis. *J Am Coll Cardiol* 2024; 84(18):B346. Full Text

Background: Transcatheter aortic valve replacement (TAVR) has shown a clear benefit in patients with symptomatic, severe aortic stenosis (AS), yet there is a paucity of data on end-stage renal disease (ESRD) patients. Methods: This retrospective single-center study at a quaternary valve center evaluated the outcomes of ESRD patients undergoing TAVR from 2012-present. We first analyzed rates of major adverse cardiac event (MACE) outcomes, structural valve degeneration (SVD), and structural valve reintervention (SVR) for all ESRD patients (unadjusted cohort). We then performed propensity matching to compare a subset of ESRD patients (adjusted cohort) with non-ESRD chronic kidney disease (CKD) patients. Preoperative risk was determined using the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM). Results: The unadjusted ESRD cohort of 95 patients demonstrated high preoperative risk (9.67%) with correlating high MACE outcome rates during the index hospitalization. At long-term follow-up, the SVD and SVR rates were 26.3% and 3.2%, respectively. There was no correlation between preoperative risk and time to SVD. After propensity matching the adjusted cohorts for preoperative risk (ESRD 7.63% and non-ESRD CKD 7.67%), a total of 54 patients were included in this subanalysis. These ESRD patients demonstrated a nonsignificant trend toward higher death rates during the index hospitalization (P = 0.09), as well as significantly higher MACE outcomes (P < 0.01) and bleeding events (P = 0.02). At the 1-year follow-up period, death (P = 0.03), MACE (P < 0.01), and SVD rates (0.04) were significantly higher in the ESRD cohort. No SVR was reported in either matched cohort. [Formula presented] Conclusion: In those undergoing TAVR, ESRD patients are at higher risk of MACE outcomes and SVD than non-ESRD CKD patients. Despite this, rates of SVR are low. This study helps risk stratify ESRD patients considered for TAVR and prognosticate post-TAVR valve outcomes in both the short-term and long-term follow-up period. Categories: STRUCTURAL: Valvular Disease: Aortic.

Internal Medicine

Rangavajla G, **Abdelhai O**, **Nguyen F**, **Giustino G**, **Fang J**, **Dawdy J**, **Gonzalez PE**, **Villablanca P**, **Lee J**, **Parikh S**, **Zweig B**, and **O'Neill B**. TCT-170 Conduction System Disorders After Transcatheter Tricuspid Valve Replacement. *J Am Coll Cardiol* 2024; 84(18):B419-B420. Full Text

Background: Transcatheter tricuspid valve replacement with the Evoque valve was recently approved by the U.S. Food and Drug Administration as a transcatheter therapy for severe tricuspid regurgitation, but initial data suggest a high rate of conduction system disorders (CSDs). As real-world data are limited, we aimed to characterize predictors of post-TTVR CSD and associations with clinical outcomes. Methods: Patients undergoing Evoque at Henry Ford Hospital February-May 2024 were included; those with aborted procedures, prior bundle branch blocks (BBB), or prior pacemakers (PPM) were excluded. Predictors of new CSD, defined as new BBB or complete heart block (CHB) were assessed, and we analyzed the association between CSD and a composite of death or heart failure hospitalization. Results: Of 28 total Evoque patients, 18 were excluded (aborted procedure: 6, prior BBB: 3, prior PPM: 12). Of the 10 studied patients, 5 developed new CSD: 4 with RBBB and 1 with CHB requiring new PPM. Percent

oversizing of the valve relative to the native annulus was not associated with CSD; however, greater baseline LVEF was associated (Figure 1A, P <0.05). New CSD post-Evoque was not associated with death or heart failure hospitalization over a median 11-day (IQR 3-32) follow-up (Figure 1B). [Formula presented] Conclusion: Although sample size and follow-up time were limited, we report early real-world data of post-Evoque CSD. Baseline LVEF, but not percent oversizing, was associated with new CSD. We aim to conduct further studies to better inform patient selection by identifying reliable predictors and clinical outcomes of post-Evoque CSD. Categories: STRUCTURAL: Valvular Disease: Tricuspid.

Nephrology

Bromberg J, Demko ZP, Kaur N, Marshall K, Armer-Cabral M, Tabriziani H, Bhorade S, Gauthier P, and **Samaniego-Picota M**. Increases in donor-derived cell-free DNA prior to biopsy proven rejection in kidney transplant. *Transplantation* 2024; 108(9):277-278. Full Text

J. Bromberg, Department of Surgery, University of Maryland, School of Medicine, Baltimore, MD, United States

Introduction: The most common clinical indicators for kidney allograft rejection include serum creatinine and proteinuria. Unfortunately, both are lagging indicators that increase once injury has already occurred. Donor-derived cell-free DNA (dd-cfDNA) has been validated as a marker for detection of allograft active rejection (AR) in kidney transplant recipients as well as other solid organ transplants. We sought to test whether dd-cfDNA is a leading indicator of rejection in kidney transplant recipients (KTR). Method: KTR with a biopsy (Bx) and >1 dd-cfDNA tests in the six months prior to the Bx from a 1,631 patient interim analysis cohort of the ProActive registry study (ClinicalTrials.gov NCT04091984) were included. Dd-cfDNA results (the ProsperaTM test) and serum creatinine (SCr) results were grouped by time prior to biopsy and stratified by ultimate Bx finding: ABMR, TCMR, and non-rejection. Results: 424 patients had a Bx and >1 dd-cfDNA result (1,013 total) drawn 0-180 days prior to Bx. 94.5% of dd-cfDNA tests (958/1,013) had a matched SCr test performed at the same visit. The cohort was 59.9% male, 52.1% white and had a median age of 52.0 years. Clinical Bx diagnoses included 26 ABMR, 62 TCMR, and 336 non-rejection. Median dd-cfDNA fraction (dd-cfDNA%) was significantly elevated five months prior to an ABMR Bx and two months prior to a TCMR Bx, compared to non-rejection (Figure 1A). SCr levels were not significantly elevated at any time point prior to Bx in cases with rejection (Figure 1B). Of the 336 patients with a non-rejection Bx, 11.3% (n=38) subjects had one increased dd-cfDNA test result (defined as >1%), and 5.3% (n=18) had two or more increased dd-cfDNA test results during the 6 month period prior to Bx. At the time of a non-rejection Bx, the median eGFR was significantly lower in patients with two or more prior increased dd-cfDNA test results (45.4 [30.5-52.6]) compared to patients with either zero (58.5 [47.2-72.4]) (p=0.00018), or one prior increased dd-cfDNA test result (60.2 [48.3-72.0]) (p=0.0006) (Figure 2). Conclusion: These data support the hypothesis that dd-cfDNA% is a leading indicator of rejection, and was elevated up to five months prior to a biopsy proven ABMR rejection and two months prior to a biopsy proven TCMR rejection. In patients with a non-rejection biopsy, increased ddcfDNA was significantly associated with reduced eGFR. Earlier detection of AR by dd-cfDNA may allow for earlier treatment of rejection. (Figure Presented).

Nephrology

Offerle L, Acevedo D, van de Ridder M, **Abraham E**, and Abbas S. Evaluating the Effectiveness of a Narrative Medicine Curriculum for Neurology Residents (P6-7.005). *Neurology* 2024; 102(17_supplement_1). Full Text

L. Offerle, Corewell Health - Grand Rapids, Michigan State University Neurology, United States

Objective: To explore how Neurology residents apply Narrative Medicine when first introduced and to propose an objective method to evaluate a new curriculum's effectiveness. Background: Narrative Medicine provides physicians an opportunity for self-reflection and processing the complexities of meaningful experiences. It is most effective when introduced in the training phase; it may reduce burnout, increase empathy, improve communication, and enable diversity, equity, and inclusion (DEI) application. The effectiveness of Narrative Medicine curricula thus far has been evaluated through participant surveys. An objective method of evaluation is needed to support educators in demonstrating its benefits.

Design/Methods: Prior to the implementation of a formal Narrative Medicine curriculum, eleven Neurology residents in various stages of training were given six reflective writing prompts regarding their interactions with patients and the patients' families. Participants were provided with 10 minutes to respond to each prompt during a 2-hour workshop. We developed six original tools to explore the depth of the reflections and create an objective scoring system to be used for comparison after curriculum implementation. These tools include word count, repetition, idiomatic expressions, tone, voice, and the percentage of the question answered. Each category was scored independently by two investigators to ensure validity. Results: The length of reflections varied, with a mean of 143 words per prompt, ranging from single digits to a maximum of 371 words. Each resident provided at least one original response; all also repeated ideas through their subsequent narratives. Only 2 out of the 66 responses were void of idiomatic expressions. There were a variety of tones used including humorous, sarcastic, and serious; most individual participants did not shift tones. Of the 66 responses, only 2 did not respond to all components of the posed questions. Conclusions: We propose a novel method of objectively evaluating the implementation of a Narrative Medicine curriculum into Neurology resident education.

Neurology
Albanna A, **Jummah A**, **Fana M**, **Qureshi M**, **Agarwal U**, **Milller D**, and **Iqbal Z**. Prolonged and Reversible Encephalopathy Secondary to an Arteriovenous Fistula: A Case Report (P10-5.021). *Neurology* 2024; 102(17_supplement_1). Full Text

A. Albanna, Neurology, Henry Ford Hospital, United States

Objective: Intracranial dural arteriovenous fistula (AVF) is a rare condition; it is usually described as an arterio-venous shunt within the dura with sinus or cortical drainage. AVFs can occur anywhere in the central nervous system. Most commonly, they are found at the transverse sinus, and this location is reported in 50% of all cases. Symptoms of the Dural AVFs vary widely according to their location. Progressive thalamic dementia due to venous hypertension of thalamic draining veins is an example. Herein, we present a patient with reversible progressive encephalopathy due to this pathology. Background: This is a 55-year-old man who was admitted for progressive encephalopathy for 3 months. Inpatient work-up included a negative Computed Tomography of the head, unremarkable infectious, toxic and metabolic abnormalities including cerebrospinal fluid analysis, patient underwent MRI of the brain with contrast showing bilateral thalamic infarcts. MR angiography showed dural AVF at the torcular herophili, with high-grade stenosis of the junction of straight sinus and torcula Herophili. The patient underwent cerebral angiography showing a complex dural AVF at the tentorium and left sigmoid sinus, this was with a retrograde venous arterialization through the internal cerebral veins, the straight vein and vein of Galen. Embolization of the fistula was done intra-procedurally, with a gradual improvement of his mental status over 4 months when followed up on in the office. Design/Methods: N/A Results: N/A Conclusions: Bilateral thalamic infarcts due to underlying venous hypertension caused by dural AVF can present as a subacute or even a chronic encephalopathy. Since the symptoms are not specific, the diagnosis might be challenging. This condition must be added to the differential list when no other obvious etiology can be found. Early diagnosis and management are generally associated with good prognosis. .

Neurology
Bagher-Ebadian H, **Brown SL**, Acharya P, **Ewing JR**, Chetty IJ, **Movsas B**, and **Thind K**. A Probabilistic Unsupervised Model to Assess Pharmacokinetic Changes in Cerebral Tumors before and after Radiation Therapy. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e98-e99. Full Text

Department of Radiation Oncology, Henry Ford Health, Detroit, MI
Department of Radiology, Michigan State University, East Lansing, MI
Oakland University, Rochester, MI
Department of Neurology, Henry Ford Health, Detroit, MI
Department of Radiation Oncology, Cedars-Sinai Medical Center, Los Angeles, CA

Neurology

Choudhury O, **Mohamedelkhair A**, and **Howell B**. A Rare Case of Ramsay Hunt Syndrome Presenting as SUNCT (P3-12.001). *Neurology* 2024; 102(17_supplement_1). Full Text

O. Choudhury, Henry Ford Hospital neurology, United States

Objective: To present a case of Ramsey hunt syndrome that presented with SUNCT type of headache Background: Ramsay Hunt syndrome represents reactivation of latent varicella zoster virus in the geniculate ganglion, but sometimes extends to involve other cranial nerves Frequently reported symptoms are unilateral and ipsilateral facial paralysis, and painful vesicles in the auditory canal or on the auricle. Design/Methods: Case report Results: A health 55-year-old female who presented initially with acute-onset pressure-like right ear pain associated with rhinorrhea. On day 4 of symptoms, she reported worsening of symptoms, with change of pain to be excruciating, and sharp limited to 5 seconds or less per attack, innumerable times throughout the day, with associated symptoms of increased lacrimation and ipsilateral conjunctival injection. On examination, she exhibited mild scleral injection of the right eye, reduced sensation to pinprick over the right (V2) and (V1), which appeared worse during attacks, with subtle right lower motor neuron facial weakness. CT head without contrast and CTA were unremarkable. A presumed diagnosis of SUNCT was made, and patient was provided with Lamotrigine and Indomethacin, which improved symptom partially then was discharged. 3 days later she noticed facial weakness and was prescribed a course of oral steroids for 6 days. The following day, she noticed a vesicular rash developing in the pinna of the right ear, for which she was given ten-day course of Valacyclovir then All of her symptoms gradually improved till completely resolved over the next 4 weeks. Conclusions:The patient did meet the criteria for a SUNCT diagnosis according to the (ICHD-3) criteria. Additionally, she symptomsconsistent with Ramsey-Hunt syndrome with findings of vesicular rash, facial pain and facial weakness. Our case broadensthe understanding of SUNCT, allowing one to consider RHS or herpes zoster as part of the differential for SUNCT.

Neurology

Elfaham A, and **Jumah A**. Unusual Case of Recurrent Falls Secondary to Tumefactive Perivascular Spaces (P9-4.006). *Neurology* 2024; 102(17_supplement_1). Full Text

A. Elfaham, Henry Ford Health, United States

Objective: Report an unusual case of recurrent falls secondary to obstructive hydrocephalus, attributed to tumefactive perivascular spaces. Background: Perivascular spaces also known as Virchow Robin spaces are benign, fluid-filled structures surrounding blood vessels in the white matter of the brain. They are usually small and not easily identified on brain imaging. Tumefactive Perivascular Spaces (TPVS) are characterized by the significant dilation and enlargement of these perivascular spaces. When the dilation is large enough, they can be visualized on MRI. The appearance of TPVS can resemble the appearance of more serious conditions like brain tumors and demyelinating disease making them clinically significant. Additionally, in 43% of giant TPVS, hydrocephalus can be seen. Obstructive hydrocephalus can be due to a myriad of conditions, but enlarged perivascular spaces is unusual. Most common presentation of obstructive hydrocephalus secondary to TPVS is headaches; however, as our case illustrates, poor balance and recurrent falls can be the presenting complaint. Design/Methods: NA Results: A 36-year-old man with no significant medical history presented to the Emergency Department with recurrent falls and imbalance for 6 weeks. Neurological exam was unremarkable with intact brainstem, normal strength, sensation, and reflexes; but, he had extreme difficulty maintaining a steady posture. MRI showed cystic foci filled with CSF in the right midbrain, cerebral peduncle, thalamus, and dentate nucleus but without transependymal flow on FLAIR sequences, suggestive of chronic TPVS. These lesions were causing mass effect and hence, an obstructive hydrocephalus. DWI and apparent diffusion coefficient sequences did not reveal any signal restriction. The patient was admitted and underwent endoscopic third ventriculostomy. After three months, he showed remarkable improvement of his symptoms. Conclusions: TPVS are oftentimes easily misinterpreted as a sinister process given the complications patients present with. Surgery is the mainstay of treatment and remarkable improvement can be achieved after third ventriculostomy for patients who are symptomatic.

Neurology
Eltous L, **Idris A**, **Elfaham A**, and **Jumah A**. Neurosyphilis in Disguise (P4-13.003). *Neurology* 2024; 102(17_supplement_1). Full Text

L. Eltous, Jordan University of Science and Technology, Jordan

Objective: Neurosyphilis can mimic different diseases, not only in its clinical presentation but also on imaging. Treponema Pallidum is also known as the great imitator . Having an ultimate diagnosis of neurosyphilis is quite critical as this can affect management drastically. Herein, we discuss the case of a 69-year-old female who was treated for neurosyphilis, while having an atypical imaging finding of anterior temporal lobe enhancement that simulated an infection with HSV. Background: A 69-year-old female with untreated syphilis infection (diagnosed almost 20 years prior presentation), was brought in with progressive decline in memory and confusion over one month. According to the family, the patient was unable to recall the name of her children or attend to her daily activities. On initial examination, she was alert but not oriented to herself, family members, location nor time, she had perseveration while answering questions, was able to only mimic commands. The rest of her examination was otherwise unremarkable. MRI of the brain with contrast showed anterior temporal lobes, insular cortex and pons T2 and FLAIR hyperintensities, that were all enhancing. Syphilis serology was positive and reactive for IgG/IgM. Treponema pallidum hemagglutination test was positive, and HIV was negative. CSF studies showed protein of 94.6 mg/dL, WBC of 15 cells/mm3 with lymphocytic predominance, RBC of 35 cu/mm, VDRL in the CSF was negative. Viral studies in the CSF were all negative. Benzathine penicillin G 24 million units was given for the total of 14 days with improvement in her mental status on follow up at one and two months. Design/Methods: N/A Results: N/A Conclusions:This unusual imaging finding of anterior temporal lobe hyperintensities with enhancement, plus the clinical presentationmake it worth listing neurosyphilis next to many disease processes including HSV on the differential list.

Neurology
Eltous L, **Idris A**, **Elfaham A**, and **Jumah A**. Lumbar Puncture, Pneumocephalus, and a Transient Cranial Nerve Palsy: A Case Report (P4-15.003). *Neurology* 2024; 102(17_supplement_1). Full Text

L. Eltous, Jordan University of Science and Technology, Jordan

Objective: Minimally invasive and surgical spine procedures are commonplace with various risks and complications. Cranial nerve palsies, however, are infrequently encountered, particularly after procedures such as lumbar punctures, epidural anesthesia, or intrathecal injections and are understandably worrisome for clinicians and patients as they may be interpreted as secondary to a sinister etiology. However, a less commonly considered source is pneumocephalus which may, in rare cases abut cranial nerves and cause a palsy as a benign and often self-resolving complication. Background: A middle-aged patient with a new diagnosis of high-grade mature T-cell non-Hodgkin lymphoma was admitted to the hospital for chemotherapy initiation. The patient received the first cycle of CHOP chemotherapy and a first infusion intrathecal methotrexate infusion and post-procedurally, she developed a new onset of painless right-sided horizontal diplopia. The intrathecal injection was performed in prone positioning using a fluoroscopic guided 20-gauge spinal needle into the L2-L3 space. Next, approximately 10ml of CSF fluid was collected followed by 12mg of methotrexate injection. CSF studies returned unremarkable. Upon physical examination, there was a notable partial right-sided abducens palsy without any other focal neurological deficits. Non-contrast CT scan of the head demonstrated a pneumocephalus anterior to the pons and at the level of the clivus abutting the right abducens nerve (Figure 1). Follow-up brain MRI with contrast was unremarkable for other potential causes of this acute palsy presentation, including infections, stroke, or herniation from intracranial hypotension. The patient was monitored and managed expectantly without any acute interventions and upon follow-up in 24 hours there was complete resolution of her symptoms. Design/Methods: N/A Results:N/AConclusions:Pneumocephalus causing a cranial nerve palsy is very rare. Its complications may be as trivial as headaches, to morecomplex presentations such a cranial nerve palsy, to exceedingly dangerous complications like tension pneumocephalus.Signs and symptoms resolve spontaneously with conservative management.

Neurology
Gerbasi M, Tu L, Chertavian E, Nejati M, and **LeWitt P**. Real-world Evidence of Efficacy, Use, and Discontinuation of Pharmacotherapies for the Treatment of Essential Tremor (P3-3.006). *Neurology* 2024; 102(17_supplement_1). Full Text

M. Gerbasi, Sage Therapeutics, Inc., United States

Objective: To conduct a literature review using real-world evidence on the most common pharmacotherapies used in treating essential tremor (ET). Background: ET is among the most common movement disorders in the US. Current treatments include pharmacological treatments and surgical interventions, though many patients continue to lack adequate tremor control. Syntheses of published real-world evidence on ET pharmacotherapies are lacking. Design/Methods: We conducted a comprehensive literature review of English-language studies published between 1966-2022 using PubMed. The review targeted non-clinical trial studies of adults with ET evaluating propranolol, primidone, gabapentin, and/or topiramate, and reporting at least upper limb tremor efficacy, safety/adverse events, tolerability, and/or treatment patterns. Studies reporting 10 subjects were excluded. Results: We identified 236 studies. Following title and screening, 75 full-text studies were assessed, with 15 included in data extraction. Patient- or clinician-validated scales were used in 2/15 studies. Activities of daily living and quality of life outcomes were not commonly reported. Up to 81% and 55% of patients used propranolol and primidone, respectively. Gabapentin (30%) and topiramate (20%) were used less frequently. Though clinical response definitions varied, propranolol demonstrated response in 37-56% of patients, and primidone in 43-55% of patients among studies with 50 evaluable patients. Approximately one-quarter of patients reported responding to gabapentin or topiramate. Discontinuation rates varied widely across studies, from 10-70% for both propranolol and primidone. Gabapentin and topiramate had discontinuation rates from 26-86% and 26-58%, respectively. Usage, efficacy, and discontinuation were not characterized by line of therapy (i.e. initial vs subsequent treatments) in the assessed studies. Conclusions: Currently available ET pharmacotherapies may not provide adequate efficacy for many patients, highlighting substantial unmet need. We identified several gaps in the published evidence base, including evaluation of commonly-used ET medications by line of therapy and reporting on validated measures to enable comparisons to new ET pharmacotherapies.

Neurology
Goorman S, **Zaman I**, **Schultz L**, **Memon A**, and **Ho E**. Obturator Neuropathy: A Retrospective Review of 36 Patients (P8-11.008). *Neurology* 2024; 102(17_supplement_1). Full Text

S. Goorman, Wayne State University, Henry Ford Hospital - Detroit, MI, United States

Objective: The primary objective of this research study is to gain understanding of electrophysiological findings and value of repeat EMG/NCS for prognostication in patients with obturator neuropathy. Background: Obturator neuropathy presents as an uncommon cause of lower extremity weakness with other symptoms including medial thigh numbness, weakness of thigh adduction, and lower extremity pain. Design/Methods: This single center retrospective study aimed to summarize various clinical features of obturator neuropathy. A total of 36 patients with obturator neuropathies diagnosed over a 20-year period, August 2002 to July 2022 were evaluated. Demographic, clinical, and electrographic data were collected, and descriptive statistics were used to analyze the variables of interest. The variables of interest included etiology, symptoms, physical exam signs, time to diagnosis from symptom onset, treatment, age, race, sex, insurance, prognosis, and electromyography (EMG) findings. Results: Of the 36 patients evaluated, surgery related trauma (n≤21; 58%) was the most common etiology, and lower extremity pain (n≤30; 86%) was the most common symptom. Based on diagnoses made through EMG, 23 patients (79%) had pure obturator neuropathy. Treatments led to improvement or complete resolution in 18 (50%) patients while 11 (31%) had no relief. No significant difference in time to diagnosis was observed based on sex, race, or insurance type Conclusions:Obturator neuropathies are commonly associated with lower extremity weakness leading to diffi culties in ambulation.Surgical trauma was the most common cause in our patient group, followed by cancer related causes. Electrodiagnosticfi ndings, mainly EMG studies, aid in the defi nitive diagnosis. The lack of statistically signifi cant differences between race,sex, or insurance in our patient group suggests an equitable process of evaluation of patient from their initial

presentationwith a provider to a defi nitive diagnosis. The lack of symptomatic improvement in 31% of patients in our groupdemonstrates the continued need for advancements in nerve repair and regrowth.

Neurology
Ho E, **Goorman S**, **Zaman I**, **Memon A**, and **Schultz L**. Laryngeal Neuropathy: A Retrospective Review of 52 Patients (P8-11.009). *Neurology* 2024; 102(17_supplement_1). Full Text

E. Ho, Henry Ford Hospital, United States

Objective: The primary objective of this research study is to gain understanding of electrophysiological findings and value of repeat EMG/NCS for prognostication in patients with laryngeal neuropathies. Background: Laryngeal neuropathy presents as an infrequently diagnosed cause of vocal dysfunction with symptoms including cough, voice changes, difficulty swallowing, and throat pain. Design/Methods: This single center retrospective study aimed to summarize various clinical features of laryngeal neuropathy A total of 52 patients with laryngeal and vagal neuropathies diagnosed over a 22-year period, 2000 to 2022 were evaluated. Demographic, clinical and electrodiagnostic data were collected, and descriptive statistics were used to analyze the variables of interest. The variables of interest included etiology, symptoms, time to diagnosis from symptom onset, treatment, race, sex, prognosis, and electromyography (EMG) findings. Results: Of the 52 patients evaluated, surgery related trauma (n≤23; 44%) was the most common etiology, and speech difficulty (n≤49; 94%) was the most common symptom. Based on diagnoses made through EMG, 25 patients (48%) had vagal neuropathy, 8 (15%) had recurrent vagal neuropathy, 13 (25%) had other laryngeal conditions. Treatments including surgical repair, speech therapy, medical therapy, and several others led to improvement or complete resolution in 23 (44%) patients. No significant difference in time to diagnosis was observed based on sex or race. Patients with post-surgical etiology had a significantly shorter time to diagnosis (p≤.015). Conclusions:Laryngeal neuropathies are commonly associated with vocal cord dysfunction leading to signifi cant speech impairment.Surgical trauma was the most common cause in our patient group, followed by idiopathic causes. Electrodiagnosticfi ndings, including EMG studies, aid in the defi nitive diagnosis. The shorter time to diagnosis in patients who develop post-surgical manifestation may be due to in-patient post-surgical status enabling faster evaluation.

Neurology
Jumah A, and **Idris A**. The National Institute of Health Stroke Scale: A Teaching Tool (P8-5.008). *Neurology* 2024; 102(17_supplement_1). Full Text

A. Jumah, Henry Ford Hospital, United States

Objective: The National Institute of Health Stroke Scale (NIHSS) is the most frequently used score in assessing the severity of stroke, as it is a very reliable and reproducible in assessing a corresponding neurological deficit. Not only this, but this scoring system is also extremely helpful in the communication between vascular neurologists, emergency personnel, and neuroradiologists when discussing stroke treatment. Teaching NIHSS to medical students and residents from other specialties spending time in neurology is absolutely necessary, and to recall the score components for a quick neurological assessment during stroke codes is of an utmost importance. Background: The illustration seen here (Figure) is an easy and a creative way to remember the components of the NIHSS in an efficient manner. From top to bottom, starting from the left to right; the letter L stands for level of consciousness, the letter O is split diagonally to remember asking both questions regarding Age and Month. The letter C indicates following commands. After this, the eyes indicate smooth pursuit assessment looking for gaze preference. The letter V indicates visual fields and the number 7 is for the 7 cranial nerve. Below this is a four-component assessment of upper and lower extremity strength, coordination, sensory function as well as inattention. Finally, both T letters stand for tongue reminding the examiner to assess for aphasia as well as dysarthria. Design/Methods: N/A Results:N/AConclusions:This was designed initially for medical students rotating in neurology to calculate stroke scales in an effi cient manner as thediffi culty in the remembering the components of the neurological examination was frequently encountered. This tool ishelpful for medical doctors as well as nurses, not only those working in neurology fl oors but also in the

emergencydepartment and the medical general practice units, used to provide a quick and effi cient assessment for patients withpossible stroke.

Neurology
Mann K, **Qureshi K**, Farooq M, and Koehler T. Ischemic Stroke Timing and COVID-19 Infection: A Case Series (P11-5.009). *Neurology* 2024; 102(17_supplement_1). Full Text

K. Mann, Neuroscience Program, Saint Mary'S Health, United States

Objective: To describe demographic, clinical characteristics and outcomes of patients experiencing stroke with concomitant COVID-19 infection in a community-based teaching hospital. Background: It has been proven that COVID-19 patients are at risk of developing ischemic stroke due to mechanisms including embolic phenomenon from a hypercoagulable state, vasculitis, and cardiomyopathy. We aim to describe incidence of stroke, radiographic patterns and timing of stroke in relation to COVID-19 infection specifically in West Michigan. Design/Methods: We conducted a single centre descriptive case series of patients with stroke and concomitant COVID-19 infection between March 2020 and December 2021. Data collected included demographic and clinical characteristics, time between COVID diagnosis and stroke and discharge disposition. Summary statistics are reported. Results: A total of 50 patients were reviewed; average age 68.9+16.3 years, 50% male and predominantly white 85.7% (36/42). Thirtynine patients were diagnosed with stroke at admission and 11 patients experienced stroke post-admission. Forty-two (84%) patients were diagnosed with COVID-19 within two weeks prior to or after stroke; with 70% occurring within 7 days. Eight patients were diagnosed with COVID-19 within a median of 20 days prior to or after stroke (range: 16-51 days). Thirty-seven patients had documented COVID-19 severity, 17 (46%) had moderate to critically severe illness. Thirty-eight (76%) patients had documented hypertension. Thirty-one (62%) patients experienced embolic stroke. Five patients died, 18 were discharged home and 27 were discharged to rehab or a long-term care facility. Conclusions: Like other findings in the literature, there appears to be a high incidence of stroke within 14 days of COVID infection, with most occurring within one week of diagnosis. Most of the strokes were embolic in nature. Most patients had severe symptoms of covid as well. .

Neurology
Mohamedelkhair A, **Ali A**, and **Elfaham A**. Rare Case of Complete Facial Diplegia After Botulinum Toxin Injections for Chronic Migraine (P10-12.002). *Neurology* 2024; 102(17_supplement_1). Full Text

A. Mohamedelkhair, Henry Ford Hospital neurology, United States

Objective: To present a case of facial diplegia as a rare adverse effect of botulinum toxin injections for chronic migraine. Background: OnabotulinumtoxinA injections are well-tolerated FDA-approved treatment of chronic migraine, with reported side effects included neck pain, brow asymmetry and eyelid droop. Adverse effects to alternative neurotoxins, incobotulinumtoxinA, are not well-studied in randomized controlled trials. Nonetheless, they are often used for treatment of chronic migraine offlabel. Design/Methods: Case Report Results: A 55 year old female with chronic migraine received botulinum toxin injections for treatment with a positive therapeutic response She had previously received 7 sessions with onabotulinumtoxinA using the FDA-approved PREEMPT protocol, and was switched to incobotulinumtoxinA due to institutional formulary change. Approximately 12 days after her third treatment with incobotulinumtoxinA, she gradually developed weakness of her facial muscles that she perceived to be facial swelling due to an allergic reaction. She had trouble closing her eyes, chewing food, and with facial expression. After visits to the emergency department and her PCP, patient followed up with neurology where she was noted to have complete facial diplegia with minimal facial movement. She started to improve after 3-4 weeks, and, her weakness completely resolved by 8 weeks. Further treatment with incobotulinumtoxinA was not pursued, and the patient was switched to a monoclonal cGRP antibody with good response. The patient was felt to have had an facial diplegia as a idiosyncratic reaction to incobotulinumtoxinA, 150 kiloDalton toxin injections with the use of standardized PREEMPT protocol. Conclusions: To our knowledge, this is the first reported case of complete facial diplegia occurring as an indiosyncratic reaction to botulinum toxin therapy for chronic migraine. Importantly, this occurred with use

of incobotulinumtoxinA, which is an offlabel but often used substitute for chronic migraine and has a lower molecular weight (150 kiloDalton) compared with onabotulinumtoxinA (900 kiloDalton). .

Neurology
Nofar J, **Davis K**, Mathew P, and **Ali A**. The Use of OnabotulinumtoxinA for the Treatment of Chronic Migraine During Pregnancy: An American Headache Society Survey Study (P7-12.003). *Neurology* 2024; 102(17_supplement_1). Full Text

J. Nofar, Neurology, Henry Ford Health, United States

Objective: To generate a statistical snapshot of physicians' perspectives and treatment practices regarding use of onabotulinumtoxinA (onabotA) for treating chronic migraine during pregnancy. Background: OnabotA is an FDA-approved neurotoxin for treating chronic migraine. However, limited data exists regarding the safety of onabotA in pregnancy. The therapeutic options for migraine during pregnancy are currently limited and few studies have been conducted to explore physicians' practices regarding the use of botulinum toxin in pregnancy. Design/Methods: A 15-question survey exploring physicians' clinical practices using botulinum toxin injections for chronic migraine was distributed online to members of the American Headache Society. The final 4 questions pertained to use in pregnancy. Descriptive analysis was performed. Results: A total of 168 respondents (162 from the United States and 6 from Canada) completed the survey (response rate 10.1% [168/1665]). Of the respondents, 96 (58%) reported not using OnabotA during pregnancy; 97 (59%) reported continuing use of onabotA while a patient is actively trying to become pregnant; 94 (57%) reported discontinuation of onabotA treatment when a patient become pregnant; 117 (71%) reported that they have or would consider resuming onabotA treatment during pregnancy should a patient experience refractory headache after discontinuation of the treatment. Conclusions: Of the providers sampled, a slight majority avoided use of onabotA during pregnancy, however would use or consider using onabotA should the patient develop refractory headache after discontinuation of onabotA due to pregnancy. Additionally, the majority of providers did not discontinue onabotA while a patient is actively trying to become pregnant.

Neurology
Nofar J, **Sitto M**, **Ali A**, and **Sallowm Y**. Occipital Nerve Block Leading to the Discovery of Carcinosarcoma (P10-12.008). *Neurology* 2024; 102(17_supplement_1). Full Text

J. Nofar, Neurology, United States

Objective: NA Background: Occipital nerve blocks are routinely performed for the treatment of various headache disorders. When conventional medications are not sufficient, minimally invasive methods such as occipital nerve blocks become a viable treatment option. The targeted nerves can be reached using anatomical landmarks or imaging. We present a case of an occipital nerve block inadvertently leading to the discovery of a high-grade neoplasm. Design/Methods: 78-year-old female complaining of headache for 2 years. It was moderate to severe intensity, originated from the left > right occipital region, and radiated anteriorly. Quality was sharp/shooting/stabbing. She was previously diagnosed with occipital neuralgia by outside provider and had undergone two occipital nerve blocks, with significant but temporary relief. She was evaluated by neurology at our institution, who concurred with the diagnosis of bilateral occipital neuralgia, and referred her for bilateral occipital nerve blocks. Using standard protocol, a 25-gauge, 1.5-inch needle was advanced 0.5 inches on the left, but no contact was made with the occipital bone. The thickness of the scalp was re-evaluated by palpation and was normal. A lateral X-ray was taken to assess the distance between the needle tip and the periosteum, and demonstrated an abnormal appearance of the occipital bone. The procedure was aborted. Results: Non-contrast CT head demonstrated destructive osseous changes involving the majority of the occipital bone with extraosseous soft tissue extension. MRI brain with and without gadolinium demonstrated an expansile, heterogeneous lesion involving the occipital calvarium without intracranial enhancement. CT-guided biopsy confirmed neoplasm favoring carcinosarcoma. Conclusions: Occipital nerve blocks are commonly performed without prior imaging or image-guidance. This case raises the potential need of pre-intervention screening (e.g. x-ray) or ultrasound guidance, particularly in elderly patients with new-onset occipital neuralgia. This would

accommodate varying skull sizes, pathologies, and anatomical variations, which can improve the effectiveness of the block, minimize recurrence, and avoid complications. .

Neurology
Qureshi M, **Jum'ah A**, **Albanna A**, and **Malik S**. Reversible Cerebral Vasoconstriction Syndrome Secondary to Loperamide Ingestion: A Case Report (P3-12.009). *Neurology* 2024; 102(17_supplement_1). Full Text

M. Qureshi, Henry Ford Hospital, United States

Objective: To describe a unique case of RCVS secondary to the antidiarrheal agent loperamide. Background: Reversible cerebral vasoconstriction syndrome (RCVS) is a cerebrovascular disorder characterized by diffuse, multifocal vasoconstriction of the cerebral circulation. While RCVS may be idiopathic, the leading cause is exposure to certain drugs. RCVS is self-limiting and almost always reversible. The main mechanism underlying the pathophysiology of vasoconstriction is cerebrovascular dysregulation of vascular tone. Design/Methods: A 73-year-old woman presented with severe vertigo of 3 days duration. CT angiography of the head and neck showed focal stenoses at the bilateral posterior cerebral arteries, the left superior cerebellar artery, and the right inferior cerebellar artery. Symptoms resolved after fluid administration. Two weeks later, magnetic resonance (MR) imaging of the brain, head and neck with contrast showed resolution of intracranial stenoses and absence of intracranial insults and vascular enhancement. Patient had been experiencing vomiting and diarrhea for one week before her ED presentation and had been using the antidiarrheal agent loperamide in 2 mg doses four times daily for 6 days, which resolved the diarrhea. Results: Our patient's RCVS with diffuse vasoconstriction was most likely caused by excessive use of the over-the-counter antidiarrheal agent loperamide, which is an opioid receptor antagonist that works in the gut, halting peristaltic movements and water secretion. Although loperamide's vasoconstrictive effects have been reported as possibly inducing myocardial ischemia, to our knowledge, loperamide associated with cerebral vasoconstriction and RCVS has not been reported Conclusions:RCVS is a syndrome which classically presents with headache, but presentation can be varied. Therefore it is important tokeep in mind the image findings of multi-focal stenosis which later resolves. We propose that Loperamide, an anti-diarrhealagent, is a causative agent for RCVS, as seen in our patient. Reviewing current medications for suspected RCVS is extremelyimportant, and immediately eliminating the causative agent is imperative.

Neurology
Varelas P, Kananeh M, **Brady P**, Holden D, Ata A, **Mehta C**, Greer D, and **Rehman M**. The Relationship Between Diabetes Insipidus and Renal Function in Brain Dead Patients (P1-2.003). *Neurology* 2024; 102(17_supplement_1). Full Text

P. Varelas, Albany Med-Department of Neurology, United States

Objective: Examine if different degrees of renal dysfunction may impact the manifestation of Diabetes Insipidus (DI) in Brain Dead (BD) patients. Background: It has been reported that up to 50% of BD patients do not have signs of clinical DI, which suggests remaining hypothalamic/pituitary activity. However these studies have never accounted for presence or absence of renal dysfunction in those patients Design/Methods: All adult patients declared BD over 12 years at a tertiary center were evaluated. DI was diagnosed by polyuria (>300 ml urine output for 2 consecutive hours), low urine specific gravity (< 1.005) and increasing serum sodium. Renal function was assessed by the estimated glomerular filtration rate (eGFR), calculated using the simplified Modification of Diet in Renal Disease (sMDRD) equation (validated for ages > 18) Results: 192/266 BD patients were included in the analysis after excluding those with missing data, < 18-years-old or on vasopressin infusions (for hypotension). 122 (63.5%) developed DI. The proportion with DI decreased significantly with decreasing eGFR: for eGFR > 60ml/min, DI was present in 77.2%; for eGFR 15-60ml/min in 54.5%, and for eGFR < 15ml/min in 32% ($p < 0.001$). There were 14 patients with eGFR < 9.7 ml/min (all with serum creatinine > 7.1 mg/dL); none experienced DI. Using logistic regression, for every 10 ml/min increase in eGFR the odds of DI increased by 1.2 times (95% CI: 1.10 to 1.32, $p < 0.001$) Conclusions: Presence of hypothalamic/pituitary activity (based on the absence of DI) may be less common than previously thought in BD patients, as kidney dysfunction

significantly impacts DI manifestation. DI is observed less frequently in BD patients who have renal injury, and some patients with severe renal dysfunction never develop clinical DI. Renal dysfunction should be accounted for when considering the presence or absence of DI in brain death.

Neurology

Zeidman L. IVIG Effective in Non-Length Dependent Skin Biopsies in Small Fiber Neuropathy with Plexin D1, TS-HDS, and FGFR-3 Antibodies (P9-11.007). *Neurology* 2024; 102(17_supplement_1). Full Text

L. Zeidman, Henry Ford Health, United States

Objective: To demonstrate efficacy of Intravenous Immunoglobulin (IVIG) in pure small fiber neuropathy (SFN) patients who had trisulfated heparin disaccharide (TS-HDS), fibroblast growth factor-3 (FGFR-3), or Plexin D1 antibodies (seropositive). Background: SFN has an increasing prevalence and over 30% of cases may be immune-mediated. TS-HDS, FGFR-3, and Plexin D1 autoantibodies have been shown to be present in 44-55% of cryptogenic SFN cases, suggesting an immune-mechanism. Some reports have shown IVIG to be an effective treatment. Design/Methods: In a retrospective review, all pure SFN cases tested for the 3 antibodies from January 2021-May 2022 were tabulated, and cases who underwent IVIG treatment were separated and analyzed for changes in length-dependent (LD)-, non-length dependent (NLD)-, and composite-epidermal nerve fiber density (ENFD) on skin biopsy (composite is an average of all sites), as well as SFN-specific questionnaire and pain scores. Results: 92 patients with pure SFN had antibody testing (68% seropositive, 32% seronegative). 17 seropositive patients underwent IVIG treatment. Of these, 2 patients stopped treatment due to side effects (severe headaches or allergic reaction), and the remaining 15 completed at least 6 months of IVIG. Of these, 12 had a post-IVIG skin biopsy, and of these, 11 (92%) had a 55.1% mean improved composite ENFD (p=0.01). NLD-ENFD specimens improved by 42.3% (p=0.02) and LD-ENFD specimens improved by 99.7% (p=0.01). Composite ENFD in Plexin D1-SFN patients improved by 139% (p=0.04). Also, 14 patients had questionnaires pre-/post-IVIG and average pain decreased by 2.7 (p=0.002). Conclusions: IVIG shows disease-modifying effect in immune SFN with novel antibodies, especially Plexin D1-SFN, as well as significantly improved pain. NLD-ENFD should be examined as well as LD-ENFD to see this effect. Further randomized controlled trials looking at NLD- as well as LD-ENFD improvement, along with pain and SFN-specific questionnaires, are needed to confirm these findings.

Neurosurgery

Chernoff D, Peterson D, Van Poppel M, Boling W, Santos P, **Schwalb J**, Eisenberg H, Mehta A, Spader H, Botros J, Vrionis F, Ko A, Adelson PD, Lega B, Konrad P, and Richardson M. ID: 335853 Initial Clinical Safety and Feasibility from RESET-RA Study: Novel Neuroimmune Modulation Device for Rheumatoid Arthritis. *Neuromodulation* 2024; 27(7):S189. Full Text

Introduction: Electrical stimulation of the vagus nerve activates the inflammatory reflex to inhibit cytokines and decrease clinical signs and symptoms of chronic inflammatory disease such as rheumatoid arthritis (RA) (Genovese et al. Lancet Rheum 2020). The RESET-RA study (NCT04539964) is a randomized, double-blind, sham-controlled, multi-center, two-stage pivotal study that evaluates the safety and efficacy of a novel neuroimmune modulation device in patients with moderate-to-severe RA who are incomplete responders or are intolerant to one or more biological or targeted synthetic drugs. We report the safety data of the surgical implantation and use of this device in the first 60 subjects enrolled in the study. Methods: The device system consists of two implanted components: a miniature integrated pulse generator and a silicon sleeve positioning device that holds the generator in apposition to the left vagus nerve. There are two external components: a wireless charger and an iPad application for programming the pulse generator. Subjects were randomly assigned (1:1) after device implantation to receive active or sham stimulation. The risks of the surgical procedure, device, and stimulation were blindly assessed after 12 weeks of stimulation therapy in the first 60 subjects enrolled in the study. Results: All implant procedures were completed without intraoperative complications, infections, or surgical revisions. No unanticipated adverse events (AEs) related to the implant procedure, device, or stimulation were reported during the perioperative period and at the end of 12 weeks of follow-up. No serious AEs related to the device, stimulation, or explant procedures were reported. Vocal cord paresis and prolonged hoarseness were reported in two subjects. The former resolved following vocal cord augmentation with injectable

filler; the latter improved with speech therapy and resolved with minor sequelae and no impairment. Conclusion: Initial results through 12 weeks of follow-up demonstrated that implantation and programming of the novel neuroimmune modulation device were safe, and the surgical procedure and device were well tolerated in patients with moderate-to-severe RA.

Neurosurgery
Kotecha R, McDermott M, Lee S, Peach M, Richardson A, Floyd J, Patel T, Wardak Z, Sloan L, Ferreira C, Neil E, Hunt M, Shen C, Wasilewski A, Wanebo J, Smith K, Chamoun R, **Robin A**, **Lee I**, Leng L, Patel A, Zhu J, Hanft S, Zeller S, Aizenberg M, Rodriguez A, Choutka O, Hoang K, Nowlan A, McCracken D, Dunbar E, Brachman D, Garcia M, and Patel S. PATHOLOGIC INCIDENCE OF TUMOR POSITIVITY VS ONLY NECROSIS AFTER PRIOR RADIATION IN PATIENTS UNDERGOING SURGICAL EXCISION FOR PRESUMED BRAIN METASTASIS RECURRENCE: INSIGHT FROM A PROSPECTIVE MULTICENTER REGISTRY. *Neuro-Oncol Adv* 2024; 6(Supplement_1):i15. Full Text

R. Kotecha, Baptist Health of Miami, Miami, FL, United States

PURPOSE/OBJECTIVE(S): Determining true recurrence versus necrosis alone after previous radiation therapy (RT) for brain metastasis based on imaging alone is difficult. Proper diagnosis is essential, as further radiation is contraindicated in the setting of radiation necrosis without tumor (TUM-). To better understand the rate of pathologic tumor positivity (TUM+) vs TUM-, we examined frozen section results from a cohort of patients with prior same-site RT undergoing resection of presumed recurrent brain metastasis (RBM). MATERIALS/METHODS: Rates of intraoperative frozen section pathology disclosing tumor +/- necrosis (TUM+) or necrosis without tumor (TUM-) were examined in patients undergoing resection for presumed RBM after prior same-site RT. All cases had been prospectively enrolled on a multi-institution registry for patients undergoing resection and intraoperative cesium-131 collagen tile brachytherapy (NCT04427384)(GammaTile, GT Medical Technologies, Tempe AZ, USA). Preoperative evaluation varied by center, and patient demographics, primary site, lesion size, and prior therapies were also examined. RESULTS: From 10/2020 to 2/2024 60 patients (64 lesions) underwent resection and intraoperative frozen section pathologic evaluation. Per patient, primary sites were 53% lung, 15% melanoma, 13% breast, 7% renal, and 10% other. F:M ratio was 31:29; median age 62, maximum preoperative diameter 2.9 cm, and median time from prior RT 15.4 months. Across all histologies TUM+ was seen in 88% (53/60) and TUM- in 12% (7/60). Rates of TUM- by primary type were highest for lung (16%), breast (13%), and melanoma (11%). The TUM- rate for lung metastasis was 16% vs 7% for non-lung origin. All TUM- patients received RT and prior chemotherapy, immunotherapy, or both. CONCLUSION: For all previously irradiated metastasis, pathology demonstrated a 12% rate of TUM-. As all cases necessitated surgery, the adverse event grading would be ≥ Gr 4. These findings highlight the importance of pathologic confirmation before undertaking re-irradiation for presumed radiographic recurrence.

Neurosurgery
Um H, Ismail M, Hill V, Puri S, Yu J, Lu L, Nayate A, **Rogers L**, Prasanna P, Bardhan M, Li C, Basree M, Baschnagel A, McMillan A, Bhatia A, Ahluwalia M, Veronesi M, and Tiwari P. AI-DRIVEN MR IMAGE FEATURES VERSUS RANO-BM CRITERIA IN DISTINGUISHING RECURRENT BRAIN METASTASES FROM RADIATION TREATMENT EFFECT: A COMPARATIVE, MULTIINSTITUTIONAL STUDY. *Neuro-Oncol Adv* 2024; 6(Supplement_1):i10. Full Text

H. Um, University of Wisconsin-Madison, Madison, WI, United States

A significant challenge in brain metastases (BM) management is distinguishing radiation-induced treatment effect (TE) from tumor recurrence (TR). TE mimics the appearance of TR on follow-up MRI, making radiographic diagnosis unreliable. The standardized Response Assessment in Neuro-Oncology for brain metastases (RANO-BM) is suboptimal due to high inter-reader variability. We compared the performance of artificial intelligence (AI)-driven MRI features with that of RANO-BM criteria in differentiating TE from TR. We hypothesize AI-features from routine MRI can capture the pathophysiologic differences between TE and TR, occult on structural MRI and hence overlooked in standard-of-care evaluation. A total of 261 lesions with pathologically-confirmed diagnoses in 189 patients

were retrospectively analyzed. 201 lesions (111 TR,90 TE) from Cleveland Clinic and University Hospitals, Cleveland were used for training a machine learning model. 60 lesions (33 TR,27 TE) from University of Wisconsin- Madison were used for model testing. MRI (Gd-T1w, T2w, FLAIR) were preprocessed, and lesions were expertly segmented into enhancing lesion, edema, and necrosis. 856 texture features were extracted from each sub-compartment, and a random forest classifier was employed for 3-fold cross-validation. Top-performing features and RANO-BM criteria were evaluated on the test set. Results show T1 features from edema were most discriminatory in differentiating TR from TE (training-AUC=0.86, testaccuracy= 71.7%, test-sensitivity=78.8%). Using RANO-BM, 9 cases were excluded due to lack of longitudinal imaging to estimate lesion growth. Additionally, since no lesions decreased in sum of longest diameter, none were classified as partial response while the remaining 51 cases were classified as stable disease (n=14, (8 TR,6 TE)) or TR (n=37, accuracy=54.1%). Interestingly, 78.6% of the stable lesions were accurately classified using our AI-model as TE or TR, missing only 3 cases (2 TR,1 TE). Our results suggest AI-driven models on clinical MRI scans may reliably distinguish TR from TE, demonstrating potential utility in clinical practice.

Obstetrics, Gynecology and Women's Health Services

Abuzeid MI, Joseph S, Hitaj J, and Rizk BM. Reproductive Outcome after Metroplasty of T-Shaped Uterus in Infertile Patients. *Fertil Steril* 2024; 122(4):e402. Full Text

OBJECTIVE: To determine reproductive outcome after hysteroscopic metroplasty in infertile patients with T-shaped uterus. MATERIALS AND METHODS: This retrospective study included 35 consecutive patients (2020-2023) who presented with reproductive failure and were found to have T-shaped uterus. 35 patients had infertility with 12 also having recurrent pregnancy loss (RPL). All patients underwent hysteroscopic metroplasty (unilateral or bilateral) for T-shaped uterus; 26 also underwent septoplasty for additional partial septate uterus (PSU) [European Society of Human Reproduction and Embryology/European Society for Gynecological Endoscopy classification of Müllerian anomalies, 2013]. Postoperative transvaginal 3D ultrasound scan (TV 3D US) with saline infusion sonohysterogram (SIH) was performed for evaluation of the uterine cavity. Depending on the underling etiology, couples were offered to try to conceive naturally, with fertility medication (Letrozole), intrauterine insemination after controlled ovarian stimulation, or in vitro fertilization. Pregnancy outcome and any intra or postoperative complications were documented. RESULTS: Mean age (years), BMI (kg/m2), duration of infertility (years) and AMH (ng/mL) were 33.6 + 4.7, 26.2 + 5.5, 3.5 + 4.2 and 4.0 + 4.3 respectively. Metroplasty for T-shaped was unilateral in 74.3% and bilateral in 25.7%. In 26 patients PSU was also present. The mean mid-fundal protrusion length (mm) was 12.1 + 3.0 and 92.3% had an indentation apex angle that was >90 degrees. Septoplasty was performed in the 26 patients who underwent unilateral metroplasty. Postoperative SIH with TV 3D US revealed minimal filmy synechia in 22.9%, requiring a second hysteroscopy and lysis of adhesions. No other intra or postoperative complications were reported. Postoperative pregnancy, miscarriage and best outcome delivery/ongoing rates were 77.1%, 25.9% and 62.9 % respectively. CONCLUSIONS: This pilot study suggests that hysteroscopic metroplasty of T-shaped uterus with septoplasty, if PSU is found, may improve reproductive outcome in infertile patients and those with infertility and RPL. IMPACT STATEMENT: The data in this pilot study should increase the awareness of the presence of T-shaped uterus or the presence of both T-shaped uterus and PSU in some infertile patients and those with RPL. Hysteroscopic correction of such Müllerian anomalies may improve reproductive outcomes.

Obstetrics, Gynecology and Women's Health Services

Ali-Fehmi R, Toboni M, Ketch P, Krause H, Wu S, Zaiem F, Wallbillich J, Morris R, Gogoi R, Wong T, **Kheil M**, Oberley MJ, Winer I, Chapel D, Hirst J, Jones N, Thaker PH, Powell M, and Herzog T. Frequency and outcomes of co-mutations according to ProMisE classifiers in endometrial cancer. *Gynecol Oncol* 2024; 190:S170. Full Text

Objectives: Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE) classifies endometrial cancer (EC) into four molecular subtypes: DNA polymerase epsilon (POLE)-mutated, mismatch repair deficient (MMRd), wild-type and mutant p53 (TP53mut). There is a limited understanding of prognosis when tumors have alterations in multiple classifiers. Here in this study, we reported the frequency and outcomes of multi-classifier tumors in addition to high-grade biomarkers (loss of heterozygosity [LOH] and

cyclin E1 amplification [CCNE1-amp]). Methods: A total of 5158 EC underwent whole-exome sequencing. MMRd was defined as a complete loss of ≥1 IHC stain (MLH1, MSH2/6, or PMS2). MSI-High (determined from 7000 targeted microsatellite loci) was used as a surrogate for MMRd. TP53mut was defined as any pathogenic or likely pathogenic (PLP) single nucleotide variation (SNV) or an insertion or deletion (indel). POLEmut was defined as PLP mutations in the exonuclease domain. Autosomal chromosomes were split into 552 segments, and the LOH within each segment was calculated (LOH-High [H] ≥ 16 %). CCNE1-amp was defined as ≥6 gene copies. Real-world overall survival (OS) was obtained from insurance claims and calculated from tissue collection to last contact; Kaplan-Meier estimates were calculated for molecularly defined patients. Results: Concurrence between MMRd, TP53mut, and POLEmut was calculated with overlapping subtypes occurring in 4.1 % of cases (MMRd and TP53mut, n = 172 [3.3 %]; MMRd and POLEmut, n = 8 [0.2 %]; TP53mut and POLEmut, n = 29 [0.6 %]) (Table 1). Tumors that were exclusively TP53mut had significantly lower median OS as compared to TP53mut/POLEmut and POLEmut alone (median OS: 30 vs 56 months vs median not reached [MNR], respectively, P = 0.009) (Fig. 1a). The median OS was not significantly different between TP53mut/MMRd, TP53mut, and MMRd (MNR vs 30 vs 40 months, P = 0.02) (Fig. 1b). Nor was there a significant difference in OS for TP53mut versus TP53mut/CCNE1-amp tumors (median OS: 30 [n = 662] vs 65 months [n = 61], P = 0.29) (Fig. 1c). No significant difference was observed between TP53mut, TP53mut/LOH-H, and LOH-H tumors (median OS: 30 vs 29.1 vs 45.5 months; P = 0.27) (Fig. 1d). Conclusions: We report on the co-occurrence of MMR, LOH, TP53, POLE, and CCNE1 alterations in a large cohort of EC. We note that co-occurrence POLEmut/TP53mut favors POLEmut alone in contrast to TP53mut alone and follows the ProMisE algorithm. The co-occurrence of MMRd/TP53mut tumors is not significantly different than either alone. Future work should investigate treatment options for these distinct subtypes. [Formula presented]

Obstetrics, Gynecology and Women's Health Services

Daviskiba S, and **Abuzeid MI**. Variations in Hysteroscopic Appearance of Partial Septate Uteri and Arcuate Uteri. *Fertil Steril* 2024; 122(4):e436. Full Text

OBJECTIVE: To provide hysteroscopic examples of arcuate uteri and partial septate uteri to supplement classification diagrams and to emphasize "gray area" of the current classification systems that are not inclusive of all patients. METHODOLOGY: Video examples are of patients that underwent diagnostic hysteroscopy as part of a workup for infertility and recurrent pregnancy loss. Hysteroscopy was performed under general anesthesia to ensure that adequate cavity distension and visualization could be performed, which may otherwise be limited by patient discomfort during in-office hysteroscopy. An ACMI 0°or 12°7mm hysteroscope lens (Division of Olympus; Maple Grove, MN, USA) was used for all cases. Normal saline was used as initial distension media, unless septum division was being performed, in which case it was switched to 1.5% glycine. A straight resectoscope loop electrode and hysteroscopic scissors were used for measurement and division of the septum. Using the hysteroscopic uterine palpator as a reference, standardized measurements of the instruments were established to allow for indirect and direct measurements of the septum length. Indirect measurement was obtained by measuring from the level of the tubal ostia to the apex using the instruments above. Using Pythagorean's theorem, indirect measurement was multiplied by 60% to get an estimate of the septum length. Indirect measurement was performed after septum incision by measuring from the apex (starting point of incision) to the base of the incised septum. CONCLUSIONS: There is a wide variety of hysteroscopic presentations of the partial septate uterus, with many patients not aligning with existing classification. ASRM defines a lower proportion of septate uteri as compared to the ESHRE-ESGE & CUME, leaving a large proportion of patients in the gray-zone (neither diagnosed as normal/arcuate nor partial septate uteri). With this uncertainty in diagnostic classification, current ASRM guidelines may exclude patients who could potentially benefit from intervention. As recent committee opinion has established, septum incision can be beneficial to patients with recurrent pregnancy loss. IMPACT STATEMENT: While there is no universally accepted definition to differentiate arcuate from partial septate uteri, adopting criteria focused on fundal indentation depth rather than apex angle may be more inclusive. Ultimately, additional work is needed for education of generalists and subspecialists on the various hysteroscopic appearances to improve diagnosis and steer potential treatment.

Obstetrics, Gynecology and Women's Health Services
Jee Y, **Aref I**, **Wang A**, **Huang-Vredevoogd J**, **Hijaz M**, and **Elshaikh MA**. Outcomes and Patterns of Failure for Women with FIGO Stage I-II Uterine Non-Endometroid Carcinoma after Surgical Staging, Adjuvant Chemotherapy and Vaginal Cuff Brachytherapy. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e692-e692. Full Text

Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI
Henry Ford Health, Detroit, MI
Department of Gynecologic Oncology, Henry Ford Cancer Institute, Detroit, MI

Obstetrics, Gynecology and Women's Health Services
Speak A, **Hijaz M**, **Singh H**, **Udumula M**, **Miller M**, **Munkarah A**, and **Rattan R**. Inhibiting mitochondria potentiates PARPi-triggered, STING-dependent immune response in pre-clinical models of epithelial ovarian cancer. *Gynecol Oncol* 2024; 190:S233-S234. Full Text

Objectives: In ovarian cancer patients with hereditary or somatic BRCA1/2 mutations, PARP inhibitors (PARPi) have altered the treatment landscape. DNA damage caused by PARPi in conjunction with DNA repair errors due to mutations in BRCA1/2 initiates immunologic signaling via the cGAS/STING pathway. Studies have shown that therapy with a STING agonist can boost the efficacy of olaparib in BRCA-mutated ovarian cancer cells. Current research suggests that the activity of almost all immune cells is regulated by their cellular metabolism, especially energy metabolism. We have previously shown that inhibiting mitochondria by metformin augmented the therapeutic efficacy of PARPi in BRCA-intact pre-clinical ovarian cancer models. This study examined whether mitochondrial inhibition could increase STING pathway activation by olaparib in BRCA1/2-mutated and wild-type ovarian cancer cells and mouse models. Methods: ID8 p53+/+, ID8 p53-/-, ID8 p53-/-, BRCA1-/-, and ID8 p53-/-, BRCA2-/- mouse ovarian cancer cells were treated with olaparib (5mm) or metformin (2.5mM) or a combination of both; 2′,3′-Cyclic GAMP was measured by ELISA. DNA damage (gH2AX) was evaluated by flow cytometry. Mitochondrial function was assessed by an XF seahorse analyzer. Treated cells were co-cultured with naïve CD8 T cells and profiled by flow cytometry. All cell lines were used to validate the response in vivo. Results: Olaparib increased γH2AX ($P < 0.001$) in the ID8 p53-/-, BRCA2-/- cells relative to ID8 p53-/-, BRCA1-/- and wild-types, and metformin further augmented this effect ($P < 0.0001$); while the lowest DNA damage was induced in BRCA and p53 intact ID8 p53+/+ ($P < 0.001$) cells. Increased DNA damage in ID8 p53-/-, BRCA2-/- cells correlated with elevated STING by olaparib, which was further exacerbated by the addition of metformin ($P < 0.0001$). When co-cultured with naïve splenic CD8 T cells, all cell lines activated CD8 effector and cytotoxic function (CD8+IFNg+, $P < 0.0001$; CD8+perforin+, $P < 0.001$; CD8+granzyme B+, $P < 0.001$) and STING response (CD8+STING+, $P < 0.000$; CD8+TBK+, $P < 0.001$). The effector activity and STING were highly elevated in CD8 T cells when co-cultured with olaparib-treated ID8 p53-/-, BRCA2-/- compared to ID8 p53-/-, BRCA1-/- and wild-type ID8 cells; this effect was further enhanced by the addition of metformin. Metabolic phenotyping revealed that CD8 T cells treated with olaparib and metformin exhibited an increase in glycolysis linked with a greater STING response. Similar results were replicated by CPI-613, another mitochondrial inhibitor. Conclusions: Olaparib activates cGAS/STING differently in ovarian cancer cells with BRCA1 and BRCA2 mutations. Mitochondrial inhibition promotes DNA damage and STING pathway activation induced by olaparib. Overall, the combination of metabolic modulators with PARPi may offer a possible therapeutic strategy for boosting the immunomodulatory effect of PARPi.

Orthopedics/Bone and Joint Center
Jurayj A, **Castle J**, **Kasto J**, **Gaudiani M**, **Nerys-Figueroa J**, **Mahylis J**, and **Muh S**. Assessing Minimum Two-Year Follow-Up PROMIS Scores After Total Shoulder Arthroplasty. Is There A Difference Between One- And Two-Year Outcomes? *JSES Int* 2024; 8(6):1334. Full Text

Aim: The goal of this study was to determine if there are significant differences in Patient-Reported Outcomes Measurement Information System (PROMIS) Upper Extremity (UE) function and PROMIS Pain Interference (PI) between one and two years after primary shoulder arthroplasty. Background: Historically, academic journals and the United States Food and Drug Administration required 2-year outcomes for publications and approving implants as safe for total shoulder arthroplasty. However, recent literature has

challenged this dogma by demonstrating that patients often plateau at 1 year for common PRO's, such as VAS and ASES. These results have yet to be proven using the Patient Reported Outcome Information System (PROMIS) scores, however. Methods: We retrospectively identified 199 patients from a single-center, multi-surgeon database who underwent primary anatomic and reverse total shoulder arthroplasty from 2017-2022 and had 1-year and 2-year PROMIS scores. Forty-six of these patients had 1- and 2-year follow-up where clinical outcomes were measured. Patients undergoing revision surgeries, hemiarthroplasty, and those lacking both 1-year and 2-year PROMIS scores were excluded. Statistical analysis was done using non-parametric analysis tests such as the Mann-Whitney U Test. A sub-analysis was done on patients with 1- and 2-year clinical follow-up results. Results: In the entire cohort of patients, there was no significant difference in PROMIS UE between 1- and 2-year post-operative scores ($p = 0.224$). There was statistically significant worsening in PROMIS PI between 1- and 2-years ($p = 0.015$), with an increase from 55.2 to 56.6. However, this does not reach the minimal clinical important difference of 8 points. Patients with diabetes (N = 54) experienced a statistically significant worsening in PROMIS UE and PROMIS PI between 1 and 2 years compared to patients without diabetes ($p = 0.008$). Sub-analysis of patients with 1- and 2-year clinical follow-up visits (N = 46) showed no statistical difference in PROMIS UE and PROMIS PI at 2 years ($p> 0.05$). They also exhibited no significant difference in clinical data such as VAS pain score, range of motion, and strength showed no significant difference between 1- and 2-year data ($p > 0.05$). Conclusion: Patients undergoing total shoulder arthroplasty demonstrate no significant differences in PROMIS-Upper Extremity and Pain Interference between 1-year and 2-year follow-up. These results suggest that patients likely reach their maximal benefit of PROMIS scores at the 1 year follow up timepoint.

Orthopedics/Bone and Joint Center

Kasto J, **Castle J**, **Evans H**, **Nerys-Figueroa J**, **Jurayj A**, **Wines W**, **Mahylis J**, and **Muh S**. A Non-Opioid Multimodal Pain Protocol Achieves Equivalent Pain Control After Total Shoulder Arthroplasty: A Randomized-Controlled Trial. *JSES Int* 2024; 8(6):1369. Full Text

Aim: The aim of this study was to evaluate the efficacy of a postoperative non-opioid multimodal pain protocol compared to an opioid protocol in terms of patient opioid utilization, postoperative pain control, and adverse effects for patients who underwent shoulder arthroplasty. Background: Orthopaedic surgeons are among the highest prescribers of opioid medications. Significant effort has been made to curtail the number of opioids prescribed through improved awareness of opioid stewardship and the development of multimodal pain management protocols. However, there remains a paucity of prospective data demonstrating the efficacy of a non-opioid protocol after total shoulder arthroplasty. Methods: We performed a prospective, randomized controlled trial including patients undergoing anatomic or reverse total shoulder arthroplasty. Patients were excluded if they underwent revision surgery, fracture, or received opioids within 3 months of surgery. All patients received standardized preoperative analgesic medications, general anesthesia, and an intraoperative periarticular injection without a regional block. Patients were randomly assigned to a postoperative non-opioid multimodal pain protocol or an opioid protocol containing 28 tablets of 5mg oxycodone in addition to the multimodal regimen. Patients completed visual analog scale (VAS) pain and Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference (PI) surveys, and were queried for opioid usage and recorded adverse effects of medications for 10 days postoperatively. An intention-to-treat analysis was performed. Results: A total of 74 patients were enrolled and included in the analysis with 37 in each cohort. There were no significant differences in VAS pain (2.1 ± 1.9 multimodal vs. 2.5 ± 1.8 opioid; $P > 0.05$) or PROMIS-PI scores (60.4 ± 7.7 multimodal vs. 60.4 opioid ± 6.7; $P > 0.05$) between treatment groups at 10-days postoperatively. The morphine milligram equivalents (MME) consumed between discharge and 10 days postoperatively for the opioid group was 32.9 ± 49.1 compared to 2.4 ± 6.9 for the non-opioid group ($P < 0.001$). The most common medication side effects for both groups were constipation (52.9% [18/34] multimodal vs. 72.2% [26/36] opioid) and drowsiness although there were no significant differences in the duration of side effects or the number of days without any side effects ($P > 0.05$) between treatment groups. Age, sex, race, and body mass index were all similar between both treatment groups. Conclusion: A non-opioid multimodal pain protocol is safe and achieves similar pain control with significantly reduced MMEs consumed after shoulder arthroplasty.

Orthopedics/Bone and Joint Center
Kasto J, **Castle J**, **Nerys-Figueroa J**, **Pratt B**, **Frei A**, **Bolton M**, **Jurayj A**, **Mahylis J**, **Moutzouros V**, and **Muh S**. The Effects Of Social Determinants Of Health Among Patients Undergoing Shoulder Stabilization Surgery. *JSES Int* 2024; 8(6):1368. Full Text

Aim: The purpose of this study was to investigate the impact of the social determinants of health (SDOH) on the number of shoulder dislocation events before patients underwent surgical stabilization. Background: SODH is comprised of a patient's environmental conditions including social and economic factors which influence access to healthcare and resources. Growing evidence in orthopaedic surgery has revealed that SDOH factors lead to differential access to care and ultimately health disparities after surgery. Previous literature has demonstrated that the number of previous dislocations before shoulder stabilization surgery increases the risk of recurrent instability after the surgical procedure. Methods: A retrospective review of patients who underwent shoulder stabilization surgery at a single center between 1/1/2018 to 5/1/2023 were identified. Patient demographic, characteristic, and social determinant data were collected using the electronic medical record from a single metropolitan health system. Area of deprivation index (ADI) data were collected using online mapping data based on patient zip codes. The number of dislocation events and the date of the first dislocation were recorded. Operative variables collected included date of surgery and the procedure performed to determine the time from dislocation to clinical presentation and from clinical presentation to shoulder stabilization surgery. Patients were stratified in ADI quartiles (Q1=least deprived to Q4=most deprived) and descriptive characteristics were summarized. Results: A total of 445 patients were who had at least one shoulder dislocation and underwent shoulder stabilization surgery were included. Baseline patient characteristics varied among the ADI quartiles with average age at surgery (in years; Q1=20.5, Q2=24.6, Q3=25.0, Q4=26.4, p<0.01), average body mass index (in kg/m2; Q1=26.2, Q2=26.1, Q3=26.9, Q4=28.2, p<0.01), average weeks from first shoulder dislocation to clinical presentation (Q1=43.4 ± 92.1, Q2= 100.0 ± 196.0, Q3= 87.5 ± 133.4, Q4= 107.5 ± 168.4, p<0.03), and the occurrence of having one shoulder instability event versus multiple events before undergoing stabilization surgery (multiple instability events, Q1=35 [62.5%], Q2=72 [56.7%], Q3=77 [65.8%], Q4=108 [74.5%]; p=0.02). Patient sex and time from clinical presentation to stabilization surgery were not significant between ADI quartiles. Non-White patients were overrepresented in the most-deprived quartile (Q4=99, [68.3%]) compared to the least-deprived quartile (Q1=17 [30.4%]; p<0.01). Conclusion: This study demonstrated that marginalized groups suffered more shoulder dislocation events before undergoing shoulder stabilization surgery and presented to an orthopaedic surgeon later than their less-deprived counterparts. Upon presentation to an orthopaedic surgeon, time from presentation to surgery was not different emphasizing the importance of health care accessibility.

Otolaryngology – Head and Neck Surgery
Bachler J, **Wang A**, **Poisson L**, **Adjei Boakye E**, **Tam S**, **Gadgeel S**, **Movsas B**, and **Potugari B**. EP.17B.03 Impact of Social Economic Status on Patient Reported Outcomes (PROs) In Non-Small Cell Lung Cancer (NSCLC). *J Thorac Oncol* 2024; 19(10):S716-S716. Full Text

Henry Ford Health, Detroit/MI/USA

Otolaryngology – Head and Neck Surgery
Czarnecki E, **Bhatnagar AR**, **Mattour A**, **Chang S**, **Kwon D**, **Ulreich C**, **Movsas B**, and **Siddiqui F**. The Impact of an Outpatient Urgent Care Clinic in Patients Treated for Head and Neck Cancer. *Int J Radiat Oncol Biol Phys* 2024; 120(2):S149-S149. Full Text

Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI
Henry Ford Health System, Detroit, MI
Department of Otolaryngology, Henry Ford Cancer Institute, Detroit, MI
Department of Surgical Oncology, Henry Ford Cancer Institute, Detroit, MI
Department of Radiation Oncology, Henry Ford Health, Detroit, MI

Otolaryngology – Head and Neck Surgery
Devpura S, **Ghanem AI**, **Gilbert M**, **AlKhatib SAR**, **Bagher-Ebadian H**, **Tam S**, **Wu V**, **Thind K**, and **Siddiqui F**. HPV-DNA Titers and Tumor Volume Correlation in Human Papillomavirus Related Oropharyngeal Squamous Cell Carcinoma. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e747-e747. Full Text

Department of Radiation Oncology, Henry Ford Health, Detroit, MI
Alexandria Clinical Oncology Department, Alexandria University, Alexandria, Egypt
Department of Otolaryngology, Henry Ford Health, Detroit, MI
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI

Otolaryngology – Head and Neck Surgery
Dunn M, Fridman I, Kinlaw AC, **Neslund-Dudas C**, **Tam S**, and Elston Lafata J. Identifying barriers to being offered and accepting a telehealth visit for cancer care: Unpacking the multi-levels of documented racial disparities in telehealth use. *J Clin Oncol* 2024; 20(10_suppl):382-382. Full Text

The University of North Carolina Gillings School of Global Public Health, Chapel Hill, NC
Lineberger Comprehensive Cancer Center, The University of North Carolina at Chapel Hill, Chapel Hill, NC
Division of Pharmaceutical Outcomes and Policy, The University of North Carolina Eshelman School of Pharmacy, Chapel Hill, NC
Henry Ford Health, Detroit, MI

Otolaryngology – Head and Neck Surgery
Elston Lafata J, Fridman I, Kinlaw AC, Jordan LCJ, **Tam S**, Smith AB, Wood WA, Stein JN, Dunn M, and **Neslund-Dudas C**. The association of oncology telehealth visits with acute care events and follow-up appointments. *JCO Oncol Pract* 2024; 20(10_suppl):384-384. Full Text

The University of North Carolina at Chapel Hill, Chapel Hill, NC
Lineberger Comprehensive Cancer Center, The University of North Carolina at Chapel Hill, Chapel Hill, NC
Henry Ford Health, Detroit, MI
UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC
The University of North Carolina Gillings School of Global Public Health, Chapel Hill, NC

Pathology and Laboratory Medicine
Cook B, **Jaehne AK**, Naiman M, **Wilson I**, **Veryser D**, **Kelly W**, **Ghosh S**, and **Rivers E**. Value Of Monocyte Distribution Width In Bacteremia Assessment In Emergency Department Patients. *Clin Chem* 2024; 70:1. Full Text

[Cook, B.; Jaehne, A. K.; Wilson, I.; Veryser, D.; Kelly, W.; Ghosh, S.; Rivers, E.] Henry Ford Hosp, Detroit, MI USA. [Naiman, M.] Beckman Coulter, Brea, CA USA.

Pathology and Laboratory Medicine
Cook B, **Jones S**, and **Ellacott T**. Can You Believe Your Troponin? Using Laboratory Automation and Programmed Rules to Reduce Non-Repeatable False Positive Troponin Results. *Clin Chem* 2024; 70(Supplement_1):I6-I6. Full Text

[Cook, B.; Jones, S.; Ellacott, T.] Henry Ford Hosp, Detroit, MI USA.

Public Health Sciences
Bachler J, **Wang A**, **Poisson L**, **Adjei Boakye E**, **Tam S**, **Gadgeel S**, **Movsas B**, and **Potugari B**. EP.17B.03 Impact of Social Economic Status on Patient Reported Outcomes (PROs) In Non-Small Cell Lung Cancer (NSCLC). *J Thorac Oncol* 2024; 19(10):S716-S716. Full Text

Henry Ford Health, Detroit/MI/USA

Public Health Sciences
Cook B, **Jaehne AK**, Naiman M, **Wilson I**, **Veryser D**, **Kelly W**, **Ghosh S**, and **Rivers E**. Value Of Monocyte Distribution Width In Bacteremia Assessment In Emergency Department Patients. *Clin Chem* 2024; 70:1. Full Text

[Cook, B.; Jaehne, A. K.; Wilson, I.; Veryser, D.; Kelly, W.; Ghosh, S.; Rivers, E.] Henry Ford Hosp, Detroit, MI USA. [Naiman, M.] Beckman Coulter, Brea, CA USA.

Public Health Sciences
Dunn M, Fridman I, Kinlaw AC, **Neslund-Dudas C**, **Tam S**, and Elston Lafata J. Identifying barriers to being offered and accepting a telehealth visit for cancer care: Unpacking the multi-levels of documented racial disparities in telehealth use. *J Clin Oncol* 2024; 20(10_suppl):382-382. Full Text

The University of North Carolina Gillings School of Global Public Health, Chapel Hill, NC
Lineberger Comprehensive Cancer Center, The University of North Carolina at Chapel Hill, Chapel Hill, NC
Division of Pharmaceutical Outcomes and Policy, The University of North Carolina Eshelman School of Pharmacy, Chapel Hill, NC
Henry Ford Health, Detroit, MI

Public Health Sciences
Elston Lafata J, Fridman I, Kinlaw AC, Jordan LCJ, **Tam S**, Smith AB, Wood WA, Stein JN, Dunn M, and **Neslund-Dudas C**. The association of oncology telehealth visits with acute care events and follow-up appointments. *JCO Oncology Practice* 2024; 20(10_suppl):384-384. Full Text

The University of North Carolina at Chapel Hill, Chapel Hill, NC
Lineberger Comprehensive Cancer Center, The University of North Carolina at Chapel Hill, Chapel Hill, NC
Henry Ford Health, Detroit, MI
UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC
The University of North Carolina Gillings School of Global Public Health, Chapel Hill, NC

Public Health Sciences
Ghanem AI, **Aref I**, **Lin CH**, **Khalil-Moawad R**, **Elshaikh M**, and **Elshaikh MA**. The Role of Adjuvant Radiotherapy and Chemotherapy for Surgically Staged Non-Myoinvasive Uterine Serous Carcinoma with Negative Peritoneal Washings. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e686-e686. Full Text

Department of Radiation Oncology, Henry Ford Health, Detroit, MI
Alexandria Clinical Oncology Department, Alexandria University, Alexandria, Egypt
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI
Department of Public Health Sciences, Henry Ford Health, Detroit, MI
Department of Radiation Oncology, Henry Ford Health-Cancer, Detroit, MI

Public Health Sciences
Godbole MM, **Abu Rous F**, **Ghosh S**, **Chitale D**, and **Gadgeel S**. EP.13E.04 Racial Disparities in Genomic Subtypes of Small Cell Lung Cancer Patients. *J Thorac Oncol* 2024; 19(10):S682. Full Text

Introduction: Recent studies have identified 4 distinct subtypes of small cell lung cancer (SCLC) defined by the expression of several transcription factors. Immunohistochemistry (IHC) based analysis can help define these genomic subtypes. Previous analyses included very few samples from Black patients with SCLC. We present the initial results of IHC expression of relevant transcription factors in tumor samples from Black and White SCLC patients. Methods: SCLC patients diagnosed between January 2018 and January 2023 at Henry Ford Health were included. Demographics, including self-defined race, clinical characteristics and therapeutic details were retrieved from electronic medical record. A tissue microarray (TMA) was constructed using standard published protocols (1.0 mm cores in triplicate). The constructed

TMA and an additional subset of whole sections were used for IHC staining for ASCL1, NEUROD1, POU2F3 and YAP1. IHC scoring was performed using H-score (score ≥10 was considered positive). Chi-square statistics and independent t-test was used for statistical analysis in the SPSS 28 software. Results: Of 258 patients with SCLC, adequate tissue for IHC scoring of all transcriptional factors was obtained for 58 patients (32 on TMA; 26 on whole sections). Of these, 28 were male and 30 female, mean age was 68 years (range: 52-86). 98% of patients were current or former smokers. Nine patients were Black and 49 were White. No statistical differences were observed for demographics, stage at diagnosis and presence of brain metastases between Black and White patients. YAP1 expression was more common in tumors of Black patients compared to tumors of White patients (33% vs 12%, p=0.136), while the expression of POU2F3 (0 vs 13%, p=0.575) and NEUROD1 (22% vs 45%, p=0.282) were more common in White patients. Positivity for more than one marker was noted in 22% of Black vs 8% of White patients (p=0.231). POU2F3 negative patients had significantly better overall survival than positive patients (p=0.034). Other markers did not show a statistically significant difference in survival. Survival analysis stratified by race was not conducted due to limited sample size. Conclusions: The initial results of our study show that the prevalence of genomic subsets of SCLC defined by IHC expression of relevant transcription factors differs between self-defined Black and White patients. We are evaluating more samples to confirm our initial results. If these differences persist with further analysis, this data could suggest differences in SCLC biology among different racial groups and may have therapeutic implications. [Formula presented] Keywords: Small cell lung cancer, Genomic subtypes, IHC

Public Health Sciences

Goorman S, **Zaman I**, **Schultz L**, **Memon A**, and **Ho E**. Obturator Neuropathy: A Retrospective Review of 36 Patients (P8-11.008). *Neurology* 2024; 102(17_supplement_1). Full Text

S. Goorman, Wayne State University, Henry Ford Hospital - Detroit, MI, United States

Objective: The primary objective of this research study is to gain understanding of electrophysiological findings and value of repeat EMG/NCS for prognostication in patients with obturator neuropathy. Background: Obturator neuropathy presents as an uncommon cause of lower extremity weakness with other symptoms including medial thigh numbness, weakness of thigh adduction, and lower extremity pain. Design/Methods: This single center retrospective study aimed to summarize various clinical features of obturator neuropathy. A total of 36 patients with obturator neuropathies diagnosed over a 20-year period, August 2002 to July 2022 were evaluated. Demographic, clinical, and electrographic data were collected, and descriptive statistics were used to analyze the variables of interest. The variables of interest included etiology, symptoms, physical exam signs, time to diagnosis from symptom onset, treatment, age, race, sex, insurance, prognosis, and electromyography (EMG) findings. Results: Of the 36 patients evaluated, surgery related trauma (n≤21; 58%) was the most common etiology, and lower extremity pain (n≤30; 86%) was the most common symptom. Based on diagnoses made through EMG, 23 patients (79%) had pure obturator neuropathy. Treatments led to improvement or complete resolution in 18 (50%) patients while 11 (31%) had no relief. No significant difference in time to diagnosis was observed based on sex, race, or insurance type Conclusions:Obturator neuropathies are commonly associated with lower extremity weakness leading to diffi culties in ambulation.Surgical trauma was the most common cause in our patient group, followed by cancer related causes. Electrodiagnosticfi ndings, mainly EMG studies, aid in the defi nitive diagnosis. The lack of statistically signifi cant differences between race,sex, or insurance in our patient group suggests an equitable process of evaluation of patient from their initial presentationwith a provider to a defi nitive diagnosis. The lack of symptomatic improvement in 31% of patients in our groupdemonstrates the continued need for advancements in nerve repair and regrowth.

Public Health Sciences

Gui H, Huang Y, Tao S, **Meng Z**, Liu Y, **Levin A**, **Ahmedani B**, and Wang Q. 15. Genetic Relationships and Biological Pathways Underlying Suicidality and Comorbid Mental Disorders: A Comprehensive Cross-Phenotype Analysis. *Eur Neuropsychopharmacol* 2024; 87:55. Full Text

Background: The co-occurrence of mental disorders and suicidality are frequently seen in epidemiology. One explanation lies in shared genetic liabilities, hence we aimed to investigate the phenotypic and genetic associations between multiple mental disorders and different levels of suicidality. Methods: Using

UK Biobank (UKB) European individual data, we first evaluated the phenotypic and polygenic relationships between 12 mental disorders and gradient scales of suicidality (spanning suicidal ideation, suicide attempts, and suicidal death). Second, we used existing genome-wide association study (GWAS) summary statistics to estimate genetic correlations and to identify pleiotropic genes using a combination of statistical genetics tools. Summary statistics were accessed from: 1) the Psychiatric Genomics Consortium (major depressive disorder [MDD], bipolar disorder [BD], anxiety disorders [ANX], obsessive-compulsive disorder [OCD], anorexia nervosa [AN], autism spectrum disorder [ASD], attention deficit hyperactivity disorder [ADHD], schizophrenia [SCZ], cannabis use disorder [CUD], and post-traumatic stress disorder [PTSD]), 2) the Million Veterans Program (alcohol use disorder [AUD] and opioid use disorder [OUD]), and 3) their joint analysis (suicidality). Third, using shared genetic liabilities as instrument, we evaluated evidence for causal relationship between mental disorders and suicidality by structural equation models and Mendelian randomizations. Last, we accessed the All of Us (AoU) diverse cohort data for replication in non-European populations. Results: For UKB, 150,861 eligible individuals were retained after standard GWAS quality control. Eight out 12 mental disorders (MDD, BD, ANX, AUD, OCD, AN, ASD and ADHD) showed both significant phenotypic and polygenic correlations with gradient suicidality (false discovery rate < 0.05). Among them, the impact of MDD and BD on suicidality were the most obvious (for MDD: OR=5.78 and 1.26 for phenotypic and polygenic level; for BD: OR=12.98 and 1.14 for phenotypic and polygenic level). Using GWAS summary statistics, we also observed positive global genetic correlations between those 8 mental disorders and suicidality (rg ranging from 0·25 to 0·68, p < 0.001). Across pairs of suicidality and mental disorders, we identified 23 functional genes (including novel ones like BPTF, NOL11 and CACNG5) shared by five or more pairs. These genes were significantly enriched in two Gene Ontology sets: developmental process and regulation of biological process. We also identified unique genes within each pair which were enriched in different pathways (e.g., glutamatergic synapse for suicidality-MDD, negative regulation of biological process for suicidality-BD, and actin cytoskeleton for suicidality-AUD). Causal models indicated potential causality from genetic diatheses of MDD, BD, AUD, ADHD, and ASD to risk of suicidality. Multiple cross-phenotype associations with suicidality were also replicated in AoU African and Asian populations (e.g., p < 0.05 for MDD and BD polygenic associations). Discussion: This study underscores the urgent need to address the shared and distinct genetic architecture of suicidality and related mental conditions. The combination of longitudinal population-level biobanks and disease-ascertained GWAS are warranted to enhance our understanding of their relationships. Our findings will provide insights into future suicide prevention and management among individuals with and without mental disorders. Disclosure: Nothing to disclose.

Public Health Sciences

Ho E, **Goorman S**, **Zaman I**, **Memon A**, and **Schultz L**. Laryngeal Neuropathy: A Retrospective Review of 52 Patients (P8-11.009). *Neurology* 2024; 102(17_supplement_1). Full Text

E. Ho, Henry Ford Hospital, United States

Objective: The primary objective of this research study is to gain understanding of electrophysiological findings and value of repeat EMG/NCS for prognostication in patients with laryngeal neuropathies. Background: Laryngeal neuropathy presents as an infrequently diagnosed cause of vocal dysfunction with symptoms including cough, voice changes, difficulty swallowing, and throat pain. Design/Methods: This single center retrospective study aimed to summarize various clinical features of laryngeal neuropathy A total of 52 patients with laryngeal and vagal neuropathies diagnosed over a 22-year period, 2000 to 2022 were evaluated. Demographic, clinical and electrodiagnostic data were collected, and descriptive statistics were used to analyze the variables of interest. The variables of interest included etiology, symptoms, time to diagnosis from symptom onset, treatment, race, sex, prognosis, and electromyography (EMG) findings. Results: Of the 52 patients evaluated, surgery related trauma (n≤23; 44%) was the most common etiology, and speech difficulty (n≤49; 94%) was the most common symptom. Based on diagnoses made through EMG, 25 patients (48%) had vagal neuropathy, 8 (15%) had recurrent vagal neuropathy, 13 (25%) had other laryngeal conditions. Treatments including surgical repair, speech therapy, medical therapy, and several others led to improvement or complete resolution in 23 (44%) patients. No significant difference in time to diagnosis was observed based on sex or race. Patients with post-surgical etiology had a significantly shorter time to diagnosis (p≤.015). Conclusions:Laryngeal neuropathies are commonly associated with vocal cord dysfunction leading to signifi cant speech

impairment.Surgical trauma was the most common cause in our patient group, followed by idiopathic causes. Electrodiagnosticfi ndings, including EMG studies, aid in the defi nitive diagnosis. The shorter time to diagnosis in patients who develop post-surgical manifestation may be due to in-patient post-surgical status enabling faster evaluation.

Radiation Oncology
AlKhatib SAR, Bjelac OC, Akperov K, Hande V, and Abdel-Wahab M. Radiotherapy Resources in Central Asia: An International Atomic Energy Agency Update. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e2-e2. Full Text

Henry Ford Health, Detroit, MI
IAEA, Vienna, Austria
National Centre of Oncology, Baku, Azerbaijan
Nagasaki University, Japan, Japan
International Atomic Energy Agency, Vienna, Austria

Radiation Oncology
Bachler J, **Wang A**, **Poisson L**, **Adjei Boakye E**, **Tam S**, **Gadgeel S**, **Movsas B**, and **Potugari B**. EP.17B.03 Impact of Social Economic Status on Patient Reported Outcomes (PROs) In Non-Small Cell Lung Cancer (NSCLC). *J Thorac Oncol* 2024; 19(10):S716-S716. Full Text

Henry Ford Health, Detroit/MI/USA

Radiation Oncology
Bagher-Ebadian H, **Brown SL**, Acharya P, **Ewing JR**, Chetty IJ, **Movsas B**, and **Thind K**. A Probabilistic Unsupervised Model to Assess Pharmacokinetic Changes in Cerebral Tumors before and after Radiation Therapy. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e98-e99. Full Text

Department of Radiation Oncology, Henry Ford Health, Detroit, MI
Department of Radiology, Michigan State University, East Lansing, MI
Oakland University, Rochester, MI
Department of Neurology, Henry Ford Health, Detroit, MI
Department of Radiation Oncology, Cedars-Sinai Medical Center, Los Angeles, CA

Radiation Oncology
Bauman J, Harris J, Uppaluri R, Yao M, Chen J, Jordan R, Geiger JL, Jujjavarapu S, Chakravati A, Phan M, **Siddiqui F**, Kulkarni A, Upadhyay P, Vujanovic L, Isett B, Sica GL, Reeder C, Le QT, and Ferris RL. Cellular Immune and Genomic Biomarkers in NRG-HN003, a Phase I Study Adding Pembrolizumab to Adjuvant Cisplatin and Radiation Therapy (CRT) in Pathologically High-Risk Head and Neck Cancer (HNSCC). *Int J Radiat Oncol Biol Phys* 2024; 120(2):S129-S130. Full Text

George Washington University Cancer Center, Washington, DC
American College of Radiology, Philadelphia, PA
Department of Surgery/Otolaryngology, Brigham & Women's Hospital and Dana-Farber Cancer Institute, Boston, MA
University Hospitals Cleveland Medical Center, Cleveland, OH
UCSF, San Francisco, CA
University of California San Francisco, San Francisco, CA
Department of Hematology and Medical Oncology, Taussig Cancer Center, Cleveland Clinic, Cleveland, OH
OSF Healthcare, Peoria, IL
The Ohio State University, Columbus, OH
University of Oklahoma Health Sciences Center, Oklahoma City, OK
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI
University of Pittsburgh, Pittsburgh, PA
Department of Pathology, University of Pittsburgh, Pittsburgh, PA

UPMC Hillman Cancer Center, Pittsburgh, PA
Stanford University, Stanford, CA
University of Pittsburgh Medical Center, Pittsburgh, PA

Radiation Oncology
Chuong MD, **Parikh PJ**, Low D, **Kim J**, Mittauer KE, Bassetti MF, Glide-Hurst C, Raldow A, Yang Y, Portelance L, Zaki B, Kim H, Mancias JD, Ng J, Pfeffer RM, Mueller A, Kelly P, Boldrini L, Fuss M, and Lee P. Quality of Life after Ablative 5-Fraction Radiation Therapy from the Phase 2 SMART Pancreas Trial. *Int J Radiat Oncol Biol Phys* 2024; 120(2):S174-S175. Full Text

Miami Cancer Institute, Miami, FL
Henry Ford Health - Cancer, Detroit, MI
Department of Radiation Oncology, University of California, Los Angeles, Los Angeles, CA
Department of Radiation Oncology, Miami Cancer Institute, Baptist Health South Florida, Miami, FL
Department of Human Oncology, University of Wisconsin Hospitals and Clinics, Madison, WI
Department of Radiation Oncology, University of California, Los Angeles, CA
Department of Radiation Oncology, University of Miami, Miami, FL
Dartmouth Cancer Center, Dartmouth-Hitchcock Medical Center, Lebanon, NH
Department of Radiation Oncology, Washington University School of Medicine, Saint Louis, MO
Department of Radiation Oncology, Brigham and Women's Hospital/Dana-Farber Cancer Institute, Boston, MA
Weill Cornell Medicine Sandra and Edward Meyer Cancer Center, New York, NY
Assuta Medical Center, Tel Aviv, Israel
Department of Radiation Oncology, Sidney Kimmel Medical College & Cancer Center at Thomas Jefferson University, Philadelpha, PA
Department of Radiation Oncology, Orlando Health Cancer Institute, Orlando, FL
Department of Radiology, Radiation Oncology and Hematology, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome, Italy
ViewRay, Demver, CO
Department of Radiation Oncology, Lennar Foundation Comprehensive Cancer Center, City of Hope National Medical Center, Irvine, CA

Radiation Oncology
Cousins MM, Dykstra MP, Griffith K, Mietzel M, Kendrick D, Trumpower E, **Dusseau D**, Dominello MM, Mierzwa ML, Covington E, Pierce LJ, and Hayman JA. Relationship between Cannabis Use and Opioid Use in Patients with Cancer Metastatic to Bone in a Large Multicenter Cohort from a State with Legalized Adult Non-Medical Cannabis. *Int J Radiat Oncol Biol Phys* 2024; 120(2):S28-S28. Full Text

Department of Radiation Oncology, University of Michigan, Ann Arbor, MI
Department of Radiation Oncology, Self Regional Healthcare, Greenwood, SC
Michigan Radiation Oncology Quality Consortium Coordinating Center, Ann Arbor, MI
Department of Biostatistics, University of Michigan, Ann Arbor, MI
Department of Radiation Oncology, Henry Ford Health System, Jackson, MI
Department of Radiation Oncology, Karmanos Cancer Center, Detroit, MI

Radiation Oncology
Czarnecki E, **Bhatnagar AR**, **Mattour A**, **Chang S**, **Kwon D**, **Ulreich C**, **Movsas B**, and **Siddiqui F**. The Impact of an Outpatient Urgent Care Clinic in Patients Treated for Head and Neck Cancer. *Int J Radiat Oncol Biol Phys* 2024; 120(2):S149-S149. Full Text

Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI
Henry Ford Health System, Detroit, MI
Department of Otolaryngology, Henry Ford Cancer Institute, Detroit, MI
Department of Surgical Oncology, Henry Ford Cancer Institute, Detroit, MI
Department of Radiation Oncology, Henry Ford Health, Detroit, MI

Radiation Oncology
Devpura S, **Ghanem AI**, **Gilbert M**, **AlKhatib SAR**, **Bagher-Ebadian H**, **Tam S**, **Wu V**, **Thind K**, and **Siddiqui F**. HPV-DNA Titers and Tumor Volume Correlation in Human Papillomavirus Related Oropharyngeal Squamous Cell Carcinoma. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e747-e747. Full Text

Department of Radiation Oncology, Henry Ford Health, Detroit, MI
Alexandria Clinical Oncology Department, Alexandria University, Alexandria, Egypt
Department of Otolaryngology, Henry Ford Health, Detroit, MI
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI

Radiation Oncology
Ghanem AI, **Aref I**, **Lin CH**, **Khalil-Moawad R**, **Elshaikh M**, and **Elshaikh MA**. The Role of Adjuvant Radiotherapy and Chemotherapy for Surgically Staged Non-Myoinvasive Uterine Serous Carcinoma with Negative Peritoneal Washings. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e686-e686. Full Text

Department of Radiation Oncology, Henry Ford Health, Detroit, MI
Alexandria Clinical Oncology Department, Alexandria University, Alexandria, Egypt
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI
Department of Public Health Sciences, Henry Ford Health, Detroit, MI
Department of Radiation Oncology, Henry Ford Health-Cancer, Detroit, MI

Radiation Oncology
Gilbert M, **Crutchfield A**, **Luo B**, **Thind K**, **Ghanem AI**, and **Siddiqui F**. Using a Large Language Model (LLM) for Automated Extraction of Discrete Elements from Clinical Notes for Creation of Cancer Databases. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e625-e625. Full Text

Department of Radiation Oncology, Henry Ford Health, Detroit, MI
Alexandria Clinical Oncology Department, Alexandria University, Alexandria, Egypt
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI

Radiation Oncology
Hall R, **Czarnecki E**, **Bhatnagar AR**, **Snyder K**, **Siddiqui F**, and **Thind K**. Treatment Planning Feasibility Study for Lattice SBRT of Locally Advanced Head and Neck Cancer. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e133-e134. Full Text

Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI
Department of Radiation Oncology, Henry Ford Health, Detroit, MI

Radiation Oncology
Huang Y, **Zhao B**, **Noora BS**, **Gallagher I**, **Doemer AJ**, **Thind K**, and **Feldman AM**. Intrafraction Motion Management of CBCT Guided Online Stereotactic Adaptive Prostate Cancer Radiotherapy. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e138-e139. Full Text

Department of Radiation Oncology, Henry Ford Health, Detroit, MI

Radiation Oncology
Jee Y, **Aref I**, **Wang A**, **Huang-Vredevoogd J**, **Hijaz M**, and **Elshaikh MA**. Outcomes and Patterns of Failure for Women with FIGO Stage I-II Uterine Non-Endometroid Carcinoma after Surgical Staging, Adjuvant Chemotherapy and Vaginal Cuff Brachytherapy. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e692-e692. Full Text

Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI
Henry Ford Health, Detroit, MI
Department of Gynecologic Oncology, Henry Ford Cancer Institute, Detroit, MI

Radiation Oncology

Khanmohammadi R, **Ghanem AI**, **Verdecchia K**, **Hall R**, **Elshaikh MA**, **Movsas B**, **Bagher-Ebadian H**, **Chetty IJ**, Ghassemi MM, and **Thind K**. A Novel Localized Student-Teacher LLM for Enhanced Toxicity Extraction in Radiation Oncology. *Int J Radiat Oncol Biol Phys* 2024; 120(2):e632-e633. Full Text

Department of Computer Science and Engineering, Michigan State University, East Lansing, MI
Department of Radiation Oncology, Henry Ford Health, Detroit, MI
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI
Department of Radiation Oncology, Cedars-Sinai Medical Center, Los Angeles, CA

Radiation Oncology

Truong MT, Torres-Saavedra P, Gillison M, Caudell JJ, Gibson MK, Waldron J, Xia P, Chung CH, Kong CS, Yao M, Jordan R, Subramaniam RM, Lewin JS, Geiger JL, Kang H, Blakaj DM, Mell LK, Harris J, **Movsas B**, and Yom SS. Quality of Life (QOL) of Patients with Human Papillomavirus (HPV)-Associated Oropharyngeal Squamous Cell Carcinoma (OPSCC) in NRG-HN002. *Int J Radiat Oncol Biol Phys* 2024; 120(2):S121-S122. Full Text

Department of Radiation Oncology, Boston Medical Center, Boston, MA
The American College of Radiology, Philadelphia, PA
The University of Texas MD Anderson Cancer Center, Houston, TX
H. Lee Moffitt Cancer Center and Research Institute, Department of Radiation Oncology, Tampa, FL
Vanderbilt University Medical Center and Vanderbilt Ingram Cancer Center, Nashville, TN
Department of Radiation Oncology, Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada
Department of Radiation Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH
H. Lee Moffitt Cancer Center, Tampa, FL
Department of Pathology, Stanford University, Stanford, CA
University Hospitals Cleveland Medical Center, Cleveland, OH
University of California San Francisco, San Francisco, CA
University of Notre Dame, Sydney, Australia
MD Anderson Cancer Center, Houston, TX
Department of Hematology and Medical Oncology, Taussig Cancer Center, Cleveland Clinic, Cleveland, OH
University of California, San Francisco, CA
Department of Radiation Oncology, James Cancer Hospital, The Ohio State University, Columbus, OH
University of California San Diego, La Jolla, CA
American College of Radiology, Philadelphia, PA
Department of Radiation Oncology, Henry Ford Health, Detroit, MI

Radiation Oncology

Tsakiridis T, Hu C, Skinner H, Santana-Davila R, Lu B, Erasmus JJ, **Doemer AJ**, Videtic GM, Wang F, Hesselle M, Lee RY, Werner-Wasik M, Schaner PE, McCormack SE, Esparaz BT, McGarry RC, Brownstein J, Struve T, Lyness JA, and Bradley JD. MA01.07 Long-Term Analysis of NRG-LU001, Randomized Phase II Trial of Concurrent Chemoradiotherapy (ccrt) -/+ Metformin in Locally Advanced NSCLC. *J Thorac Oncol* 2024; 19(10):S53-S54. Full Text

McMaster University, Hamilton, Ontario, Canada, Hamilton/ON/CA
Johns Hopkins, Baltimore/MD/USA
NRG Oncology Statistics and Data Management Center, Philadelphia/PA/USA
UPMC Hillman Cancer Center, Pittsburgh/PA/USA
Seattle Cancer Care Alliance, Seattle/WA/USA
University of Missouri, Columbia/MO/USA
MD Anderson Cancer Center, Houston, Texas, Houston/TX/USA
Henry Ford Hospital, Detroit/MI/USA
Cleveland Clinic, Cleveland/OH/USA
University of Kansas Cancer Center, Oakland Park/KS/USA

Saint Francis Cancer Center, Greenville/SC/USA
The Cancer Center of Hawaii-Liliha, Honolulu/OK/USA
Bodine Cancer Center, Philadelphia/PA/USA
Norris Cotton Cancer Center, Lebanon/NH/USA
Metro Minnesota Community Oncology Research Consortium, Saint Louis Park/MO/USA
Heartland Cancer Research NCORP, Decatur/IL/USA
University Of Kentucky, Lexington/KY/USA
Ohio State University Comprehensive Cancer Center, Columbus/OH/USA
University of Cincinnati, Cincinnati/OH/USA
Perelman Center for Advanced Medicine, University of Pennsylvania, Philadelphia/PA/USA

Radiation Oncology
Yousif A, Pudar J, **Elshaikh M**, **Khalil-Moawad R**, and **Elshaikh M**. First-degree family history of cancer in women with stage I endometrial carcinoma: Prevalence and prognostic impact. *Gynecol Oncol* 2024; 190:S139-S140. Full Text

Objectives: The significance of a family history of malignancy in endometrial cancer patients has been inconsistently reported in the literature. Most cases of uterine cancer are sporadic; however, familial clustering is observed in around 5 % of cases. In our cohort, we examined the first-degree family history of cancer in women with stage I uterine endometrioid carcinoma. Methods: Our study cohort included 1741 patients. All underwent a hysterectomy and oophorectomy, and they were managed with observation or adjuvant radiotherapy alone; 701 (40 %) patients reported family history (FH) of cancer in their first-degree relatives (FDR), and 1030 reported no or unknown FH of cancer in their FDR. Descriptive statistical analysis was performed to characterize our study cohort. Results: Table 1 shows the total number of patients, 1731, among whom 701 (40 %) reported a positive family history compared to 1030 (60 %) who reported a negative family history of cancers. Both groups had similar age and race distribution. Maternal FH of cancer was reported in 50 % of patients and paternal in 34 %. Breast, colon, and endometrial cancers were most frequently reported in mothers and sisters of endometrial cancer patients, respectively. In contrast, lung, prostate, and colon cancers were the top 3 cancers in endometrial cancer patients' fathers. Cancer recurrence was slightly increased in patients with FH of cancer in their FDR (8 % vs 7 %). Conclusions: First-degree family history of cancer is common in patients with stage I endometrial cancer. Genetic counseling for patients with endometrial cancer should be considered in this population. Further research is needed to elucidate its prognostic role in endometrial cancer patients. [Formula presented]

Sleep Medicine
Speak A, **Hijaz M**, **Singh H**, **Udumula M**, **Miller M**, **Munkarah A**, and **Rattan R**. Inhibiting mitochondria potentiates PARPi-triggered, STING-dependent immune response in pre-clinical models of epithelial ovarian cancer. *Gynecol Oncol* 2024; 190:S233-S234. Full Text

Objectives: In ovarian cancer patients with hereditary or somatic BRCA1/2 mutations, PARP inhibitors (PARPi) have altered the treatment landscape. DNA damage caused by PARPi in conjunction with DNA repair errors due to mutations in BRCA1/2 initiates immunologic signaling via the cGAS/STING pathway. Studies have shown that therapy with a STING agonist can boost the efficacy of olaparib in BRCA-mutated ovarian cancer cells. Current research suggests that the activity of almost all immune cells is regulated by their cellular metabolism, especially energy metabolism. We have previously shown that inhibiting mitochondria by metformin augmented the therapeutic efficacy of PARPi in BRCA-intact pre-clinical ovarian cancer models. This study examined whether mitochondrial inhibition could increase STING pathway activation by olaparib in BRCA1/2-mutated and wild-type ovarian cancer cells and mouse models. Methods: ID8 p53+/+, ID8 p53-/-, ID8 p53-/-, BRCA1-/-, and ID8 p53-/-, BRCA2-/- mouse ovarian cancer cells were treated with olaparib (5mm) or metformin (2.5mM) or a combination of both; 2′,3′-Cyclic GAMP was measured by ELISA. DNA damage (gH2AX) was evaluated by flow cytometry. Mitochondrial function was assessed by an XF seahorse analyzer. Treated cells were co-cultured with naïve CD8 T cells and profiled by flow cytometry. All cell lines were used to validate the response in vivo. Results: Olaparib increased γH2AX ($P < 0.001$) in the ID8 p53-/-, BRCA2-/- cells relative to ID8 p53-/-, BRCA1-/- and wild-types, and metformin further augmented this effect ($P < 0.0001$); while the lowest DNA damage

was induced in BRCA and p53 intact ID8 p53+/+ (P < 0.001) cells. Increased DNA damage in ID8 p53-/-, BRCA2-/- cells correlated with elevated STING by olaparib, which was further exacerbated by the addition of metformin (P < 0.0001). When co-cultured with naïve splenic CD8 T cells, all cell lines activated CD8 effector and cytotoxic function (CD8+IFNg+, P < 0.0001; CD8+perforin+, P < 0.001; CD8+granzyme B+, P < 0.001) and STING response (CD8+STING+, P < 0.000; CD8+TBK+, P < 0.001). The effector activity and STING were highly elevated in CD8 T cells when co-cultured with olaparib-treated ID8 p53-/-, BRCA2-/- compared to ID8 p53-/-, BRCA1-/- and wild-type ID8 cells; this effect was further enhanced by the addition of metformin. Metabolic phenotyping revealed that CD8 T cells treated with olaparib and metformin exhibited an increase in glycolysis linked with a greater STING response. Similar results were replicated by CPI-613, another mitochondrial inhibitor. Conclusions: Olaparib activates cGAS/STING differently in ovarian cancer cells with BRCA1 and BRCA2 mutations. Mitochondrial inhibition promotes DNA damage and STING pathway activation induced by olaparib. Overall, the combination of metabolic modulators with PARPi may offer a possible therapeutic strategy for boosting the immunomodulatory effect of PARPi.

Sleep Medicine

Thorpy MJ, **Roth T**, Kushida CA, Morse AM, Harsh J, Ortiz LE, Dubow J, Gudeman J, and Dauvilliers Y. Consistent Efficacy of Once-Nightly Sodium Oxybate Regardless of Patient Demographic and Baseline Disease Characteristics. *Sleep Med* 2024; 115(17):211-211. Full Text

Albert Einstein Coll Med, New York, NY USA
Henry Ford Hlth Syst, Sleep Disorders & Res Ctr, Detroit, MI USA
Stanford Univ, Sch Med, Stanford, CA USA
Janet Weis Childrens Hosp, Geisinger Commonwealth Sch Med, Geisinger Med Ctr, Danville, PA USA
Colorado Sleep Inst, Boulder, CO USA
Johns Hopkins All Childrens Hosp, St Petersburg, FL USA
Avadel Pharmaceut, Chesterfield, MO USA
Univ Montpellier, Sleep Wake Disorders Ctr, Gui de Chauliac Hosp, Dept Neurol,INM,INSERM, Montpellier, France

Objective: Once-nightly sodium oxybate (ON-SXB; FT218; LUMRYZ™) was investigated in patients with narcolepsy in the phase 3 REST-ON trial (NCT02720744). This post-hoc analysis assessed ON-SXB efficacy across participant subgroups. Background: All tested doses of ON-SXB resulted in significant improvements (all P<0.001) for the coprimary endpoints of change from baseline in mean sleep latency on the Maintenance of Wakefulness Test (MWT), Clinical Global Impression-Improvement (CGI-I) rating of much or very much improved, weekly number of cataplexy attacks (NCA), and in the secondary endpoint Epworth Sleepiness Scale (ESS) score. Design/Methods: Participants (≥16 years) with narcolepsy type 1 (NT1) or 2 (NT2) were randomized 1:1 to receive ON-SXB (4.5 g [1 week], 6 g [2 weeks], 7.5 g [5 weeks], and 9 g [5 weeks]) or placebo. Least squares mean differences (LSMD [95% CI]) in change from baseline with ON-SXB vs placebo for MWT, NCA, and ESS, and odds ratios (ORs) for CGI-I, across demographic and disease characteristic subgroups were calculated. Data from the modified intent-to-treat (mITT) population (all randomized participants with ≥1 efficacy measure after receiving the 6.0-g dose) were analyzed. Results: The mITT population included 190 participants (ON-SXB, n=97; placebo, n=93). ON-SXB 9 g significantly improved mean sleep latency on the MWT (minutes; P<0.05) for age, sex, race, BMI, narcolepsy type, and alerting agent use subgroups (LSMD range: 4.0 - 10.0). ORs significantly favored ON-SXB 9 g on CGI-I (P<0.05) for low/high age, white/non-white race, alerting agent use, female sex, high BMI, and NT1 (range: 3.3-7.1). ON-SXB 9 g significantly improved NCA (P<0.05) for all subgroups (LSMD range: -5.5 to -7.6) except non-white and male. All subgroups showed significant improvements on ESS score with ON-SXB 9 g except NT2 (LSMD [95% CI]: -2.72 [-6.09, 0.65]). Conclusions: These findings demonstrate the robust efficacy of once-at-bedtime ON-SXB across participant subgroups. .

Surgery

Allen K, Rogers T, Greenbaum A, Kirker E, McCabe J, Cheema M, Logsdon D, **Alnajjar R**, Paone G, Harrington K, Lederman R, and Chhatriwalla A. TCT-891 Transcarotid Versus Transcaval Access for Transcatheter Aortic Valve Replacement Using a Balloon Expandable Valve: Propensity-Matched Analysis From a Real-World Registry. *J Am Coll Cardiol* 2024; 84(18):B375. Full Text

Background: Transcarotid and transcaval access for transcatheter aortic valve replacement (TAVR) have demonstrated superior outcomes to transaxillary/transthoracic access; however, comparisons of transcarotid vs transcaval alternate access are lacking. Methods: The Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry was queried for patients undergoing transcarotid and transcaval TAVR with the SAPIEN 3 (Edwards Lifesciences) valve platform between November 2018 and September 2023. Procedural, in-hospital, 30-day, and 1-year outcomes, including CMS linkage, were evaluated and then compared using 3:1 propensity score matching. Results: The study included 5,712 patients (transcarotid 5,297; transcaval 415) with a well-matched propensity matched cohort of 1,218 transcarotid and 406 transcaval patients. Overall, this high-risk cohort of patients had a high burden of comorbidities. Transcarotid and transcaval patients had similar mortality at 30 days (4.1% vs 5.5%; P = 0.25) and 1-year (19.4% vs 19.2%; P = 0.87) and similar stroke rates at 30-days (5.6% vs 3.8%; P = 0.15) and 1 year (7.8% vs 5.6%; P = 0.13). Transcarotid access was performed more frequently with general anesthesia (94.9% vs 60.1%; P < 0.0001), admitted to the ICU more often (79.7% vs 66.2%; P = 0.002) and had longer mean ICU times (36.2 h vs 26.7 h; P = 0.03). Procedure time (88.0 vs 119.0 min; P < 0.0001), fluoroscopy time (15.8 vs 36.2 min; P < 0.0001), contrast volume (75.8 mL vs 128.9 mL; P < 0.0001), life-threatening bleeding (1.6% vs 3.9%; P = 0.006) and need for blood transfusion (12.2% vs 20.7%; P < 0.0001) were lower with transcarotid access. Most patients in both groups were discharged home after TAVR (>85%) with a similar median LOS of 2.0 days. Transcarotid access was associated with a lower 30-day rate of new PPM/ICD (7.3% vs 10.9%; P = 0.04) and 30-day readmission rate (11.0% vs 14.9%; P = 0.03). Conclusion: Transcarotid and transcaval access for TAVR with the SAPIEN 3 family valves is associated with similar 30-day and 1-year mortality and stroke. Depending on patient anatomy and Heart Team expertise, both are appropriate and the preferred approaches when TAVR requires nonfemoral access. Categories: STRUCTURAL: Valvular Disease: Aortic.

Surgery

Czarnecki E, **Bhatnagar AR**, **Mattour A**, **Chang S**, **Kwon D**, **Ulreich C**, **Movsas B**, and **Siddiqui F**. The Impact of an Outpatient Urgent Care Clinic in Patients Treated for Head and Neck Cancer. *Int J Radiat Oncol Biol Phys* 2024; 120(2):S149-S149. Full Text

Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI
Henry Ford Health System, Detroit, MI
Department of Otolaryngology, Henry Ford Cancer Institute, Detroit, MI
Department of Surgical Oncology, Henry Ford Cancer Institute, Detroit, MI
Department of Radiation Oncology, Henry Ford Health, Detroit, MI