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HENRY FORD HEALTH

Henry Ford Health Publication List – April 2024

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health personnel. Searches were conducted in PubMed, Embase, Web of Science, CINAHL, and Google Books during the month, and then imported into EndNote for formatting. There are 159 unique citations listed this month, including 115 articles and 44 conference abstracts.

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

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Articles

Conference Abstracts

Articles

Administration
Parke DM, Ogbolu Y, and Rowthorn V. Global learning: A post-COVID-19 approach to advance health equity. *Glob Public Health* 2024; 19(1):2340507. PMID: 38626120. Full Text

Henry Ford Health, Detroit, MI, USA.
Center for Health Equity and Outcomes Research, University of Maryland Baltimore, Baltimore, MD, USA.

The COVID-19 pandemic has accelerated acceptance of learning from other countries, especially for high-income countries to learn from low- and middle-income countries, a practice known as global learning. COVID-19's rapid disease transmission underscored how connected the globe is as well as revealed stark health inequities which facilitated looking outside of one's borders for solutions. The Global Learning for Health Equity (GL4HE) Network, supported by Robert Wood Johnson Foundation, held a 3-part webinar series in December 2021 to understand the current state of global learning and explore how global learning can advance health equity in the post-COVID-19 era. This paper reflects on these cutting-edge discussions about the current state of global learning, drawing upon the highlights, perspectives, and conclusions that emerged from these webinars. The paper also comments on best practices for global learning, including adapting for context, addressing biases, funding considerations, ensuring bidirectional partnerships, community engagement, and adopting a multidisciplinary approach.

Administration
Sikorskii A, **Tam S**, Given B, Given CW, **Adjei Boakye E**, **Zatirka T**, **Nair M**, **Su WK**, **Jogunoori S**, **Watson P**, **Movsas B**, and **Chang S**. Thresholds in PROMIS Scores Anchored to Subsequent Unscheduled Health Service Use Among People Diagnosed With Cancer. *JCO Oncol Pract* 2024; Epub ahead of print. PMID: 38564704. Full Text

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Health Alliance Plan, Henry Ford Health, Detroit, MI.
Division of Hospital Medicine, Henry Ford Health, Detroit, MI.
Radiation Oncology, Henry Ford Cancer, Henry Ford Health, Detroit, MI.
Henry Ford Cancer Patient Reported Outcomes Committee, Henry Ford Cancer Head and Neck Cancer Program, Detroit, MI.

PURPOSE: To establish thresholds in the Patient-Reported Outcomes Measurement Information System (PROMIS) pain interference, physical function, fatigue, and depression scores on the basis of their association with subsequent use of the emergency department (ED) or urgent care by people diagnosed with cancer. METHODS: Retrospective data from 952 people seen at Henry Ford Cancer and insured through the Health Alliance Plan were analyzed using generalized linear mixed-effects models. The log odds of ED or urgent care use during 14 or 30 days after each patient-reported outcome (PRO) assessment were related to PRO scores, while adjusting for comorbidity, sociodemographic, and tumor characteristics. RESULTS: Pain interference and physical function were associated with subsequent ED or urgent care visits, but fatigue and depression were not, and the results for 14- and 30-day visits were similar. Thresholds anchored in the likelihood of these visits differed according to cancer stage. For people with advanced cancer, a pain interference score of 60 or higher (odds ratio [OR] 3.75, [95% CI, 1.53 to 7.87]) and a physical function score lower than 40 (OR 2.94, [95% CI, 1.22 to 7.06]) produced the largest ORs with narrowest CIs for 30-day visits. For people with nonadvanced cancer, the thresholds of

65 for pain interference (OR 2.64, [95% CI, 1.40 to 5.01]) and 35 for physical function (OR 1.87, [95% CI, 1.01 to 3.45]) produced largest ORs with narrowest CIs for 30-day visits. CONCLUSION: These anchor-based thresholds in PROMIS scores can inform clinicians' actions with the goal of preventing ED or urgent care visits.

Allergy and Immunology
Finkel KA, **Jung H**, **Kim H**, and **Coleman DT**. Protracted anaphylaxis and cytokine release syndrome 6 days after rituximab desensitization. *Ann Allergy Asthma Immunol* 2024; Epub ahead of print. PMID: 38615738. Full Text

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Anesthesiology
Dexter F, Epstein RH, Marian AA, and **Guerra-Londono CE**. Preventing Prolonged Times to Awakening While Mitigating the Risk of Patient Awareness: Gas Man Computer Simulations of Sevoflurane Consumption From Brief, High Fresh Gas Flow Before the End of Surgery. *Cureus* 2024; 16(3):e55626. PMID: 38586680. Full Text

Anesthesia, University of Iowa, Iowa City, USA.
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Prolonged times to tracheal extubation are associated with adverse patient and economic outcomes. We simulated awakening patients from sevoflurane after long-duration surgery at 2% end-tidal concentration, 1.0 minimum alveolar concentration (MAC) in a 40-year-old. Our end-of-surgery target was 0.5 MAC, the Michigan Awareness Control Study's threshold for intraoperative alerts. Consider an anesthetist who uses a 1 liter/minute gas flow until surgery ends. During surgical closure, the inspired sevoflurane concentration is reduced from 2.05% to 0.62% (i.e., MAC-awake). The estimated time to reach 0.5 MAC is 28 minutes. From a previous study, 28 minutes exceeded ≥95% of surgical closure times for all 244 distinct surgical procedures (N=23,343 cases). Alternatively, the anesthetist uses 8 liters/minute gas flow with the vaporizer at MAC-awake for 1.8 minutes, which reduces the end-tidal concentration to 0.5 MAC. The anesthetist then increases the vaporizer to keep end-tidal 0.5 MAC until the surgery ends. An additional simulation shows that, compared with simulated end-tidal agent feedback control, this approach consumed 0.45 mL extra agent. Simulation results are the same for an 80-year-old patient. The extra 0.45 mL has a global warming potential comparable to driving 26 seconds at 40 kilometers (25 miles) per hour, comparable to route modification to avoid potential roadway hazards.

Anesthesiology
Guerra-Londono CE, Cata JP, **Nowak K**, and Gottumukkala V. Prehabilitation in Adults Undergoing Cancer Surgery: A Comprehensive Review on Rationale, Methodology, and Measures of Effectiveness. *Curr Oncol* 2024; 31(4):2185-2200. PMID: 38668065. Full Text

Department of Anesthesiology, Pain Management & Perioperative Medicine, Henry Ford Health, Detroit, MI 48202, USA.
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Cancer surgery places a significant burden on a patients' functional status and quality of life. In addition, cancer surgery is fraught with postoperative complications, themselves influenced by a patient's

functional status. Prehabilitation is a unimodal or multimodal strategy that aims to increase a patient's functional capacity to reduce postoperative complications and improve postoperative recovery and quality of life. In most cases, it involves exercise, nutrition, and anxiety-reducing interventions. The impact of prehabilitation has been explored in several types of cancer surgery, most commonly colorectal and thoracic. Overall, the existing evidence suggests prehabilitation improves physiological outcomes (e.g., lean body mass, maximal oxygen consumption) as well as clinical outcomes (e.g., postoperative complications, quality of life). Notably, the benefit of prehabilitation is additional to that of enhanced recovery after surgery (ERAS) programs. While safe, prehabilitation programs require multidisciplinary coordination preoperatively. Despite the existence of numerous systematic reviews and meta-analyses, the certainty of evidence demonstrating the efficacy and safety of prehabilitation is low to moderate, principally due to significant methodological heterogeneity and small sample sizes. There is a need for more large-scale multicenter randomized controlled trials to draw strong clinical recommendations.

Anesthesiology
Olson J, Ko A, **Nowak KA**, **Latack K**, and Bozimowsky G. Using Simulation Training to Reduce Skill Decay Among Certified Registered Nurse Anesthetists. *J Contin Educ Nurs* 2024; 55(4):187-194. PMID: 38063801. Full Text

BACKGROUND: Skill decay refers to the loss of skills and knowledge resulting from lack of consistent use. Among certified registered nurse anesthetists (CRNAs), skill decay can lead to negative results. One method that has been shown to mitigate skill decay is low-dose, high-frequency (LDHF) simulation. There is a gap in the LDHF simulation literature regarding CRNAs to determine its effectiveness in reducing skill decay or increasing confidence levels. METHOD: This study used a quasi-experimental pretest-posttest follow-up design. The pretests and posttests were evaluated using a Wilcoxon signed rank test to determine CRNAs' proficiency and confidence in central venous catheter (CVC) insertion before and after a simulated refresher training course. RESULTS: The CRNAs showed a significant improvement in CVC insertion proficiency, from a 50% pretest average to a 94% posttest average ($p < .0001$), and they retained proficiency 6 months later (91%, $p = .0109$). There was no significant change in CRNAs' confidence level following the training ($p = .4486$). CONCLUSION: A program of LDHF simulation training is an important activity in meeting the continuing education/training needs of CRNAs in improving and retaining CVC insertion proficiency. This study demonstrates the efficacy of a LDHF simulation program for CRNAs and helps to bridge the gap in the literature on the use of LDHF simulation among CRNAs. [J Contin Educ Nurs. 2024;55(4):187-194.].

Behavioral Health Services/Psychiatry/Neuropsychology
Ahmedani BK, **Frank C**, and **Zervos J**. Zero Suicide International: An opportunity across Asia. *Asian J Psychiatr* 2024; 104056. Epub ahead of print. PMID: 38679537. Full Text

Henry Ford Health, Center for Health Policy & Health Services Research, United States; Henry Ford Health, Behavioral Health Services, United States. Electronic address: bahmeda1@hfhs.org.
Henry Ford Health, Behavioral Health Services, United States.
Henry Ford Health, Global Health Initiative, United States.

Behavioral Health Services/Psychiatry/Neuropsychology
Boggs JM, Richards J, Simon G, Aguirre-Miyamoto EM, Barton LJ, Beck A, Beidas RS, Bruschke C, Buckingham ETt, Buttlaire S, Clarke G, Coleman K, Flores JP, **Frank C**, Penfold RB, Richardson L, Ryan JM, Schoenbaum M, Sterling S, Stewart C, Yarborough BJH, **Yeh HH**, and **Ahmedani B**. Suicide Screening, Risk Assessment, and Lethal Means Counseling During Zero Suicide Implementation. *Psychiatr Serv* 2024; Epub ahead of print. PMID: 38566561. Full Text

Kaiser Permanente Colorado, Aurora (Boggs, Beck, Buckingham, Richardson); Kaiser Permanente Washington, Seattle (Richards, Simon, Penfold, Stewart); Kaiser Permanente Southern California, Pasadena (Aguirre-Miyamoto, Barton, Coleman); Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago (Beidas); Kaiser Permanente Program Office, Oakland, California (Bruschke); Kaiser Permanente Northern California, Oakland (Buttlaire, Sterling); Kaiser Permanente Northwest, Portland, Oregon (Clarke, Ryan, Yarborough); Department of Mental Health,

Johns Hopkins Bloomberg School of Public Health, Baltimore (Flores); Henry Ford Health System, Detroit (Frank, Yeh, Ahmedani); NIMH, Bethesda (Schoenbaum).

OBJECTIVE: The authors measured implementation of Zero Suicide (ZS) clinical practices that support identification of suicide risk and risk mitigation, including screening, risk assessment, and lethal means counseling, across mental health specialty and primary care settings. METHODS: Six health care systems in California, Colorado, Michigan, Oregon, and Washington participated. The sample included members ages ≥13 years from 2010 to 2019 (N=7,820,524 patients). The proportions of patients with suicidal ideation screening, suicide risk assessment, and lethal means counseling were estimated. RESULTS: In 2019, patients were screened for suicidal ideation in 27.1% (range 5.0%-85.0%) of mental health visits and 2.5% (range 0.1%-35.0%) of primary care visits among a racially and ethnically diverse sample (44.9% White, 27.2% Hispanic, 13.4% Asian, and 7.7% Black). More patients screened positive for suicidal ideation in the mental health setting (10.2%) than in the primary care setting (3.8%). Of the patients screening positive for suicidal ideation in the mental health setting, 76.8% received a risk assessment, and 82.4% of those identified as being at high risk received lethal means counseling, compared with 43.2% and 82.4%, respectively, in primary care. CONCLUSIONS: Six health systems that implemented ZS showed a high level of variation in the proportions of patients receiving suicide screening and risk assessment and lethal means counseling. Two opportunities emerged for further study to increase frequency of these practices: expanding screening beyond patients with regular health care visits and implementing risk assessment with lethal means counseling in the primary care setting directly after a positive suicidal ideation screening.

Behavioral Health Services/Psychiatry/Neuropsychology

Karr JE, Zuccato BG, Ingram EO, Considine CM, **Merker B**, and Abeare CA. Cognitive, Sleep-Arousal, Physical, and Affective Domain Scores on the Post-Concussion Symptom Scale: Added Utility in Detecting Symptom Elevations among Student-Athletes with a Remote History of Concussion. *Arch Clin Neuropsychol* 2024; Epub ahead of print. PMID: 38594912. Full Text

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OBJECTIVE: The evaluation of self-reported symptoms is a standard component of concussion assessment and management. Clinicians typically evaluate a total symptom severity score rather than scores corresponding to specific symptom domains (i.e., cognitive, sleep-arousal, physical, and affective symptoms). This study examined (i) whether elevations in specific symptom domains would be missed when interpreting only the total symptom severity score and (ii) if a single symptom domain elevation was more common than having elevated symptoms across multiple domains. METHOD: Adolescent student-athletes (N = 1,008) with concussion history (i.e., ≥6 months since last concussion) completed the Post-Concussion Symptom Scale (PCSS). The PCSS total score and cognitive, sleep-arousal, physical, and affective domain scores were calculated. To determine if symptoms were elevated, scores were compared to normative data matched on gender and pre-existing conditions, with scores considered elevated if they were ≥84th percentile. The frequency of total and domain score elevations were calculated and stratified by gender and number of prior concussions (i.e., 1 or ≥2 prior concussions). RESULTS: Overall, 26% of student-athletes had an elevated symptom domain score without being elevated on the total score. The most common symptom presentation was to have a single elevated symptom domain (21%), followed by two (11%), three (8%), or four elevated domains (6%). CONCLUSIONS: Interpreting PCSS symptom domains may be beneficial in detecting student-athletes with elevated symptoms following a remote concussion. Roughly a quarter of student-athletes have domain-specific symptom elevations that would be missed by interpreting the total score alone.

Behavioral Health Services/Psychiatry/Neuropsychology

Miller-Matero LR, **Santullano D**, **Rich M**, **Valler M**, **Hecht LM**, **Tobin ET**, and **Ahmedani BK**. Association of health literacy with chronic pain and pain-related distress. *Prof Psychol Res Pr* 2024; 55(2):89-94. PMID: Not assigned. Request Article

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Research suggests health literacy should be considered when treating chronic pain. The purpose of this secondary analysis was to examine the relationship of health literacy with pain and psychological functioning and to determine whether health literacy status was associated with outcomes after a brief psychological intervention for chronic pain. Participants with chronic musculoskeletal pain (N = 60) were randomized to a five-session psychological intervention or control group between September 2018 and February 2020. Participants completed a baseline and postassessment, which included measures of health literacy status (i.e., adequate vs. lower level), pain severity, pain interference, pain catastrophizing, depression, anxiety, and pain acceptance. Participants were mostly female (78.3%) and Black (88.3%) with a mean age of 62.2 years. At baseline, lower levels of health literacy were associated with greater pain severity (p = .003), pain catastrophizing (p = .03), and depressive symptoms (p = .02). Among those randomized to the intervention group, health literacy status was not related to engagement in the intervention. However, those with adequate levels of health literacy were more likely to have lower depressive symptoms (p = .045) and higher acceptance of pain (p = .01) at postintervention compared to those with lower levels. Among individuals with chronic pain, those with lower levels of health literacy may have worse pain and psychological functioning. Those with lower levels may also not benefit as much from standardized psychological interventions for pain management. Clinicians delivering psychological interventions for chronic pain may want to consider screening for health literacy status and adapt the intervention to ensure understanding.

Behavioral Health Services/Psychiatry/Neuropsychology
Wolfe D. Psychotherapy Is Essential to Psychiatry Training. *Acad Psychiatry* 2024; Epub ahead of print. PMID: 38587777. Request Article

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Cardiology/Cardiovascular Research
Al-Ogaili A, Alexandrou M, Rempakos A, Mutlu D, Choi JW, Poommipanit P, Khatri JJ, **Alaswad K**, **Basir MB**, Chandwaney RH, Gorgulu S, ElGuindy AM, Elbarouni B, Jaber W, Rinfret S, Nicholson W, Jaffer FA, Aygul N, Azzalini L, Kearney KE, Frizzell J, Davies R, Goktekin O, Rangan BV, Mastrodemos OC, Sandoval Y, Nicholas Burke M, and Brilakis ES. Retrograde chronic total occlusion percutaneous coronary intervention via ipsilateral collaterals. *Catheter Cardiovasc Interv* 2024; 103(6):863-872. PMID: 38563074. Full Text

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St. Boniface General Hospital, Winnipeg, Manitoba, Canada.
Emory University Hospital Midtown, Atlanta, Georgia, USA.
Massachusetts General Hospital, Boston, Massachusetts, USA.
Selcuk University, Konya, Turkey.
Division of Cardiology, Department of Medicine, University of Washington, Seattle, Washington, USA.
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Memorial Bahcelievler Hospital, Istanbul, Turkey.

BACKGROUND: There is limited data on retrograde chronic total occlusion (CTO) percutaneous coronary intervention (PCI) via ipsilateral epicardial collaterals (IEC). AIMS: To compare the clinical and

angiographic characteristics, and outcomes of retrograde CTO PCI via IEC versus other collaterals in a large multicenter registry. METHODS: Observational cohort study from the Prospective Global registry for the study of Chronic Total Occlusion Intervention (PROGRESS-CTO). RESULTS: Of 4466 retrograde cases performed between 2012 and 2023, crossing through IEC was attempted in 191 (4.3%) cases with 50% wiring success. The most common target vessel in the IEC group was the left circumflex (50%), in comparison to other retrograde cases, where the right coronary artery was most common (70%). The Japanese CTO score was similar between the two groups (3.13 ± 1.23 vs. 3.06 ± 1.06, p = 0.456); however, the IEC group had a higher Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS-CTO) score (1.95 ± 1.02 vs. 1.27 ± 0.92, p < 0.0001). The most used IEC guidewire was the SUOH 03 (39%), and the most frequently used microcatheter was the Caravel (43%). Dual injection was less common in IEC cases (66% vs. 89%, p < 0.0001). Technical (76% vs. 79%, p = 0.317) and procedural success rates (74% vs. 79%, p = 0.281) were not different between the two groups. However, IEC cases had a higher procedural complications rate (25.8% vs. 16.4%, p = 0.0008), including perforations (17.3% vs. 9.0%, p = 0.0001), pericardiocentesis (3.1% vs. 1.2%, p = 0.018), and dissection/thrombus of the donor vessel (3.7% vs. 1.2%, p = 0.002). CONCLUSION: The use of IEC for retrograde CTO PCI was associated with similar technical and procedural success rates when compared with other retrograde cases, but higher incidence of periprocedural complications.

Cardiology/Cardiovascular Research

Alexandrou M, Mutlu D, Rempakos A, Al Ogaili A, Choi JW, Poommipanit P, **Alaswad K**, **Basir MB**, Davies R, Jaffer FA, Dattilo P, Azzalini L, Aygul N, Reddy N, Jefferson BK, Gorgulu S, Khatri JJ, Young LD, Krestyaninov O, Khelimskii D, Frizzell J, Elbarouni B, Rangan BV, Mastrodemos OC, Burke MN, Sandoval Y, and Brilakis ES. Ranolazine in chronic total occlusion percutaneous coronary intervention. *J Invasive Cardiol* 2024; Epub ahead of print. PMID: 38691399. Request Article

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Massachusetts General Hospital, Boston, Massachusetts, USA.
Medical Center of the Rockies, Loveland, CO, USA.
Division of Cardiology, Department of Medicine, University of Washington, Seattle, Washington, USA.
Selcuk University, Konya, Turkey.
Kettering Medical Center, Dayton, Ohio, USA.
Tristar Hospitals, Tennessee, USA.
Biruni University Medical School, Istanbul, Turkey.
Cleveland Clinic, Cleveland, Ohio, USA.
Meshalkin Novosibirsk Research Institute, Novosibirsk, Russia.
St. Vincent Hospital, Indianapolis, USA.
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Ranolazine is an anti-anginal medication given to patients with chronic angina and persistent symptoms despite medical therapy. We examined 11 491 chronic total occlusion (CTO) percutaneous coronary interventions (PCI) that were performed at 41 US and non-US centers between 2012 and 2023 in the PROGRESS-CTO Registry. Patients on ranolazine at baseline had more comorbidities, more complex lesions, lower procedural and technical success (based on univariable but not multivariable analysis), and higher incidence of major adverse cardiac events (MACE) (on both univariable and multivariable analysis).

Cardiology/Cardiovascular Research

Alhuneafat L, Khalid MU, **Jabri A**, Deicke MD, Virk S, Jacobs MW, Hsich E, **Alqarqaz M**, Dunlap ME, Kassis-George H, and Link C. Early pandemic in-hospital outcomes and mortality risk factors in COVID-19 solid organ transplant patients. *Proc (Bayl Univ Med Cent)* 2024; 37(3):414-423. PMID: 38628349. Full Text

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BACKGROUND: Solid organ transplant (SOT) recipients with COVID-19 have a higher risk of mortality than those without COVID-19. However, it is unclear how SOT patient outcomes compare to the general population without SOT who contract COVID-19. METHODS: We used the National Inpatient Sample from January to December 2020 to investigate inpatient outcomes seen in SOT recipients after contracting COVID-19 compared to nontransplant patients. We identified our study sample using ICD-10 CM and excluded those <18 years of age and those with dual organ transplants. Inpatient outcomes were compared in SOT and non-SOT COVID cohorts, and we further evaluated predictors of mortality in the SOT with COVID population. RESULTS: Out of the 1,416,445 COVID-19 admissions included in the study, 8315 (0.59%) were single SOT recipients. Our analysis that adjusted for multiple baseline characteristics and comorbidities demonstrated that COVID-19 in SOT patients was associated with higher rates of acute kidney injury (adjusted odds ratio [aOR] 2.34, 95% confidence interval [CI] 1.81-3.02, $P < 0.01$), lower rates of acute respiratory distress syndrome (aOR 0.68, 95% CI 0.54-0.85, $P < 0.01$), and similar rates of cardiac arrest, pulmonary embolism, circulatory shock, cerebrovascular events, and in-hospital mortality. Age >65 was associated with mortality in SOT patients. CONCLUSION: In this nationally representative sample, SOT patients presenting with COVID-19 experienced similar rates of mortality compared to those without SOT. SOT patients were more likely to develop acute kidney injury. Further research is needed to understand the complex relationship between transplant patient outcomes and COVID-19.

Cardiology/Cardiovascular Research

Altibi AM, Alhuneafat L, **Jabri A**, Al-Abdouh A, and Ghanem F. Cerebral embolic protection device utilization and outcomes in transcatheter aortic valve replacement: A nationally representative propensity matched analysis. *Cardiovasc Revasc Med* 2024; Epub ahead of print. PMID: 38653674. Full Text

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INTRODUCTION: In patients undergoing transcatheter aortic valve replacement (TAVR), cerebral embolic protection devices (CEPD) are used to possibly diminish the risk of periprocedural stroke. Trends and outcomes of CEPD usage in TAVR are not well characterized. METHODS: National readmission databases (NRD) 2017-2019 was used to identify hospital admissions for TAVR using ICD-10 codes, with versus without Sentinel CEPD. Primary outcomes of the study were in-hospital and 30-day stroke. Secondary outcomes include in-hospital mortality, 30-day mortality, 30-day readmission rate, and other procedural complications. We matched both cohorts using propensity score matching (PSM) and performed logistic regression to compute the odds ratios (ORs) and corresponding 95 % confidence intervals (CI). RESULTS: Out of 190,837 TAVR admissions in the United States, 10,643 (5.6 %) patients had TAVR with Sentinel CEPD. After propensity score matching, our cohort included 10,503 patients with CEPD and 10,541 without CEPD. Trends in CEPD utilization are noted in Fig. 1. In the PSM cohort,

Sentinel CEPD was not associated with decreased risk of in-hospital stroke (1.9 % vs. 1.8 %, OR: 0.98, 95 % CI: 0.76-1.26, p = 0.88), 30-day stroke (2.1 % vs. 2.1 %, OR: 1.01, 95 % CI: 0.78-1.30, p = 0.96), or 30-day mortality (1.3 % vs. 1.0 %, OR: 0.74, 95 % CI: 0.51-1.07, p = 0.11) when compared to TAVR without CEPD. Other in-hospital and short-term outcomes post-TAVR were not impacted by Sentinel CEPD usage, including acute kidney injury, vascular complications, paravalvular leak, cardiogenic shock, circulatory support, or permanent pacemaker (Table 1). CONCLUSION: In this nationally representative cohort, Sentinel CEPD utilization during transfemoral TAVR for stroke prevention was not associated with reduced odds of in-hospital stroke, 30-day stroke, or 30-day mortality. Future studies should focus on optimizing patient selection for CEPD and establishing predictive models to identify the subset of TAVR patients with higher risk for periprocedural stroke who might benefit from CEPD.

Cardiology/Cardiovascular Research

Aslam S, **Cowger J**, Shah P, Stosor V, Copeland H, Reed A, Morales D, Giblin G, Mathew J, Morrissey O, Morejon P, Nicoara A, and Molina E. The International Society of Heart and Lung Transplantation (ISHLT): 2024 infection definitions for durable and acute mechanical circulatory support devices. *J Heart Lung Transplant* 2024; Epub ahead of print. PMID: 38691077. Full Text

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Division of Cardiology, Henry Ford Health, Detroit, Michigan.
Inova Heart and Vascular Institute, Falls Church, Virginia.
Division of Infectious Diseases, Northwestern University Feinberg School of Medicine, Chicago, Illinois.
Department of Surgery, Lutheran Hospital of Indiana/Indiana School of Medicine, Fort Wayne, Indiana.
Respiratory & Transplant Medicine, Royal Brompton and Harefield Hospitals, Harefield, United Kingdom.
Division of Cardiothoracic Surgery, Department of Surgery, Cincinnati Children's Hospital, Cincinnati, Ohio.
Cardiology Unit, Mater Misericordiae University Hospital, Dublin, Ireland.
Cardiology Department, Royal Children's Hospital, Melbourne, Australia.
Department of Infectious Diseases, Monash University and Physician at Alfred Health, Melbourne, Australia.
Cardiology, Clinica Guayaquil, Guayaquil, Ecuador.
Division of Cardiothoracic Anesthesia, Duke University, Durham, North Carolina.
Samsky Heart Failure Center, Piedmont Heart Institute, Atlanta, Georgia.

Infections remain a significant concern in patients receiving mechanical circulatory support (MCS), encompassing both durable and acute devices. This consensus manuscript provides updated definitions for infections associated with durable MCS devices and new definitions for infections in acute MCS, integrating a comprehensive review of existing literature and collaborative discussions among multidisciplinary specialists. By establishing consensus definitions, we seek to enhance clinical care, facilitate consistent reporting in research studies, and ultimately improve outcomes for patients receiving MCS.

Cardiology/Cardiovascular Research

Bharadwaj AS, Truesdell AG, Lemor A, Thompson JB, Abu-Much A, Zhang Y, Schonning MJ, Cohen DJ, Lansky AJ, and **O'Neill WW**. Characteristics of Patients Undergoing High-Risk Percutaneous Coronary Intervention in Contemporary United States Practice. *Am J Cardiol* 2024; Epub ahead of print. PMID: 38679222. Full Text

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Cardiology/Cardiovascular Research
Danagoulian S, **Miller J**, **Cook B**, **Gunaga S**, **Fadel R**, **Gandolfo C**, Mills NL, **Modi S**, Mahler SA, Levy PD, **Parikh S**, **Krupp S**, **Abdul-Nour K**, **Klausner H**, **Rockoff S**, **Gindi R**, **Lewandowski A**, **Hudson M**, **Perrotta G**, **Zweig B**, **Lanfear D**, **Kim H**, **Shaheen E**, **Darnell G**, **Nassereddine H**, **Hawatian K**, **Tang A**, Keerie C, and **McCord J**. Is rapid acute coronary syndrome evaluation with high-sensitivity cardiac troponin less costly? An economic evaluation. *J Am Coll Emerg Physicians Open* 2024; 5(2):e13140. PMID: 38567033. Full Text

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OBJECTIVE: Protocols to evaluate for myocardial infarction (MI) using high-sensitivity cardiac troponin (hs-cTn) have the potential to drive costs upward due to the added sensitivity. We performed an economic evaluation of an accelerated protocol (AP) to evaluate for MI using hs-cTn to identify changes in costs of treatment and length of stay compared with conventional testing. METHODS: We performed a planned secondary economic analysis of a large, cluster randomized trial across nine emergency departments (EDs) from July 2020 to April 2021. Patients were included if they were 18 years or older with clinical suspicion for MI. In the AP, patients could be discharged without further testing at 0 h if they had a hs-cTnI < 4 ng/L and at 1 h if the initial value were 4 ng/L and the 1-h value ≤7 ng/L. Patients in the standard of care (SC) protocol used conventional cTn testing at 0 and 3 h. The primary outcome was the total cost of treatment, and the secondary outcome was ED length of stay. RESULTS: Among 32,450 included patients, an AP had no significant differences in cost (+$89, CI: -$714, $893 hospital cost, +$362, CI: -$414, $1138 health system cost) or ED length of stay (+46, CI: -28, 120 min) compared with the SC protocol. In lower acuity, free-standing EDs, patients under the AP experienced shorter length of stay (-37 min, CI: -62, 12 min) and reduced health system cost (-$112, CI: -$250, $25). CONCLUSION: Overall, the implementation of AP using hs-cTn does not result in higher costs.

Cardiology/Cardiovascular Research
Elshawi R, Sakr S, Al-Mallah MH, **Keteyian SJ**, **Brawner CA**, and **Ehrman JK**. FIT calculator: a multi-risk prediction framework for medical outcomes using cardiorespiratory fitness data. *Sci Rep* 2024; 14(1):8745. PMID: 38627439. Full Text

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Accurately predicting patients' risk for specific medical outcomes is paramount for effective healthcare management and personalized medicine. While a substantial body of literature addresses the prediction

of diverse medical conditions, existing models predominantly focus on singular outcomes, limiting their scope to one disease at a time. However, clinical reality often entails patients concurrently facing multiple health risks across various medical domains. In response to this gap, our study proposes a novel multi-risk framework adept at simultaneous risk prediction for multiple clinical outcomes, including diabetes, mortality, and hypertension. Leveraging a concise set of features extracted from patients' cardiorespiratory fitness data, our framework minimizes computational complexity while maximizing predictive accuracy. Moreover, we integrate a state-of-the-art instance-based interpretability technique into our framework, providing users with comprehensive explanations for each prediction. These explanations afford medical practitioners invaluable insights into the primary health factors influencing individual predictions, fostering greater trust and utility in the underlying prediction models. Our approach thus stands to significantly enhance healthcare decision-making processes, facilitating more targeted interventions and improving patient outcomes in clinical practice. Our prediction framework utilizes an automated machine learning framework, Auto-Weka, to optimize machine learning models and hyper-parameter configurations for the simultaneous prediction of three medical outcomes: diabetes, mortality, and hypertension. Additionally, we employ a local interpretability technique to elucidate predictions generated by our framework. These explanations manifest visually, highlighting key attributes contributing to each instance's prediction for enhanced interpretability. Using automated machine learning techniques, the models simultaneously predict hypertension, mortality, and diabetes risks, utilizing only nine patient features. They achieved an average AUC of 0.90 ± 0.001 on the hypertension dataset, 0.90 ± 0.002 on the mortality dataset, and 0.89 ± 0.001 on the diabetes dataset through tenfold cross-validation. Additionally, the models demonstrated strong performance with an average AUC of 0.89 ± 0.001 on the hypertension dataset, 0.90 ± 0.001 on the mortality dataset, and 0.89 ± 0.001 on the diabetes dataset using bootstrap evaluation with 1000 resamples.

Cardiology/Cardiovascular Research

Engel Gonzalez P, **Gregerson S**, **Mahmood S**, **Brooks C**, **Villablanca PA**, **Frisoli TM**, **Lee J**, **Wyman JF**, **Wang DD**, **O'Neill WW**, and **O'Neill BP**. Clinical characteristics and outcomes of alcohol septal ablation in the era of transcatheter valve interventions. *Catheter Cardiovasc Interv* 2024; 103(6):1023-1034. PMID: 38639143. Full Text

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BACKGROUND: The clinical efficacy and safety of alcohol septal ablation (ASA) for obstructive hypertrophic cardiomyopathy (HCM) have been well-established; however, less is known about outcomes in patients undergoing preemptive ASA before transcatheter mitral valve replacement (TMVR). AIMS: The goal of this study is to characterize the procedural characteristics and examine the clinical outcomes of ASA in both HCM and pre-TMVR. METHODS: This retrospective study compared procedural characteristics and outcomes in patient who underwent ASA for HCM and TMVR. RESULTS: In total, 137 patients were included, 86 in the HCM group and 51 in the TMVR group. The intraventricular septal thickness (mean 1.8 vs. 1.2 cm; $p < 0.0001$) and the pre-ASA LVOT gradient (73.6 vs. 33.8 mmHg; $p \leq 0.001$) were higher in the HCM group vs the TMVR group. The mean volume of ethanol injected was higher (mean 2.4 vs. 1.7 cc; $p < 0.0001$). The average neo-left ventricular outflow tract area increased significantly after ASA in the patients undergoing TMVR (99.2 ± 83.37 mm(2) vs. 196.5 ± 114.55 mm(2); $p = <0.0001$). The HCM group had a greater reduction in the LVOT gradient after ASA vs the TMVR group (49.3 vs. 18 mmHg; $p = 0.0040$). The primary composite endpoint was higher in the TMVR group versus the HCM group (50.9% vs. 25.6%; $p = 0.0404$) and had a higher incidence of new permanent pacemaker (PPM) (25.5% vs. 18.6%; $p = 0.3402$). The TMVR group had a higher rate of all-cause mortality (9.8% vs. 1.2%; $p = 0.0268$). CONCLUSIONS: Preemptive ASA before TMVR was performed in patients with higher degree of clinical comorbidities, and correspondingly is associated with worse short-term clinical outcomes in comparison to ASA for HCM patients. ASA before TMVR enabled percutaneous mitral interventions in a small but significant minority of patients that would have otherwise been excluded. The degree of LVOT and neoLVOT area increase is significant and predictable.

Cardiology/Cardiovascular Research

Fang JX, **O'Neill BP**, **Wang DD**, **Giustino G**, **von Buchwald CL**, **Lee JC**, **Engel Gonzalez P**, **Frisoli TM**, **O'Neill WW**, and **Villablanca PA**. Feasibility and technicality of aortic valve lithotripsy-facilitate balloon valvuloplasty in patients with severe aortic stenosis unsuitable for immediate valvular replacement. *Cardiovasc Revasc Med* 2024; Epub ahead of print. PMID: 38670866. Full Text

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BACKGROUND: Aortic valve lithotripsy can fragment aortic valve calcium deposits and potentially restore leaflet pliability in animal model and ex-vivo, but clinical data is limited. Transcatheter aortic valve implantation (TAVR) might not be feasible as an urgent procedure in critically ill patients. Balloon valvuloplasty has the major limitation of valve recoil and inducing aortic regurgitation. AIMS: To determine the clinical feasibility of aortic valve lithotripsy-facilitated balloon valvuloplasty in patients with severe aortic stenosis unsuitable for valvular replacement. METHODS: We performed lithotripsy as adjunctive therapy to balloon aortic valvuloplasty in ten consecutive patients, most of whom were deemed unfit for TAVR. Lithotripsy of the aortic valve was performed with simultaneous inflation of one to three peripheral lithotripsy balloons to deliver ultrasound pulses. Rapid pacing was not used during lithotripsy. Aortic valve velocity, gradient, and valve area were measured before and after the procedure by echocardiogram. Transvalvular pressure gradient was recorded intra-procedurally. Periprocedural and ninety-day clinical outcomes were followed. RESULTS: Procedure was technically successful in 9 out of 10 patients and aborted in one patient due to cardiogenic shock. One patient had femoral closure device related complication. There was a statistically significant decrease in valvular gradient and increase in aortic valve area. 9 out of 10 patients recovered from acute episode and were discharged. 6 patients had improvement in NYHA class. 4 patients were subsequently able to receive TAVR. 90-day mortality occurred in 3 patients. There was no stroke or bradyarrhythmia peri-procedurally and no heart failure hospitalization at 90 days. CONCLUSION: Aortic valve lithotripsy-facilitated balloon valvuloplasty has reasonable feasibility, safety and technical reproducibility and acute clinical result. Hemodynamic effect is similar to that of balloon valvuloplasty reported in the literature. Subsequent Prognosis is not altered in critically ill patients.

Cardiology/Cardiovascular Research

Fliegner MA, Hou H, Bauer TM, Daramola T, McCullough JS, Pagani FD, Sukul D, Likosky DS, **Keteyian SJ**, and Thompson MP. Interhospital Variability in Cardiac Rehabilitation Use After Cardiac Surgery Among Medicare Beneficiaries. *J Thorac Cardiovasc Surg* 2024; Epub ahead of print. PMID: 38649110. Full Text

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OBJECTIVE: Despite guideline recommendation, cardiac rehabilitation (CR) following cardiac surgery remains underutilized, and the extent of interhospital variability is not well understood. This study evaluated determinants of interhospital variability in CR use and outcomes. METHODS: This retrospective cohort study included 166,809 Medicare beneficiaries undergoing cardiac surgery who were

discharged alive between 07/01/2016 and 12/31/2018. CR participation was identified in outpatient facility claims within a year of discharge. Hospital-level CR rates were tabulated, and multilevel models evaluated the extent to which patient, organizational, and regional factors accounted for interhospital variability. Adjusted 1-year mortality and readmission rates were also calculated for each hospital quartile of CR use. RESULTS: Overall, 90,171 (54.1%) participated in at least one CR session within a year of discharge. Interhospital CR rates ranged from 0.0% to 96.8%. Hospital factors that predicted CR use included non-teaching status and lower hospital volume. Before adjusting for patient, organizational, and regional factors, 19.3% of interhospital variability was attributable to the admitting hospital. After accounting for covariates, 12.3% of variation was attributable to the admitting hospital. Patient (0.5%), structural (2.8%), and regional (3.7%) factors accounted for the remaining explained variation. Hospitals in the lowest quartile of CR use had higher adjusted 1-year mortality rates (Q1 = 6.7%, Q4 = 5.2%, $p < 0.001$) and readmission rates (Q1 = 37.6%, Q4 = 33.9%, $p<0.001$). CONCLUSION: Identifying best practices among high CR use facilities and barriers to access in low CR use hospitals may reduce interhospital variability in CR use and advance national improvement efforts.

Cardiology/Cardiovascular Research
Giustino G, **O'Neill BP**, **Wang DD**, **Frisoli T**, **Fang JX**, **Engel-Gonzalez P**, **Lee J**, **Fadel R**, **O'Neill WW**, and **Villablanca PA**. Feasibility and safety of transcaval venoarterial extracorporeal membrane oxygenation in severe cardiogenic shock. *EuroIntervention* 2024; 20(8):e511-e513. PMID: 38629421. Request Article

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Cardiology/Cardiovascular Research
Gupta K, Lemor A, Alkhatib A, **McBride P**, **Cowger J**, **Grafton G**, **Alaswad K**, **O'Neill W**, **Villablanca P**, and **Basir MB**. Use of percutaneous mechanical circulatory support for right ventricular failure. *Catheter Cardiovasc Interv* 2024; 103(6):909-916. PMID: 38584525. Full Text

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BACKGROUND: Utilization of right ventricular mechanical circulatory support (RV-MCS) devices has been limited by a lack of recognition of RV failure as well as a lack of availability and experience with RV-MCS. AIMS: We report a single-center experience with the use of percutaneous RV-MCS and report predictors of adverse outcomes. METHODS: This was a single-center retrospective cohort study. Data from consecutive patients who received RV-MCS for any indication between June 2015 and January 2022 were included. Data on baseline comorbidities, hemodynamics, and laboratory values were collected. The primary outcome was in-hospital mortality analyzed as a logistic outcome in a multivariable model. These variables were further ranked by their predictive value. RESULTS: Among 58 consecutive patients enrolled, the median age was 66 years, 31% were female and 53% were white. The majority of the patients (48%) were hospitalized for acute on chronic heart failure. The majority of the patients were SCAI SHOCK Stage D (67%) and 34 (64%) patients had MCS placed within 24 h of the onset of shock. Before placement of RV-MCS, median central venous pressure (CVP) and RV stroke work index were 20 mmHg and 8.9 g m/m(2), respectively. Median serum lactate was 3.5 (1.6, 6.2) mmol/L. Impella RP was implanted in 50% and ProtekDuo in the remaining 50%. Left ventricular MCS was concomitantly used in 66% of patients. Twenty-eight patients (48.3%) died. In these patients, median serum lactate was significantly higher (4.1 [2.3, 13.0] vs. 2.2 [1.4, 4.0] mmol/L, $p = 0.007$) and a trend toward higher median CVP (24 [18, 31] vs. 19 [14, 24] mmHg, $p = 0.052$). In the multivariable logistic model, both serum lactate and CVP before RV-MCS placement were independent predictors of in-hospital mortality. Serum lactate had the highest predictive value. CONCLUSION: In our real-world cohort, 52% of patients treated with RV-MCS survived their index hospitalization. Serum lactate at presentation and CVP were the strongest predictors of in-hospital mortality.

Cardiology/Cardiovascular Research

Haddadin F, Birnbaum G, Alhuneafat L, **Jabri A**, Ulhaq O, Giorgberidze I, and Afshar H. A case of helix-fixation leadless pacemaker dislodgment and retrieval: The importance of achieving appropriate postimplant impedance. *HeartRhythm Case Reports* 2024. Epub ahead of print. PMID: Not assigned. Full Text

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Cardiology/Cardiovascular Research

Keteyian SJ, **Grimshaw C**, **Ehrman JK**, **Kerrigan DJ**, **Abdul-Nour K**, **Lanfear DE**, and **Brawner CA**. The iATTEND Trial: A Trial Comparing Hybrid Versus Standard Cardiac Rehabilitation. *Am J Cardiol* 2024; Epub ahead of print. PMID: 38670326. Full Text

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The improving ATTENDance (iATTEND) to cardiac rehabilitation (CR) trial tested the hypotheses that hybrid CR (HYCR) (combination of virtual and in-facility CR sessions) would result in greater attendance compared with traditional, facility-based only CR (FBCR) and yield equivalent improvements in exercise capacity and health status. Patients were randomized to HYCR (n = 142) or FBCR (n = 140), stratified by gender and race. Attendance was assessed as number of CR sessions completed within 6 months (primary end point) and the percentage of patients completing 36 CR sessions. Other end points (tested for equivalency) included exercise capacity and self-reported health status. HYCR patients completed 1 to 12 sessions in-facility, with the balance completed virtually using synchronized, 2-way audiovisual technology. Neither total number of CR sessions completed within 6 months (29 ± 12 vs 28 ± 12 visits, adjusted p = 0.94) nor percentage of patients completing 36 sessions (59 ± 4% vs 51 ± 4%, adjusted p = 0.32) were significantly different between HYCR and FBCR, respectively. The between-group changes for exercise capacity (peak oxygen uptake, 6-minute walk distance) and health status were equivalent. Regarding safety, no sessions required physician involvement, there was 1 major adverse event after a virtual session, and no falls required medical attention. In conclusion, although we rejected our primary hypothesis that attendance would be greater with HYCR versus FBCR, we showed that FBCR and HYCR resulted in similar patient attendance patterns and equivalent improvements in exercise capacity and health status. HYCR which incorporates virtually supervised exercise should be considered an acceptable alternative to FBCR.

Cardiology/Cardiovascular Research

Maligireddy A, **Jabri A**, Zghouzi M, Rojulpote C, VanAken G, Janga C, **Radjef R**, **Aronow H**, **Awdish R**, **Kelly B**, **Grafton G**, Paul TK, Lin CJ, Mikhalkova D, Alaswad K, **Franco-Palacios D**, **Villablanca P**, and **Aggarwal V**. Maternal and Fetal Outcomes in Pulmonary Hypertension During Pregnancy: A Contemporary Nationwide Analysis. *Am J Cardiol* 2024; Epub ahead of print. PMID: 38663575. Full Text

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Pulmonary hypertension (PH) disproportionately affects women, presenting challenges during pregnancy. Historically, patients with PH are advised to avoid pregnancy; however, recent reports have indicated that the incidence of adverse events in pregnant patients with PH may be lower than previously reported. We conducted a retrospective cohort study in pregnant patients with PH using the National Readmission Database from January 1, 2016, to December 31, 2020. PH was categorized according to the World Health Organization classification. Primary end points include maternal mortality and 30-day nonelective readmission rate. Other adverse short-term maternal (cardiovascular and obstetric) and fetal outcomes were also analyzed. Of 9,922,142 pregnant women, 3,532 (0.04%) had PH, with Group 1 PH noted in 1,833 (51.9%), Group 2 PH in 676 (19.1%), Group 3 PH in 604 (17.1%), Group 4 PH in 23 (0.7%), Group 5 PH in 98 (2.8%), and multifactorial PH in 298 (8.4%). PH patients exhibited higher rates of adverse cardiovascular events (15.7% vs 0.3% without PH, p <0.001) and mortality (0.9% vs 0.01% without PH, p <0.001). Mixed PH and Group 2 PH had the highest prevalence of adverse cardiovascular events in the World Health Organization PH groups. Patients with PH had a significantly higher nonelective 30-day readmission rate (10.4% vs 2.3%) and maternal adverse obstetric events (24.2% vs 9.1%) compared with those without PH (p <0.001) (Figure 1). In conclusion, pregnant women with PH had significantly higher adverse event rates, including in-hospital maternal mortality (85-fold), compared with those without PH.

Cardiology/Cardiovascular Research

Raad M, **Greenberg J**, **Altawil M**, **Lee J**, **Wang DD**, **Oudeif A**, **Birchak J**, **Abdelrahim E**, **Makki T**, **Mohammed M**, Chehab O, **Ignatius A**, Singh G, **Maskoun W**, **O'Neill B**, **Lahiri M**, **Eng M**, **Villablanca P**, **Wyman JF**, **Khan A**, Epstein AE, **O'Neill W**, **Schuger C**, and **Frisoli TM**. The Transcatheter Aortic Valve Replacement-Conduction Study: The Value of the His-Ventricular Interval in Risk Stratification for Post-TAVR Atrioventricular-Block. *Structural Heart* 2024. Epub ahead of print. PMID: Not assigned. Full Text

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Background: There is no clear consensus regarding the optimal risk stratification of high-degree atrioventricular block (HDAVB) after transcatheter aortic valve replacement (TAVR). Methods: This prospective study sought to determine the utility of the pre- and post-TAVR His-ventricular (HV) interval in the risk stratification of post-TAVR HDAVB. One hundred twenty-one patients underwent an electrophysiology study before and after TAVR. The primary outcome was HDAVB requiring pacemaker implantation within 30 days post-TAVR. A separate retrospective cohort was analyzed to determine the postoperative interval at which the risk of HDAVB is reduced to <5%. Results: HDAVB occurred in 12 (10%) patients. Baseline right bundle branch block (RBBB) (odds ratio [OR]: 13.6), implant depth >4 mm (OR: 3.9), use of mechanically- or self-expanding valves (OR: 6.3), and post-TAVR HV > 65 ms (OR: 4.9) were associated with increased risk of HDAVB, whereas PR intervals and pre-TAVR HV were not. In patients without baseline RBBB or new persistent left bundle branch block (LBBB), not one patient with post-TAVR HV < 65 ms developed HDAVB. In the separate retrospective cohort (N = 1049), the risk of HDAVB is reduced (<5%) on postoperative days 4 and 3 in patients with pre-TAVR RBBB and post-TAVR persistent LBBB, respectively. Conclusions: Baseline RBBB, new persistent LBBB, implant depth >4 mm, and a post-TAVR HV ≥ 65 ms were associated with a higher risk of post-TAVR HDAVB, whereas an HV ≤ 65 ms was associated with a lower risk. The pre-TAVR HV was not associated with our outcome, and the delta HV did not have practical incremental prognostic value. Among those without pre-TAVR RBBB or post-TAVR persistent LBBB, no patients with post-TAVR HV < 65 ms developed HDAVB.

Cardiology/Cardiovascular Research

Rempakos A, Alexandrou M, Mutlu D, Choi JW, Poommipanit P, Khatri JJ, Young L, Jefferson B, Gorgulu S, Jaffer FA, Chandwaney R, Davies R, Benton S, **Alaswad K**, Azzalini L, Kearney KE, Krestyaninov O, Khelimskii D, Dattilo P, Reddy N, Abi-Rafeh N, Elguindy A, Goktekin O, Rangan BV, Mastrodemos OC, Al-Ogaili A, Sandoval Y, Burke NM, Brilakis ES, and **Basir MB**. Validation of the BCIS CHIP Score in chronic total occlusion percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2024; 103(6):856-862. PMID: 38629740. Full Text

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BACKGROUND: The complex high-risk indicated percutaneous coronary intervention (CHIP) score is a tool developed using the British Cardiovascular Intervention Society (BCIS) database to define CHIP cases and predict in-hospital major adverse cardiac or cerebrovascular events (MACCE). AIM: To assess the validity of the CHIP score in chronic total occlusion (CTO) percutaneous coronary intervention (PCI). METHODS: We evaluated the performance of the CHIP score on 8341 CTO PCIs from the Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS-CTO) performed at 44 centers between 2012 and 2023. RESULTS: In our cohort, 7.8% (n = 647) of patients had a CHIP score of 0, 50.2% (n = 4192) had a CHIP score of 1-2, 26.2% (n = 2187) had a CHIP score of 3-4, 11.7% (n = 972) had a CHIP score of 5-6, 3.3% (n = 276) had a CHIP score of 7-8, and 0.8% (n = 67) had a CHIP score of 9+. The incidence of MACCE for a CHIP score of 0 was 0.6%, reaching as high as 8.7% for a CHIP score of 9+, confirming that a higher CHIP score is associated with a higher risk of MACCE. The estimated increase in the risk of MACCE per one score unit increase was 100% (95% confidence interval [CI]: 65%-141%). The AUC of the CHIP score model for predicting MACCE in our cohort was 0.63 (95% CI: 0.58-0.67). There was a positive correlation between the CHIP score and the PROGRESS-CTO MACE score (Spearman's correlation: 0.37; 95% CI: 0.35-0.39; $p < 0.001$). CONCLUSIONS: The CHIP score has modest predictive capacity for MACCE in CTO PCI.

Center for Health Policy and Health Services Research

Ahmedani BK, **Frank C**, and **Zervos J**. Zero Suicide International: An opportunity across Asia. *Asian J Psychiatr* 2024; 104056. Epub ahead of print. PMID: 38679537. Full Text

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Center for Health Policy and Health Services Research

Boggs JM, Richards J, Simon G, Aguirre-Miyamoto EM, Barton LJ, Beck A, Beidas RS, Bruschke C, Buckingham ETt, Buttlaire S, Clarke G, Coleman K, Flores JP, **Frank C**, Penfold RB, Richardson L, Ryan JM, Schoenbaum M, Sterling S, Stewart C, Yarborough BJH, **Yeh HH**, and **Ahmedani B**. Suicide Screening, Risk Assessment, and Lethal Means Counseling During Zero Suicide Implementation. *Psychiatr Serv* 2024; Epub ahead of print. PMID: 38566561. Full Text

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OBJECTIVE: The authors measured implementation of Zero Suicide (ZS) clinical practices that support identification of suicide risk and risk mitigation, including screening, risk assessment, and lethal means counseling, across mental health specialty and primary care settings. METHODS: Six health care systems in California, Colorado, Michigan, Oregon, and Washington participated. The sample included members ages ≥13 years from 2010 to 2019 (N=7,820,524 patients). The proportions of patients with suicidal ideation screening, suicide risk assessment, and lethal means counseling were estimated. RESULTS: In 2019, patients were screened for suicidal ideation in 27.1% (range 5.0%-85.0%) of mental health visits and 2.5% (range 0.1%-35.0%) of primary care visits among a racially and ethnically diverse sample (44.9% White, 27.2% Hispanic, 13.4% Asian, and 7.7% Black). More patients screened positive for suicidal ideation in the mental health setting (10.2%) than in the primary care setting (3.8%). Of the patients screening positive for suicidal ideation in the mental health setting, 76.8% received a risk assessment, and 82.4% of those identified as being at high risk received lethal means counseling, compared with 43.2% and 82.4%, respectively, in primary care. CONCLUSIONS: Six health systems that implemented ZS showed a high level of variation in the proportions of patients receiving suicide screening and risk assessment and lethal means counseling. Two opportunities emerged for further study to increase frequency of these practices: expanding screening beyond patients with regular health care visits and implementing risk assessment with lethal means counseling in the primary care setting directly after a positive suicidal ideation screening.

Center for Health Policy and Health Services Research

Danzo S, Kuklinski MR, Sterling SA, Beck A, **Braciszewski JM**, Boggs J, Briney JS, Charvat-Aguilar N, Eisenberg N, Kaffl A, Kline-Simon A, **Loree AM**, Lyons VH, Morse EF, Morrison KM, Negusse R, and Scheuer H. Anxiety, depression, and suicidal ideation among early adolescents during the COVID-19 pandemic. *J Adolesc* 2024; Epub ahead of print. PMID: 38678440. Full Text

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BACKGROUND: Anxiety and depression are among the most common and debilitating psychiatric disorders affecting youth, with both related to increased suicide risk. While rates of youth anxiety and depression were increasing before the COVID-19 pandemic, the pandemic further negatively impacted adolescent mental health. Unfortunately, few studies have examined prevalence of these concerns

among early adolescents (ages 10-13) longitudinally during the pandemic. METHOD: The current study examined self-reported anxiety and depression symptoms, and suicidal ideation amongst a general pediatrics population of 11- to 13-year-olds (n = 623) from March through September 2020 (early-pandemic) and approximately 7 months later (September 2020 through May 2021; mid-pandemic). Paired samples proportions were used to examine changes in prevalence of moderate to severe anxiety, depression, and suicidal ideation from early- to mid-pandemic. RESULTS: Results highlight high initial rates and stability in anxiety and suicidal ideation, as well as a significant increase in depression (42.9% increase; $p < .05$) among the full sample during the COVID-19 pandemic. Prevalance of concerns were greatest for females and Hispanic youth during the early-pandemic, and generally highest for females and Medicaid insured youth at mid-pandemic. DISCUSSION: Results extend recent research and underscore the need for continued monitoring of mental health concerns across development for youth who grew up during the COVID-19 pandemic; highlighting the need for sustainable, effective, and accessible early detection, prevention, and intervention strategies. Improving these services is critical to support youth who experienced pandemic-related stressors, and to prepare for supporting youth during future disruptive and isolating events.

Center for Health Policy and Health Services Research
Flores JP, **Kahn G**, Penfold RB, Stuart EA, **Ahmedani BK**, Beck A, Boggs JM, Coleman KJ, Daida YG, Lynch FL, Richards JE, Rossom RC, Simon GE, and Wilcox HC. Adolescents Who Do Not Endorse Risk via the Patient Health Questionnaire Before Self-Harm or Suicide. *JAMA Psychiatry* 2024; Epub ahead of print. PMID: 38656403. Full Text

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IMPORTANCE: Given that the Patient Health Questionnaire (PHQ) item 9 is commonly used to screen for risk of self-harm and suicide, it is important that clinicians recognize circumstances when at-risk adolescents may go undetected. OBJECTIVE: To understand characteristics of adolescents with a history of depression who do not endorse the PHQ item 9 before a near-term intentional self-harm event or suicide. DESIGN, SETTING, AND PARTICIPANTS: This was a retrospective cohort study design using electronic health record and claims data from January 2009 through September 2017. Settings included primary care and mental health specialty clinics across 7 integrated US health care systems. Included in the study were adolescents aged 13 to 17 years with history of depression who completed the PHQ item 9 within 30 or 90 days before self-harm or suicide. Study data were analyzed September 2022 to April 2023. EXPOSURES: Demographic, diagnostic, treatment, and health care utilization characteristics. MAIN OUTCOME(S) AND MEASURE(S): Responded "not at all" (score = 0) to PHQ item 9 regarding thoughts of death or self-harm within 30 or 90 days before self-harm or suicide. RESULTS: The study included 691 adolescents (mean [SD] age, 15.3 [1.3] years; 541 female [78.3%]) in the 30-day cohort and 1024 adolescents (mean [SD] age, 15.3 [1.3] years; 791 female [77.2%]) in the 90-day cohort. A total of 197 of 691 adolescents (29%) and 330 of 1024 adolescents (32%), respectively, scored 0 before self-harm or suicide on the PHQ item 9 in the 30- and 90-day cohorts. Adolescents seen in primary care (odds ratio [OR], 1.5; 95% CI, 1.0-2.1; P = .03) and older adolescents (OR, 1.2; 95% CI, 1.0-1.3; P = .02) had increased odds of scoring 0 within 90 days of a self-harm event or suicide, and adolescents with a history of inpatient hospitalization and a mental health diagnosis had twice the odds (OR, 2.0; 95% CI, 1.3-3.0; P = .001) of scoring 0 within 30 days. Conversely, adolescents with diagnoses of eating disorders were significantly less likely to score 0 on item 9 (OR, 0.4; 95% CI, 0.2-0.8; P = .007) within 90 days. CONCLUSIONS AND RELEVANCE: Study results suggest that older age, history of an inpatient mental health encounter, or being screened in primary care were associated with at-risk adolescents being less

likely to endorse having thoughts of death and self-harm on the PHQ item 9 before a self-harm event or suicide death. As use of the PHQ becomes more widespread in practice, additional research is needed for understanding reasons why many at-risk adolescents do not endorse thoughts of death and self-harm.

Center for Health Policy and Health Services Research
Miller-Matero LR, **Santullano D**, **Rich M**, **Valler M**, **Hecht LM**, **Tobin ET**, and **Ahmedani BK**. Association of health literacy with chronic pain and pain-related distress. *Prof Psychol Res Pr* 2024; 55(2):89-94. PMID: Not assigned. Request Article

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Research suggests health literacy should be considered when treating chronic pain. The purpose of this secondary analysis was to examine the relationship of health literacy with pain and psychological functioning and to determine whether health literacy status was associated with outcomes after a brief psychological intervention for chronic pain. Participants with chronic musculoskeletal pain (N = 60) were randomized to a five-session psychological intervention or control group between September 2018 and February 2020. Participants completed a baseline and postassessment, which included measures of health literacy status (i.e., adequate vs. lower level), pain severity, pain interference, pain catastrophizing, depression, anxiety, and pain acceptance. Participants were mostly female (78.3%) and Black (88.3%) with a mean age of 62.2 years. At baseline, lower levels of health literacy were associated with greater pain severity (p = .003), pain catastrophizing (p = .03), and depressive symptoms (p = .02). Among those randomized to the intervention group, health literacy status was not related to engagement in the intervention. However, those with adequate levels of health literacy were more likely to have lower depressive symptoms (p = .045) and higher acceptance of pain (p = .01) at postintervention compared to those with lower levels. Among individuals with chronic pain, those with lower levels of health literacy may have worse pain and psychological functioning. Those with lower levels may also not benefit as much from standardized psychological interventions for pain management. Clinicians delivering psychological interventions for chronic pain may want to consider screening for health literacy status and adapt the intervention to ensure understanding.

Center for Health Policy and Health Services Research
Sheriff B, Sakyi K, Malm EK, **Zabel C**, Owusu PG, Sowah LA, and Anum A. Knowledge of developmental disabilities and referral sources among health workers in two Ghanaian hospitals. *Int J Dev Disabil* 2024; 70(3):458-468. PMID: 38699501. Full Text

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Proper treatment of developmental disabilities requires health workers to have adequate knowledge of etiology and referral procedures. There is a dearth of research on knowledge of developmental disabilities among health workers in Ghana. The purpose of this study was to document knowledge about developmental disorders, causes, and referral procedures among health workers. Researchers used a successive free-listing method to interview 37 health workers. Developmental disabilities which present with physical symptoms were the most salient disorders identified among health workers, while learning disabilities and attention deficit disorder were largely overlooked. The most commonly listed developmental disabilities were cerebral palsy, Down syndrome, and autism spectrum disorder. Respondents had limited knowledge about the causes of and referral resources for developmental disabilities. Results show the need for continuing medical education, public awareness, and enhanced resources to support the identification and care of children with developmental disabilities in Ghana.

Center for Health Policy and Health Services Research

Simon GE, Rossom RC, Iturralde E, **Ahmedani BK**, Waring SC, Owen-Smith AA, Sterling SA, Miley K, Stults CD, Daida YG, Lynch FL, Beck A, Sanchez K, Coleman KJ, and Shortreed SM. Clozapine Use Among People With Psychotic Disorders Who Experience Specific Indications for Clozapine. *J Clin Psychiatry* 2024; 85(2). PMID: 38696137. Full Text

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Objective: To examine rates of clozapine use among people with psychotic disorders who experience specific indications for clozapine. Methods: Records data from 11 integrated health systems identified patients aged 18 years or older with recorded International Classification of Diseases, Tenth Revision, Clinical Modification, diagnoses of schizophrenia, schizoaffective disorder, or other psychotic disorder who experienced any of the 3 events between January 1, 2019, and December 31, 2019, suggesting indications for clozapine: a diagnosis of self-harm injury or poisoning, suicidal ideation diagnosed or in response to standardized assessments, and hospitalization or emergency department (ED) care for psychotic disorder despite treatment with 2 or more antipsychotic medications. Prescription dispensing data identified all clozapine use prior to or in the 12 months following each indication event. Analyses were conducted with aggregate data from each health system; no individual data were shared. Results: A total of 7,648 patients with psychotic disorder diagnoses experienced at least 1 indication event. Among 1,097 experiencing a self-harm event, 32 (2.9%) had any prior clozapine use, and 10 (0.9%) initiated clozapine during the following 12 months. Among 6,396 with significant suicidal ideation, 238 (3.7%) had any prior clozapine use, and 70 (1.1%) initiated clozapine over 12 months. Among 881 with hospitalization or ED visit despite pharmacotherapy, 77 (8.7%) had any prior clozapine treatment, and 41 (4.7%) initiated clozapine over 12 months. Among those with significant suicidal ideation, rates of both prior clozapine treatment and subsequent initiation varied significantly by race and ethnicity, with rates among Hispanic and non-Hispanic Black patients lower than among non Hispanic White patients. Conclusions: Initiating clozapine treatment is uncommon among people with psychotic disorders who experience events suggesting clozapine is indicated, with even lower rates among Black and Hispanic patients.

Clinical Quality and Safety

Sikorskii A, **Tam S**, Given B, Given CW, **Adjei Boakye E**, **Zatirka T**, **Nair M**, **Su WK**, **Jogunoori S**, **Watson P**, **Movsas B**, and **Chang S**. Thresholds in PROMIS Scores Anchored to Subsequent Unscheduled Health Service Use Among People Diagnosed With Cancer. *JCO Oncol Pract* 2024; Epub ahead of print. PMID: 38564704. Full Text

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PURPOSE: To establish thresholds in the Patient-Reported Outcomes Measurement Information System (PROMIS) pain interference, physical function, fatigue, and depression scores on the basis of their association with subsequent use of the emergency department (ED) or urgent care by people diagnosed with cancer. METHODS: Retrospective data from 952 people seen at Henry Ford Cancer and insured through the Health Alliance Plan were analyzed using generalized linear mixed-effects models. The log odds of ED or urgent care use during 14 or 30 days after each patient-reported outcome (PRO) assessment were related to PRO scores, while adjusting for comorbidity, sociodemographic, and tumor characteristics. RESULTS: Pain interference and physical function were associated with subsequent ED or urgent care visits, but fatigue and depression were not, and the results for 14- and 30-day visits were similar. Thresholds anchored in the likelihood of these visits differed according to cancer stage. For people with advanced cancer, a pain interference score of 60 or higher (odds ratio [OR] 3.75, [95% CI, 1.53 to 7.87]) and a physical function score lower than 40 (OR 2.94, [95% CI, 1.22 to 7.06]) produced the largest ORs with narrowest CIs for 30-day visits. For people with nonadvanced cancer, the thresholds of 65 for pain interference (OR 2.64, [95% CI, 1.40 to 5.01]) and 35 for physical function (OR 1.87, [95% CI, 1.01 to 3.45]) produced largest ORs with narrowest CIs for 30-day visits. CONCLUSION: These anchor-based thresholds in PROMIS scores can inform clinicians' actions with the goal of preventing ED or urgent care visits.

Dermatology

Alexis A, Del Rosso JQ, Forman S, Martorell A, Browning J, Laquer V, Desai SR, York JP, Chavda R, Dhawan S, Moore AY, and **Stein-Gold L**. Importance of treating acne sequelae in skin of color: 6-month phase IV study of trifarotene with an appropriate skincare routine including UV protection in acne-induced post-inflammatory hyperpigmentation. *Int J Dermatol* 2024; Epub ahead of print. PMID: 38685118. Full Text

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BACKGROUND: Acne-induced hyperpigmentation (AIH) may accompany acne vulgaris (AV) inflammation in all skin phototypes. Trifarotene has shown depigmenting properties in vivo. This study evaluated trifarotene plus skincare because it is increasingly recognized that holistic AV management should include skincare and treatments. METHODS: This is a phase IV double-blind, parallel-group study of patients (13-35 years) with moderate AV and AIH treated with trifarotene (N = 60) or vehicle (N = 63) plus skincare regimen (moisturizer, cleanser, and sunscreen) for 24 weeks. Assessments included the AIH overall disease severity (ODS) score, post-AV hyperpigmentation index (PAHPI), exit interviews, photography, and acne assessments. Standard safety assessments were included. RESULTS: Trifarotene 50 µg/g cream improved significantly from baseline in ODS score versus vehicle (-1.6 vs. -1.1,

P = 0.03) at Week 12, but scores were comparable between groups at Week 24 (primary endpoint). Trifarotene had a better reduction in PAHPI score at Week 24 (-18.9% vs. -11.3% vehicle, P < 0.01). Lesion count reductions were higher with trifarotene at Week 12 versus vehicle (P < 0.001) and at Week 24 (P < 0.05), as were IGA success rates versus vehicle at Weeks 12 (P < 0.05) and 24 (P < 0.05). Patients agreed that the skincare regimen contributed to less irritation, making treatment adherence easier. Photography showed improvements in pigmentation and erythema across all skin types. AEs were more common in the vehicle group versus trifarotene (30.2 vs. 16.7%, respectively). CONCLUSIONS: In all skin phototypes, there was more rapid improvement in the ODS and PAHPI scores with trifarotene by Weeks 12 and 24, respectively. The combination of trifarotene and skincare correlated with high patient satisfaction and adherence to the treatment protocol.

Dermatology

Bielamowicz K, **Dimitrion P**, Abla O, Bomken S, Campbell P, Collin M, Degar B, Diamond EL, Eckstein OS, El-Mallawany N, Fluchel M, Goyal G, Henry MM, Hermiston M, Hogarty M, Jeng M, Jubran R, Lubega J, Kumar A, Ladisch S, McClain KL, Merad M, **Mi QS**, Parsons DW, Peckham-Gregory E, Picarsic J, Prudowsky ZD, Rollins BJ, Shaw PH, Wistinghausen B, Rodriguez-Galindo C, and Allen CE. Langerhans cell histiocytosis: NACHO update on progress, chaos, and opportunity on the path to rational cures. *Cancer* 2024; Epub ahead of print. PMID: 38687639. Full Text

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Langerhans cell histiocytosis (LCH) is a myeloid neoplastic disorder characterized by lesions with CD1a-positive/Langerin (CD207)-positive histiocytes and inflammatory infiltrate that can cause local tissue damage and systemic inflammation. Clinical presentations range from single lesions with minimal impact to life-threatening disseminated disease. Therapy for systemic LCH has been established through serial trials empirically testing different chemotherapy agents and durations of therapy. However, fewer than 50% of patients who have disseminated disease are cured with the current standard-of-care vinblastine/prednisone/(mercaptopurine), and treatment failure is associated with long-term morbidity, including the risk of LCH-associated neurodegeneration. Historically, the nature of LCH-whether a reactive condition versus a neoplastic/malignant condition-was uncertain. Over the past 15 years, seminal discoveries have broadly defined LCH pathogenesis; specifically, activating mitogen-activated protein kinase pathway mutations (most frequently, BRAFV600E) in myeloid precursors drive lesion formation. LCH therefore is a clonal neoplastic disorder, although secondary inflammatory features contribute to the disease. These paradigm-changing insights offer a promise of rational cures for patients based on individual mutations, clonal reservoirs, and extent of disease. However, the pace of clinical trial development behind lags the kinetics of translational discovery. In this review, the authors discuss the current understanding of LCH biology, clinical characteristics, therapeutic strategies, and opportunities to improve outcomes for every patient through coordinated agent prioritization and clinical trial efforts.

Dermatology
Bonilla PS, and **de Guzman Strong C**. Nanopore Long-Read Sequencing Solves the Conundrum of FLG Genetics. *J Invest Dermatol* 2024; Epub ahead of print. PMID: 38647516. Full Text

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Dermatology
Gao D, **Ozog D**, and **Veenstra J**. Response to "Squamous Cell Carcinoma in Situ Achieves Tumor Clearance in More Mohs Stages Than Invasive Squamous Cell Carcinoma". *Dermatol Surg* 2024; Epub ahead of print. PMID: 38656894. Full Text

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Dermatology
Garbe C, Forsea AM, Amaral T, Arenberger P, Autier P, Berwick M, Boonen B, Bylaite M, Del Marmol V, Dreno B, Fargnoli MC, Geller AC, Green AC, Greinert R, Hauschild A, Harwood CA, Hoorens I, Kandolf L, Kaufmann R, Kelleners-Smeets N, Lallas A, Lebbé C, Leiter U, **Lim HW**, Longo C, Malvehy J, Moreno D, Pellacani G, Peris K, Robert C, Saiag P, Schadendorf D, Peter Soyer H, Stockfleth E, Stratigos A, Uhara H, Vieira R, Volkmer B, Weinstock MA, Whitaker D, Zalaudek I, Whiteman DC, and Brochez L. Skin cancers are the most frequent cancers in fair-skinned populations, but we can prevent them. *Eur J Cancer* 2024; 204:114074. PMID: 38691877. Full Text

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Cancers of the skin are the most commonly occurring cancers in humans. In fair-skinned populations, up to 95% of keratinocyte skin cancers and 70-95% of cutaneous melanomas are caused by ultraviolet radiation and are thus theoretically preventable. Currently, however, there is no comprehensive global advice on practical steps to be taken to reduce the toll of skin cancer. To address this gap, an expert working group comprising clinicians and researchers from Africa, America, Asia, Australia, and Europe, together with learned societies (European Association of Dermato-Oncology, Euromelanoma, Euroskin, European Union of Medical Specialists, and the Melanoma World Society) reviewed the extant evidence and issued the following evidence-based recommendations for photoprotection as a strategy to prevent skin cancer. Fair skinned people, especially children, should minimise their exposure to ultraviolet radiation, and are advised to use protective measures when the UV index is forecast to reach 3 or higher. Protective measures include a combination of seeking shade, physical protection (e.g. clothing, hat, sunglasses), and applying broad-spectrum, SPF 30 + sunscreens to uncovered skin. Intentional exposure to solar ultraviolet radiation for the purpose of sunbathing and tanning is considered an unhealthy behaviour and should be avoided. Similarly, use of solaria and other artificial sources of ultraviolet radiation to encourage tanning should be strongly discouraged, through regulation if necessary. Primary prevention of skin cancer has a positive return on investment. We encourage policymakers to communicate these messages to the general public and promote their wider implementation.

Dermatology

Gracia-Cazaña T, Aguilera J, Navarro-Bielsa A, González S, **Lim HW**, and Gilaberte Y. New trends on personalized sunscreens. *Photodermatol Photoimmunol Photomed* 2024; 40(3):e12967. PMID: 38616500. Full Text

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BACKGROUND/PURPOSE: Nowadays, there are emerging trends in customized and personalized photoprotection, focusing on the innovative approaches to enhance sun protection efficacy tailored to individual needs. METHODS: We conducted an electronic search of the following databases: MEDLINE, EMBASE, Cochrane Database of Systematic Reviews, Cochrane Skin Group Specialised Skin Register, and TESEO. Specific search terms related to personalized photoprotection and the variables of age, genetic predisposition, skin phototype, photodermatosis, and physiological conditions such as pregnancy, as well as lifestyle habits were used. RESULTS/CONCLUSION: The article highlights the challenges and opportunities in adopting personalized photoprotection strategies, aiming to promote skin health and prevent the harmful effects of UV radiation in the era of precision medicine.

Dermatology

Pelet Del Toro NM, Strunk A, Wu JJ, **Stein Gold L**, Del Rosso JQ, Brodell RT, and Han G. Topical clindamycin for acne vulgaris: analysis of gastrointestinal events. *J Dermatolog Treat* 2024; 35(1):2325603. PMID: 38568005. Full Text

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Purpose: Topical clindamycin, a lincosamide antibiotic, is commonly combined with benzoyl peroxide or a retinoid for acne vulgaris (AV) treatment. While oral and topical clindamycin carry warnings/contraindications regarding gastrointestinal (GI) adverse events (AEs), real-world incidence of GI AEs with topical clindamycin is unknown. This review provides background information and an overview of safety data of topical clindamycin for treating AV.Materials and Methods: Available safety data from published literature, previously unpublished worldwide pharmacovigilance data, and two retrospective cohort studies were reviewed.Results and Conclusions: According to pharmacovigilance data, the rate of GI adverse drug reactions with topical clindamycin-containing products was 0.000045% (64/141,084,533). Results from two retrospective medical record studies of patients with AV indicated that physicians prescribe topical clindamycin equally to patients with or without inflammatory bowel disease history, and that rates of pseudomembranous colitis in these patients were low. In 8 published pivotal clinical trials of topical clindamycin for AV, GI AEs were reported in 1.4% of participants. Limitations include under/inaccurate reporting of AEs or prescription data and limited generalizability. This review of published case reports, worldwide pharmacovigilance data, retrospective US prescription data, and clinical trials safety data demonstrates that the incidence of colitis in patients exposed to topical clindamycin is extremely low.

Dermatology

Soung J, Ständer S, Gutermuth J, Pau-Charles I, Dawson Z, Yang FE, Sun L, Pierce E, Elmaraghy H, and **Stein-Gold L**. Lebrikizumab monotherapy impacts on quality of life scores through improved itch and sleep interference in two Phase 3 trials. *J Dermatolog Treat* 2024; 35(1):2329240. PMID: 38679419. Full Text

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BACKGROUND: Lebrikizumab improved itch, interference of itch on sleep, and quality of life (QoL) in patients with moderate-to-severe atopic dermatitis (AD), in two Phase 3 trials at 16 weeks compared to placebo. OBJECTIVES: We assess improvements in itch and sleep interference due to itch and their impact on QoL measurements after treatment. METHODS: Data were analyzed from ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) in patients with moderate-to-severe AD. QoL was evaluated using Dermatology Life Quality Index (DLQI) at Week 16 in patients (>16 years of age) who were itch responders/non-responders (defined as ≥4-point improvement in Pruritus Numeric Rating Scale) or Sleep-Loss Scale responders/non-responders (defined as ≥2-point improvement in itch interference on sleep). RESULTS: In ADvocate1 and ADvocate2, significantly greater proportions of itch responders had a clinically meaningful improvement in measures related to QoL (DLQI scores (0/1), ≤5 DLQI total score and ≥4-point DLQI improvement) compared to itch non-responders. In both studies, a significantly greater proportion of Sleep-Loss Scale responders, reported a DLQI score of (0/1), DLQI total score of ≤5 and DLQI improvement of ≥4 points compared to Sleep-Loss Scale non-responders. CONCLUSIONS: Improvement in itch and sleep interference due to itch is associated with improvement in the QoL of patients after treatment with lebrikizumab for moderate-to-severe AD. ClinicalTrials.gov registration NCT04146363 (ADvocate1) and NCT04178967 (ADvocate2).

Dermatology
Strahan AG, Davies OMT, Fernández LT, Inena Gaylord IW, Mekonnen YG, Grijsen ML, Ollague JE, Sabushimike D, Polo Silveira L, Maurer T, Dodiuk-Gad RP, Singal A, **Lim HW**, Bhose A, Lubov JE, Jain S, Zehtab M, Allison T, Guerin M, Enbiale W, Rehmus W, Wanat KA, Fuller LC, Bailey E, and Freeman EE. Expanding global health dermatology leadership: launching the GLODERM international mentorship program. *Br J Dermatol* 2024; Epub ahead of print. PMID: 38666309. Full Text

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Dermatology
Waterton KA, Chan S, Yoo J, **Jackson-Richards D**, and Barbosa NS. Best Practices for Clinical Image Collection and Utilization in Patients With Skin of Color. *Cutis* 2024; 113(4):147-149. PMID: Not assigned. Full Text

Dermatology
Xiong M, **Young AT**, Fernandez A, Jones JS, and Kirby AM. Understanding Breast Cancer Surgery Through Tiktok: an Analysis of Video Content and Viewer Engagement. *Ann Surg Oncol* 2024; Epub ahead of print. PMID: 38592623. Full Text

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BACKGROUND: Breast cancer is the most common cancer in adolescents and young adults. Social media, particularly TikTok, has emerged as a crucial platform for sharing health information in this population. This study aims to characterize breast cancer surgery information on TikTok, focusing on content reliability, viewer reception, and areas for improvement. METHODS: We queried the search terms "breast cancer surgery," "mastectomy," and "lumpectomy" on TikTok, evaluating the top 50 videos for each. After watching each video, characteristics were recorded including: creator characteristics, video metrics, viewer reception, and video content. Statistical analysis was performed using Spearman's rank correlations and t-tests. RESULTS: A total of 138 videos were analyzed (excluding 12 duplicates from the initial 150). These videos received 4,895,373 likes and 109,705 comments. The most common content types were storytelling (57%) and education (20%), and the most common creator types were patients (77.3%) and physicians (10.3%). Videos with educational content by physicians were rare (6.5%). Engagement varied on the basis of video length, search terms, and creator characteristics. Overall, viewer comments predominantly expressed support and interest. CONCLUSIONS: Our study reveals that information on breast cancer surgery is widely shared on TikTok and has high viewer engagement. Factors influencing impact include video length, creator background, and search terms. While social media has democratized information sharing, there is a relative lack of physician creators providing objective and educational content. We highlight opportunities for health professionals to engage in social media as a tool for health education and ensure diverse and reliable healthcare content on these platforms.

Diagnostic Radiology

Gongala S, Garcia JA, Korakavi N, Patil N, Akbari H, Sloan A, Barnholtz-Sloan JS, Sun J, **Griffith B**, **Poisson LM**, Booth TC, Jain R, Mohan S, Nasralla MP, Bakas S, Tippareddy C, Puig J, Palmer JD, Shi W, Colen RR, Sotiras A, Ahn SS, Park YW, Davatzikos C, and Badve C. Sex-specific Differences in IDH1-Wildtype Glioblastoma patients in the ReSPOND Consortium. *AJNR Am J Neuroradiol* 2024; Epub ahead of print. PMID: 38684319. Full Text

BACKGROUND: Understanding sex-based differences in glioblastoma patients is necessary for accurate personalized treatment planning to improve patient outcomes. PURPOSE: To investigate sex-specific differences in molecular, clinical and radiological tumor parameters, as well as survival outcomes in glioblastoma, isocitrate dehydrogenase-1 wildtype (IDH1-WT), grade 4 patients. METHODS: Retrospective data of 1832 glioblastoma, IDH1-WT patients with comprehensive information on tumor parameters was acquired from the Radiomics Signatures for Precision Oncology in Glioblastoma (ReSPOND) consortium. Data imputation was performed for missing values. Sex-based differences in tumor parameters, such as, age, molecular parameters, pre-operative KPS score, tumor volumes, epicenter and laterality were assessed through non-parametric tests. Spatial atlases were generated using pre-operative MRI maps to visualize tumor characteristics. Survival time analysis was performed through log-rank tests and Cox proportional hazard analyses. RESULTS: GBM was diagnosed at a median age of 64 years in females compared to 61.9 years in males (FDR = 0.003). Males had a higher Karnofsky Performance Score (above 80) as compared to females (60.4% females Vs 69.7% males, FDR = 0.044). Females had lower tumor volumes in enhancing (16.7 cm(3) Vs. 20.6 cm(3) in males, FDR = 0.001), necrotic core (6.18 cm(3) Vs. 7.76 cm(3) in males, FDR = 0.001) and edema regions (46.9 cm(3) Vs. 59.2 cm(3) in males, FDR = 0.0001). Right temporal region was the most common tumor epicenter in the overall population. Right as well as left temporal lobes were more frequently involved in males. There were no significant differences in survival outcomes and mortality ratios. Higher age, unmethylated O6-methylguanine-DNAmethyltransferase (MGMT) promoter and undergoing subtotal resection increased the mortality risk in both males and females. CONCLUSIONS: Our study demonstrates significant sex-based differences in clinical and radiological tumor parameters of glioblastoma, IDH1-WT, grade 4 patients. Sex is not an independent prognostic factor for survival outcomes and the tumor parameters influencing patient outcomes are identical for males and females. ABBREVIATIONS: IDH1-WT =

isocitrate dehydrogenase-1 wildtype; MGMTp = O6-methylguanine-DNA-methyltransferase promoter; KPS = Karnofsky performance score; EOR = extent of resection; WHO = world health organization; FDR = false discovery rate.

Diagnostic Radiology
Khandare S, **Jalics A**, **Lawrence RL**, **Zauel R**, **Klochko C**, and **Bey MJ**. A novel 3D MRI-based approach for assessing supraspinatus muscle length. *J Biomech* 2024; 168:112110. PMID: 38677025. Full Text

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Rotator cuff (RC) tears are a common source of pain and decreased shoulder strength. Muscle length is known to affect muscle strength, and therefore evaluating changes in supraspinatus muscle length associated with RC pathology, surgical repair, and post-operative recovery may provide insights into functional deficits. Our objective was to develop a reliable MRI-based approach for assessing supraspinatus muscle length. Using a new semi-automated approach for identifying 3D location of the muscle-tendon junction (MTJ), supraspinatus muscle length was calculated as the sum of MTJ distance (distance between 3D MTJ position and glenoid plane) and supraspinatus fossa length (distance between root of the scapular spine and glenoid plane). Inter- and intra-operator reliability of this technique were assessed with intraclass correlation coefficient (ICC) and found to be excellent (ICCs > 0.96). Muscle lengths of 6 patients were determined before RC repair surgery and at 3- and 12-months post-surgery. Changes in normalized muscle length (muscle length as a percentage of pre-surgical muscle length) at 3 months post-surgery varied considerably across patients (16.1 % increase to 7.0 % decrease) but decreased in all patients from 3- to 12-months post-surgery (0.3 % to 17.2 %). This study developed a novel and reliable approach for quantifying supraspinatus muscle length and provided preliminary demonstration of its utility by assessing muscle length changes associated with RC pathology and surgical repair. Future studies can use this technique to evaluate changes over time in supraspinatus muscle length in response to clinical intervention, and associations between muscle length and shoulder function.

Diagnostic Radiology
Soliman SB. A 31-year-old Female Patient with a Thigh Skin Depression. *J Med Ultrasound* 2024; 32(1):97. PMID: 38665337. Full Text

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Emergency Medicine
Ashktorab H, Pizuorno A, Chirumamilla LG, Adeleye F, Dalivand MM, Sherif ZA, Oskrochi G, Challa SR, Jones-Wonni B, Rankine S, Ekwunazu C, Banson A, Kim R, Gilliard C, Ekpe E, Shayegh N, Nyaunu C, Martins C, Slack A, Okwesili P, Abebe M, Batta Y, Ly D, Valarie O, Smith T, Watson K, Kolawole O, Tahmazian S, Atoba S, Khushbakht M, Riley G, Gavin W, Kara A, Hache-Marliere M, Palaiodimos L, Mani VR, Kalabin A, Gayam VR, Garlapati PR, **Miller J**, Jackson F, Carethers JM, Rustgi V, and Brim H. African Americans Possessed High Prevalence of Comorbidities and Frequent Abdominal Symptoms, and Comprised A Disproportionate Share of Covid-19 Mortality among 9,873 Us- Hospitalized Patients Early in the Pandemic. *Arch Intern Med Res* 2024; 7(1):27-41. PMID: 38694760. Full Text

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BACKGROUND AND AIM: Identifying clinical characteristics and outcomes of different ethnicities in the US may inform treatment for hospitalized COVID-19 patients. Aim of this study is to identify predictors of mortality among US races/ethnicities. DESIGN SETTING AND PARTICIPANTS: We retrospectively analyzed de-identified data from 9,873 COVID-19 patients who were hospitalized at 15 US hospital centers in 11 states (March 2020-November 2020). Main Outcomes and Measures: The primary outcome was to identify predictors of mortality in hospitalized COVID-19 patients. RESULTS: Among the 9,873 patients, there were 64.1% African Americans (AA), 19.8% Caucasians, 10.4% Hispanics, and 5.7% Asians, with 50.7% female. Males showed higher in-hospital mortality (20.9% vs. 15.3%, p=0.001). Non-survivors were significantly older (67 vs. 61 years) than survivors. Patients in New York had the highest in-hospital mortality (OR=3.54 (3.03 - 4.14)). AA patients possessed higher prevalence of comorbidities, had longer hospital stay, higher ICU admission rates, increased requirement for mechanical ventilation and higher in-hospital mortality compared to other races/ethnicities. Gastrointestinal symptoms (GI), particularly diarrhea, were more common among minority patients. Among GI symptoms and laboratory findings, abdominal pain (5.3%, p=0.03), elevated AST (n=2653, 50.2%, p=<0.001, OR=2.18), bilirubin (n=577, 12.9%, p=0.01) and low albumin levels (n=361, 19.1%, p=0.03) were associated with mortality. Multivariate analysis (adjusted for age, sex, race, geographic location) indicates that patients with asthma, COPD, cardiac disease, hypertension, diabetes mellitus, immunocompromised status, shortness of breath and cough possess higher odds of in-hospital mortality. Among laboratory parameters, patients with lymphocytopenia (OR2=2.50), lymphocytosis (OR2=1.41), and elevations of serum CRP (OR2=4.19), CPK (OR2=1.43), LDH (OR2=2.10), troponin (OR2=2.91), ferritin (OR2=1.88), AST (OR2=2.18), D-dimer (OR2=2.75) are more prone to death. Patients on glucocorticoids (OR2=1.49) and mechanical ventilation (OR2=9.78) have higher in-hospital mortality. CONCLUSION: These findings suggest that older age, male sex, AA race, and hospitalization in New York were associated with higher in-hospital mortality rates from COVID-19 in early pandemic stages. Other predictors of mortality included the presence of comorbidities, shortness of breath, cough elevated serum inflammatory markers, altered lymphocyte count, elevated AST, and low serum albumin. AA patients comprised a disproportionate share of COVID-19 death in the US during 2020 relative to other races/ethnicities.

Emergency Medicine

Danagoulian S, **Miller J**, **Cook B**, **Gunaga S**, **Fadel R**, **Gandolfo C**, Mills NL, **Modi S**, Mahler SA, Levy PD, **Parikh S**, **Krupp S**, **Abdul-Nour K**, **Klausner H**, **Rockoff S**, **Gindi R**, **Lewandowski A**, **Hudson M**, **Perrotta G**, **Zweig B**, **Lanfear D**, **Kim H**, **Shaheen E**, **Darnell G**, **Nassereddine H**, **Hawatian K**, **Tang A**, Keerie C, and **McCord J**. Is rapid acute coronary syndrome evaluation with high-sensitivity cardiac troponin less costly? An economic evaluation. *J Am Coll Emerg Physicians Open* 2024; 5(2):e13140. PMID: 38567033. Full Text

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OBJECTIVE: Protocols to evaluate for myocardial infarction (MI) using high-sensitivity cardiac troponin (hs-cTn) have the potential to drive costs upward due to the added sensitivity. We performed an economic evaluation of an accelerated protocol (AP) to evaluate for MI using hs-cTn to identify changes in costs of treatment and length of stay compared with conventional testing. METHODS: We performed a planned secondary economic analysis of a large, cluster randomized trial across nine emergency departments (EDs) from July 2020 to April 2021. Patients were included if they were 18 years or older with clinical suspicion for MI. In the AP, patients could be discharged without further testing at 0 h if they had a hs-cTnI < 4 ng/L and at 1 h if the initial value were 4 ng/L and the 1-h value ≤7 ng/L. Patients in the standard of care (SC) protocol used conventional cTn testing at 0 and 3 h. The primary outcome was the total cost of treatment, and the secondary outcome was ED length of stay. RESULTS: Among 32,450 included patients, an AP had no significant differences in cost (+$89, CI: -$714, $893 hospital cost, +$362, CI: -$414, $1138 health system cost) or ED length of stay (+46, CI: -28, 120 min) compared with the SC protocol. In lower acuity, free-standing EDs, patients under the AP experienced shorter length of stay (-37 min, CI: -62, 12 min) and reduced health system cost (-$112, CI: -$250, $25). CONCLUSION: Overall, the implementation of AP using hs-cTn does not result in higher costs.

Emergency Medicine

Lall MD, **Jayaprakash N**, Carrick A, Chang BP, Himelfarb NT, Thomas Y, Wong ML, Dobiesz V, and Raukar NP. Consensus-Driven Recommendations to Support Physician Pregnancy, Adoption, Surrogacy, Parental Leave, and Lactation in Emergency Medicine. *Ann Emerg Med* 2024; Epub ahead of print. PMID: 38639673. Full Text

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The emergency department clinical environment is unique, and guidelines for promoting supportive and equitable workplace cultures ensure success and longevity for pregnant persons and parents in emergency medicine. There is paucity, variability, and dissatisfaction with current parental (historically referred to as maternity and paternity) leave policies. This paper describes the development of consensus-derived recommendations to serve as a framework for emergency departments across the country for incorporating family-friendly policies. Policies that foster a family-inclusive workplace by allowing for professional advancement without sacrificing personal values regardless of sex, gender, and gender identity are critical for emergency medicine recruitment and retention.

Family Medicine
Freedman JD, Eidelman M, Apt E, and Kotlarsky P. Review of Current Concepts in Metatarsus Adductus. *Pediatr Ann* 2024; 53(4):e152-e156. PMID: 38574072. Request Article

Metatarsus adductus (MA), the most common congenital foot deformity, involves adduction of the forefoot at the tarsometatarsal joint, with normal hindfoot alignment. Early diagnosis is important because treatment is more successful if initiated before age 9 months. Treatment of MA depends on deformity severity, in which mild to moderate deformity can be treated conservatively. Current standard of care for severe or rigid deformity involves referral by primary care physicians to specialists for management by casting and splinting. Recently, several orthoses have demonstrated equal effectiveness to casting and may allow for primary care physicians to treat MA without the need for referral. In this review article, we provide an overview of MA and discuss diagnosis and treatment. We also discuss novel devices and suggest how they may affect the future management of severe and rigid MA.

Gastroenterology
Abusuliman M, Amreia M, **Rehman S**, **Chaudhary AJ**, Abosheaishaa H, **Jamali T**, and Hanafi A. Fatal Itching and Failing Liver: A Case Report and Literature Review of Rare, Atypical DRESS (Drug Rash with Eosinophilia and Systemic Symptoms) Syndrome. *Cureus* 2024; 16(3):e55355. PMID: 38559511. Full Text

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DRESS (Drug Rash with Eosinophilia and Systemic Symptoms) syndrome is a rare, life-threatening, hypersensitivity reaction. The prolonged course and non-specific symptoms of the condition make diagnosis challenging. We present a case of DRESS syndrome that was misdiagnosed as urticaria. Investigations revealed deranged liver and kidney functions and abnormal blood count. The presented case emphasizes the need to have a high suspicion for DRESS syndrome in patients who present with jaundice, generalized rash, acute renal failure, and acute liver failure.

Gastroenterology
Dahiya DS, Wachala J, Solanki S, Solanki D, Kichloo A, Holcomb S, Mansuri U, Haq KS, Ali H, Gangwani MK, Shah YR, Varghese T, Khan HMA, Horslen SP, Schiano TD, and **Jafri SM**. Sepsis during short bowel syndrome hospitalizations: Identifying trends, disparities, and clinical outcomes in the United States. *World J Gastrointest Pathophysiol* 2024; 15(1):92085. PMID: 38682025. Full Text

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BACKGROUND: Short bowel syndrome (SBS) hospitalizations are often complicated with sepsis. There is a significant paucity of data on adult SBS hospitalizations in the United States and across the globe. AIM: To assess trends and outcomes of SBS hospitalizations complicated by sepsis in the United States. METHODS: The National Inpatient Sample was utilized to identify all adult SBS hospitalizations between 2005-2014. The study cohort was further divided based on the presence or absence of sepsis. Trends were identified, and hospitalization characteristics and clinical outcomes were compared. Predictors of mortality for SBS hospitalizations complicated with sepsis were assessed. RESULTS: Of 247097 SBS hospitalizations, 21.7% were complicated by sepsis. Septic SBS hospitalizations had a rising trend of hospitalizations from 20.8% in 2005 to 23.5% in 2014 (P trend < 0.0001). Compared to non-septic SBS hospitalizations, septic SBS hospitalizations had a higher proportion of males (32.8% vs 29.3%, P < 0.0001), patients in the 35-49 (45.9% vs 42.5%, P < 0.0001) and 50-64 (32.1% vs 31.1%, P < 0.0001) age groups, and ethnic minorities, i.e., Blacks (12.4% vs 11.3%, P < 0.0001) and Hispanics (6.7% vs 5.5%, P < 0.0001). Furthermore, septic SBS hospitalizations had a higher proportion of patients with intestinal transplantation (0.33% vs 0.22%, P < 0.0001), inpatient mortality (8.5% vs 1.4%, P < 0.0001), and mean length of stay (16.1 d vs 7.7 d, P < 0.0001) compared to the non-sepsis cohort. A younger age, female gender, White race, and presence of comorbidities such as anemia and depression were identified to be independent predictors of inpatient mortality for septic SBS hospitalizations. CONCLUSION: Septic SBS hospitalizations had a rising trend between 2005-2014 and were associated with higher inpatient mortality compared to non-septic SBS hospitalizations.

Gastroenterology
Patel-Rodrigues PA, Cundra L, Alhaqqan D, Gildea DT, Woo SM, and Lewis JH. Herbal- and Dietary-Supplement-Induced Liver Injury: A Review of the Recent Literature. *Livers* 2024; 4(1):94-118. PMID: Not assigned. Full Text

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Gastroenterology
Pohl H, Rex DK, Barber J, Moyer M, Elmunzer J, Rastogi A, Gordon S, Zolotarevsky E, Levenick JM, Aslanian H, **El Atrache M**, Von Renteln D, Bhaumik B, Keswani R, Kumta N, Pleskow DK, Smith Z, Abu Ghanimeh MK, Sanaei O, and Jensen LL. Cold snare endoscopic resection for large colon polyps – a randomized trial. *Endoscopy* 2024; 56:S7-S7. PMID: Not assigned. Request Article

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Global Health Initiative
Ahmedani BK, **Frank C**, and **Zervos J**. Zero Suicide International: An opportunity across Asia. *Asian J Psychiatr* 2024; 104056. Epub ahead of print. PMID: 38679537. Full Text

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Hematology-Oncology
Cloyd JM, Colby S, Guthrie KA, Lowy AM, Chiorean EG, **Philip P**, Sohal D, and Ahmad S. Failure to Undergo Resection Following Neoadjuvant Therapy for Resectable Pancreatic Cancer: A Secondary Analysis of SWOG S1505. *J Natl Compr Canc Netw* 2024; 1-6. Epub ahead of print. PMID: 38688309. Full Text

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BACKGROUND: Neoadjuvant therapy (NT) is increasingly used for patients with pancreatic ductal adenocarcinoma (PDAC), and yet reasons for not undergoing subsequent pancreatectomy are poorly understood. Given the importance of completing multimodality therapy, we investigated factors associated with failure to undergo surgical resection following NT for PDAC. METHODS: SWOG S1505 was a multicenter phase II randomized trial of preoperative mFOLFIRINOX or gemcitabine/nab-paclitaxel prior to planned pancreatectomy for patients with potentially resectable PDAC. Associations between clinical, demographic, and hospital-level characteristics and receipt of surgical resection were estimated via multiple logistic regression. Differences in overall survival from 18 weeks postrandomization (scheduled time of surgery) according to resection status were assessed via Cox regression models. RESULTS: Among 102 eligible patients, 73 (71.6%) underwent successful pancreatectomy, whereas 29 (28.4%) did not, primarily because of progression (n=11; 10.8%) or toxicity during NT (n=9; 8.8%). Weight loss during NT (odds ratio [OR], 0.34; 95% CI, 0.11-0.93) and the hospital's city size (small: OR, 0.24 [95% CI, 0.07-0.80] and large: OR, 0.28 [95% CI, 0.10-0.79] compared with midsize) were significantly associated with a lower probability of surgical resection in adjusted models, whereas age, sex, race, body mass index, performance status, insurance type, geographic region, treatment arm, tumor location, chemotherapy delays/modifications, and hospital characteristics were not. Surgical resection following NT was associated with improved overall survival (median, 23.8 vs 10.8 months; P<.01) even after adjusting for grade 3-5 adverse events during NT, performance status, and body mass index (hazard ratio, 0.55; 95% CI, 0.32-0.95). CONCLUSIONS: Failure to undergo resection following NT was relatively common among patients with potentially resectable PDAC and associated with worse survival. Although few predictive factors were identified in this secondary analysis of the SWOG S1505 randomized trial, further research must focus on risk factors for severe toxicities during NT that preclude surgical resection so that patient-centered interventions can be delivered or alternate treatment sequencing can be recommended.

Hematology-Oncology
Gadgeel SM, Rodríguez-Abreu D, Halmos B, Garassino MC, Kurata T, Cheng Y, Jensen E, Shamoun M, Rajagopalan K, and Paz-Ares L. Pembrolizumab Plus Chemotherapy for Metastatic Non-Small-Cell Lung

Cancer With Programmed Cell Death Ligand 1 Tumor Proportion Score Less Than 1%: Pooled Analysis of Outcomes After 5 Years of Follow-Up. *J Thorac Oncol* 2024; Epub ahead of print. PMID: 38642841. Request Article

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BACKGROUND: We report long-term outcomes from a pooled analysis of patients with previously untreated metastatic non–small-cell lung cancer (NSCLC) with programmed cell death ligand 1 (PD-L1) tumor proportion score (TPS) <1% enrolled in phase 3 studies of pembrolizumab plus chemotherapy versus placebo plus chemotherapy. METHODS: This exploratory pooled analysis included individual patient data from the KEYNOTE-189 global (NCT02578680) and Japan extension (NCT03950674) studies of metastatic nonsquamous NSCLC without EGFR or ALK alterations and the KEYNOTE-407 global (NCT02775435) and China extension (NCT03875092) studies of metastatic squamous NSCLC. Patients received pembrolizumab or placebo plus pemetrexed and cisplatin or carboplatin in KEYNOTE-189 and pembrolizumab or placebo plus carboplatin and paclitaxel or nab-paclitaxel in KEYNOTE-407. PD-L1 TPS was centrally assessed using PD-L1 IHC 22C3 pharmDX (Agilent Technologies, Carpinteria, CA). RESULTS: Overall, 442 patients were included in this analysis (pembrolizumab plus chemotherapy, n=255; chemotherapy, n=187). Median follow-up was 60.7 (range, 49.9–72.0) months. Pembrolizumab plus chemotherapy improved overall survival (OS; hazard ratio [HR], 0.64; 95% CI, 0.51–0.79) and progression-free survival (HR, 0.66; 95% CI, 0.54–0.81) versus chemotherapy. Five-year OS rates (95% CI) were 12.5% (8.6%–17.3%) versus 9.3% (5.6%–14.1%). Grade 3–5 treatment-related adverse events occurred in 59.1% of patients for pembrolizumab plus chemotherapy and 61.3% for chemotherapy. CONCLUSION: With ~5 years of follow-up, pembrolizumab plus chemotherapy provided clinically meaningful and durable improvements in survival outcomes versus chemotherapy alone in patients with previously untreated metastatic NSCLC with PD-L1 TPS <1%. These results continue to support pembrolizumab plus chemotherapy as a standard of care in this patient population.

Hematology-Oncology

Park JJ, Chu A, Li J, Ali A, McKay RR, **Hwang C**, Labriola MK, Jang A, Kilari D, Mo G, Ravindranathan D, Graham LS, Sokolova A, Tripathi A, **Pilling A**, Jindal T, Ravindra A, Cackowski FC, Sweeney PL, Thapa B, Amery TS, Heath EI, Garje R, Zakharia Y, Koshkin VS, Bilen MA, Schweizer MT, Barata PC, Dorff TB, Cieslik M, Alva AS, and Armstrong AJ. Repeat Next-Generation Sequencing Testing on Progression in Men With Metastatic Prostate Cancer Can Identify New Actionable Alterations. *JCO Precis Oncol* 2024; 8:e2300567. PMID: 38579192. Request Article

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PURPOSE: There are limited data available on the real-world patterns of molecular testing in men with advanced prostate cancer. We thus sought to evaluate next-generation sequencing (NGS) testing in the United States, focused on single versus serial NGS testing, the different disease states of testing (hormone-sensitive v castration-resistant, metastatic vs nonmetastatic), tissue versus plasma circulating tumor DNA (ctDNA) assays, and how often actionable data were found on each NGS test. METHODS: The Prostate Cancer Precision Medicine Multi-Institutional Collaborative Effort clinical-genomic database was used for this retrospective analysis, including 1,597 patients across 15 institutions. Actionable NGS data were defined as including somatic alterations in homologous recombination repair genes, mismatch repair deficiency, microsatellite instability (MSI-high), or a high tumor mutational burden ≥10 mut/MB. RESULTS: Serial NGS testing (two or more NGS tests with specimens collected more than 60 days apart) was performed in 9% (n = 144) of patients with a median of 182 days in between test results. For the second NGS test and beyond, 82.1% (225 of 274) of tests were from ctDNA assays and 76.1% (217 of 285) were collected in the metastatic castration-resistant setting. New actionable data were found on 11.1% (16 of 144) of second NGS tests, with 3.5% (5 of 144) of tests detecting a new BRCA2 alteration or MSI-high. A targeted therapy (poly (ADP-ribose) polymerase inhibitor or immunotherapy) was given after an actionable result on the second NGS test in 31.3% (5 of 16) of patients. CONCLUSION: Repeat somatic NGS testing in men with prostate cancer is infrequently performed in practice and can identify new actionable alterations not present with initial testing, suggesting the utility of repeat molecular profiling with tissue or blood of men with metastatic castration-resistant prostate cancer to guide therapy choices.

Hematology-Oncology

Yaeger R, McKean MA, Haq R, Beck JT, Taylor MH, Cohen JE, Bowles DW, **Gadgeel SM**, Mihalcioiu C, Papadopoulos KP, Diamond EL, Sturtz KB, Feng G, Drescher SK, Reddy MB, Sengupta B, Maity AK, Brown SA, Singh A, Brown EN, Baer BR, Wong J, Mou TC, Wu WI, Kahn DR, Gadal S, Rosen N, Gaudino JJ, Lee PA, Hartley DP, and Rothenberg SM. A next-generation BRAF inhibitor overcomes resistance to BRAF inhibition in patients with BRAF-mutant cancers using pharmacokinetics-informed dose escalation. *Cancer Discov* 2024; Epub ahead of print. PMID: 38691346. Full Text

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RAF inhibitors have transformed treatment for BRAF V600-mutant cancer patients, but clinical benefit is limited by adaptive induction of ERK signaling, genetic alterations that induce BRAF V600 dimerization, and poor brain penetration. Next-generation pan-RAF dimer inhibitors are limited by narrow therapeutic index. PF-07799933 (ARRY-440) is a brain-penetrant, selective, pan-mutant BRAF inhibitor. PF-07799933 inhibited signaling in vitro, disrupted endogenous mutant-BRAF:wild-type-CRAF dimers, and spared wild-type ERK signaling. PF-07799933 ± binimetinib inhibited growth of mouse xenograft tumors driven by mutant BRAF that functions as dimers and by BRAF V600E with acquired resistance to current RAF inhibitors. We treated patients with treatment-refractory BRAF-mutant solid tumors in a first-in-human clinical trial (NCT05355701) that utilized a novel, flexible, pharmacokinetics-informed dose escalation design that allowed rapid achievement of PF-07799933 efficacious concentrations. PF-07799933 ± binimetinib was well-tolerated and resulted in multiple confirmed responses, systemically and in the brain, in BRAF-mutant cancer patients refractory to approved RAF inhibitors.

Hospital Medicine
May JE, Triller DM, Inglis L, Rose AE, DiLorenzo-Agramonte V, Burnett AE, Schumock GT, **Kaatz S**, Barnes GD, and Ansell JE. Securing administrative leadership commitment for anticoagulation stewardship programs. *JACCP Journal of the American College of Clinical Pharmacy* 2024; 7(4):384-394. PMID: Not assigned. Full Text

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Anticoagulation is a leading cause of medication-related harm. As a result, there is increasing recognition of the importance of the development of anticoagulation stewardship programs to ensure safe and effective anticoagulation use across health care settings. Securing administrative leadership support to build such programs is a necessary first step but is often a significant barrier to implementation. Herein, we present a structured approach to guide providers advocating to leadership for stewardship programs at their institutions. We divide the approach into four phases: (1) Build the foundation, (2) Select stewardship initiatives, (3) Develop implementation plans, and (4) Prepare and present a business plan. Within each phase, we outline specific actions to consider, all leading up to the end goal of creating a compelling business plan to generate administrative leadership buy-in. We also provide resources to promote the understanding of institutional needs as well as broader trends across health systems that influence stewardship program development. Our aim is to provide stewardship advocates with the tools to effectively secure leadership support to facilitate the development of Anticoagulation Stewardship Programs across all health care institutions.

Hypertension and Vascular Research
Arkhipov SN, **Liao TS**, **Potter DL**, **Bobbitt KR**, **Ivanov V**, **Ortiz PA**, and **Pavlov TS**. Dissociation of Hypertension and Renal Damage After Cessation of High-Salt Diet in Dahl Rats. *Hypertension* 2024; Epub ahead of print. PMID: 38618734. Full Text

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BACKGROUND: Every year, thousands of patients with hypertension reduce salt consumption in the efforts to control their blood pressure. However, hypertension has a self-sustaining character in a

significant part of the population. We hypothesized that chronic hypertension leads to irreversible renal damage that remains after removing the trigger, causing an elevation of the initial blood pressure. METHODS: Dahl salt-sensitive rat model was used for chronic, continuous observation of blood pressure. Rats were fed a high salt diet to induce hypertension, and then the diet was switched back to normal sodium content. RESULTS: We found that developed hypertension was irreversible by salt cessation: after a short period of reduction, blood pressure grew even higher than in the high-salt phase. Notably, the self-sustaining phase of hypertension was sensitive to benzamil treatment due to sustaining epithelial sodium channel hyperactivity, as shown with patch-clamp analysis. Glomerular damage and proteinuria were also irreversible. In contrast, some mechanisms, contributing to the development of salt-sensitive hypertension, normalized after salt restriction. Thus, flow cytometry demonstrated that dietary salt reduction in hypertensive animals decreased the number of total CD45(+), CD3(+)CD4(+), and CD3(+)CD8(+) cells in renal tissues. Also, we found tubular recovery and improvement of glomerular filtration rate in the postsalt period versus a high-salt diet. CONCLUSIONS: Based on earlier publications and current data, poor response to salt restriction is due to the differential contribution of the factors recognized in the developmental phase of hypertension. We suggest that proteinuria or electrolyte transport can be prioritized over therapeutic targets of inflammatory response.

Infectious Diseases

Surie D, Yuengling KA, DeCuir J, Zhu Y, Lauring AS, Gaglani M, Ghamande S, Peltan ID, Brown SM, Ginde AA, Martinez A, Mohr NM, Gibbs KW, Hager DN, Ali H, Prekker ME, Gong MN, Mohamed A, Johnson NJ, Srinivasan V, Steingrub JS, Leis AM, Khan A, Hough CL, Bender WS, Duggal A, Bendall EE, Wilson JG, Qadir N, Chang SY, Mallow C, Kwon JH, Exline MC, Shapiro NI, Columbus C, **Vaughn IA**, **Ramesh M**, Mosier JM, Safdar B, Casey JD, Talbot HK, Rice TW, Halasa N, Chappell JD, Grijalva CG, Baughman A, Womack KN, Swan SA, Johnson CA, Lwin CT, Lewis NM, Ellington S, McMorrow ML, Martin ET, and Self WH. Severity of Respiratory Syncytial Virus vs COVID-19 and Influenza Among Hospitalized US Adults. *JAMA Netw Open* 2024; 7(4):e244954. PMID: 38573635. Full Text

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IMPORTANCE: On June 21, 2023, the Centers for Disease Control and Prevention recommended the first respiratory syncytial virus (RSV) vaccines for adults aged 60 years and older using shared clinical decision-making. Understanding the severity of RSV disease in adults can help guide this clinical decision-making. OBJECTIVE: To describe disease severity among adults hospitalized with RSV and compare it with the severity of COVID-19 and influenza disease by vaccination status. DESIGN, SETTING, AND PARTICIPANTS: In this cohort study, adults aged 18 years and older admitted to the hospital with acute respiratory illness and laboratory-confirmed RSV, SARS-CoV-2, or influenza infection were prospectively enrolled from 25 hospitals in 20 US states from February 1, 2022, to May 31, 2023. Clinical data during each patient's hospitalization were collected using standardized forms. Data were analyzed from August to October 2023. EXPOSURES: RSV, SARS-CoV-2, or influenza infection. MAIN OUTCOMES AND MEASURES: Using multivariable logistic regression, severity of RSV disease was compared with COVID-19 and influenza severity, by COVID-19 and influenza vaccination status, for a range of clinical outcomes, including the composite of invasive mechanical ventilation (IMV) and in-hospital death. RESULTS: Of 7998 adults (median [IQR] age, 67 [54-78] years; 4047 [50.6%] female) included, 484 (6.1%) were hospitalized with RSV, 6422 (80.3%) were hospitalized with COVID-19, and 1092 (13.7%) were hospitalized with influenza. Among patients with RSV, 58 (12.0%) experienced IMV or death, compared with 201 of 1422 unvaccinated patients with COVID-19 (14.1%) and 458 of 5000 vaccinated patients with COVID-19 (9.2%), as well as 72 of 699 unvaccinated patients with influenza (10.3%) and 20 of 393 vaccinated patients with influenza (5.1%). In adjusted analyses, the odds of IMV or in-hospital death were not significantly different among patients hospitalized with RSV and unvaccinated patients hospitalized with COVID-19 (adjusted odds ratio [aOR], 0.82; 95% CI, 0.59-1.13; P = .22) or influenza (aOR, 1.20; 95% CI, 0.82-1.76; P = .35); however, the odds of IMV or death were significantly higher among patients hospitalized with RSV compared with vaccinated patients hospitalized with COVID-19 (aOR, 1.38; 95% CI, 1.02-1.86; P = .03) or influenza disease (aOR, 2.81; 95% CI, 1.62-4.86; P < .001). CONCLUSIONS AND RELEVANCE: Among adults hospitalized in this US cohort during the 16 months before the first RSV vaccine recommendations, RSV disease was less common but similar in severity compared with COVID-19 or influenza disease among unvaccinated patients and more severe than COVID-19 or influenza disease among vaccinated patients for the most serious outcomes of IMV or death.

Infectious Diseases

Vandervelde R, **Mlynarek ME**, **Ramesh M**, Patel N, **Veve MP**, and **August BA**. Impact of time to treatment in first occurrence, non-severe Clostridioides difficile infection for elderly patients: are we waiting too long to treat? *Antimicrob Steward Healthc Epidemiol* 2024; 4(1):e59. PMID: 38698948. Full Text

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OBJECTIVE: Data evaluating timeliness of antibiotic therapy in Clostridioides difficile infections (CDI) are not well established. The study's purpose was to evaluate the impact of time-to-CDI treatment on disease progression. METHODS: A case-control study was performed among hospitalized patients with CDI from 1/2018 to 2/2022. Inclusion criteria were age ≥65 years, first occurrence, non-severe CDI at symptom onset, and CDI treatment for ≥72 hours. Cases included patients who progressed to severe or fulminant CDI; controls were patients without CDI progression. Time to CDI treatment was evaluated in three ways: a classification and regression tree (CART)-defined threshold, time as a continuous variable, and time as a categorical variable. RESULTS: 272 patients were included; 136 with CDI progression, 136 patients without. The median (IQR) age was 74 (69-81) years, 167 (61%) were women, and 108 (40%) were immunosuppressed. CDI progression patients more commonly were toxin positive (66 [49%] vs 52 [38%], P = .087) with hospital-acquired disease (57 [42%] vs 29 [21%], P < 0.001). A CART-derived breakpoint for optimal time-to-CDI treatment of 64 hours established early (184, 68%) and delayed treatment (88, 32%). When accounting for confounding variables, delayed CDI treatment was associated with disease progression (adjOR, 4.6; 95%CI, 2.6-8.2); this was observed regardless of how time-to-CDI-active therapy was evaluated (continuous adjOR, 1.02; categorical adjOR, 2.11). CONCLUSION: Delayed CDI treatment was associated with disease progression and could represent an important antimicrobial stewardship measure with future evaluation.

Internal Medicine
Abusuliman M, Amreia M, **Rehman S**, **Chaudhary AJ**, Abosheaishaa H, **Jamali T**, and Hanafi A. Fatal Itching and Failing Liver: A Case Report and Literature Review of Rare, Atypical DRESS (Drug Rash with Eosinophilia and Systemic Symptoms) Syndrome. *Cureus* 2024; 16(3):e55355. PMID: 38559511. Full Text

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DRESS (Drug Rash with Eosinophilia and Systemic Symptoms) syndrome is a rare, life-threatening, hypersensitivity reaction. The prolonged course and non-specific symptoms of the condition make diagnosis challenging. We present a case of DRESS syndrome that was misdiagnosed as urticaria. Investigations revealed deranged liver and kidney functions and abnormal blood count. The presented case emphasizes the need to have a high suspicion for DRESS syndrome in patients who present with jaundice, generalized rash, acute renal failure, and acute liver failure.

Internal Medicine
Bhasin A, and **Haftka-George A**. Diagnostic Challenges and Treatment Approach to Seronegative Autoimmune Encephalitis. *Cureus* 2024; 16(3):e56844. PMID: 38659526. Full Text

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Seronegative autoimmune encephalitis (AE) is a rare, immune-mediated inflammatory syndrome that presents with a wide spectrum of neuropsychiatric symptoms, such as cognitive impairment, seizures, psychosis, focal neurological defects, and altered consciousness. This disease process presents with no identifiable autoimmune antibodies, which leads to uncertain diagnosis, delayed treatment, and prolonged hospital admissions. Early diagnosis and prompt treatment of AE should not be delayed, as early recognition and treatment leads to improved outcomes and disease reversibility for these patients. In this

study, we present a case report of a 77-year-old male who presented with acutely altered mental status. This patient underwent an extensive workup and demonstrated no signs of clinical improvement throughout a prolonged hospital admission. The diagnostic challenges and treatment obstacles encountered during our care of this patient are described in this case report, along with recommendations for early diagnosis and prompt treatment for patients with suspected seronegative AE.

Internal Medicine
Engel Gonzalez P, **Gregerson S**, **Mahmood S**, **Brooks C**, **Villablanca PA**, **Frisoli TM**, **Lee J**, **Wyman JF**, **Wang DD**, **O'Neill WW**, and **O'Neill BP**. Clinical characteristics and outcomes of alcohol septal ablation in the era of transcatheter valve interventions. *Catheter Cardiovasc Interv* 2024; 103(6):1023-1034. PMID: 38639143. Full Text

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BACKGROUND: The clinical efficacy and safety of alcohol septal ablation (ASA) for obstructive hypertrophic cardiomyopathy (HCM) have been well-established; however, less is known about outcomes in patients undergoing preemptive ASA before transcatheter mitral valve replacement (TMVR). AIMS: The goal of this study is to characterize the procedural characteristics and examine the clinical outcomes of ASA in both HCM and pre-TMVR. METHODS: This retrospective study compared procedural characteristics and outcomes in patient who underwent ASA for HCM and TMVR. RESULTS: In total, 137 patients were included, 86 in the HCM group and 51 in the TMVR group. The intraventricular septal thickness (mean 1.8 vs. 1.2 cm; $p < 0.0001$) and the pre-ASA LVOT gradient (73.6 vs. 33.8 mmHg; $p \leq 0.001$) were higher in the HCM group vs the TMVR group. The mean volume of ethanol injected was higher (mean 2.4 vs. 1.7 cc; $p < 0.0001$). The average neo-left ventricular outflow tract area increased significantly after ASA in the patients undergoing TMVR (99.2 ± 83.37 mm(2) vs. 196.5 ± 114.55 mm(2); p = <0.0001). The HCM group had a greater reduction in the LVOT gradient after ASA vs the TMVR group (49.3 vs. 18 mmHg; $p = 0.0040$). The primary composite endpoint was higher in the TMVR group versus the HCM group (50.9% vs. 25.6%; $p = 0.0404$) and had a higher incidence of new permanent pacemaker (PPM) (25.5% vs. 18.6%; $p = 0.3402$). The TMVR group had a higher rate of all-cause mortality (9.8% vs. 1.2%; $p = 0.0268$). CONCLUSIONS: Preemptive ASA before TMVR was performed in patients with higher degree of clinical comorbidities, and correspondingly is associated with worse short-term clinical outcomes in comparison to ASA for HCM patients. ASA before TMVR enabled percutaneous mitral interventions in a small but significant minority of patients that would have otherwise been excluded. The degree of LVOT and neoLVOT area increase is significant and predictable.

Internal Medicine
Gupta K, Lemor A, Alkhatib A, **McBride P**, **Cowger J**, **Grafton G**, **Alaswad K**, **O'Neill W**, **Villablanca P**, and **Basir MB**. Use of percutaneous mechanical circulatory support for right ventricular failure. *Catheter Cardiovasc Interv* 2024; 103(6):909-916. PMID: 38584525. Full Text

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BACKGROUND: Utilization of right ventricular mechanical circulatory support (RV-MCS) devices has been limited by a lack of recognition of RV failure as well as a lack of availability and experience with RV-MCS. AIMS: We report a single-center experience with the use of percutaneous RV-MCS and report predictors of adverse outcomes. METHODS: This was a single-center retrospective cohort study. Data from consecutive patients who received RV-MCS for any indication between June 2015 and January 2022 were included. Data on baseline comorbidities, hemodynamics, and laboratory values were collected. The primary outcome was in-hospital mortality analyzed as a logistic outcome in a multivariable model. These variables were further ranked by their predictive value. RESULTS: Among 58 consecutive patients enrolled, the median age was 66 years, 31% were female and 53% were white. The majority of

the patients (48%) were hospitalized for acute on chronic heart failure. The majority of the patients were SCAI SHOCK Stage D (67%) and 34 (64%) patients had MCS placed within 24 h of the onset of shock. Before placement of RV-MCS, median central venous pressure (CVP) and RV stroke work index were 20 mmHg and 8.9 g m/m(2), respectively. Median serum lactate was 3.5 (1.6, 6.2) mmol/L. Impella RP was implanted in 50% and ProtekDuo in the remaining 50%. Left ventricular MCS was concomitantly used in 66% of patients. Twenty-eight patients (48.3%) died. In these patients, median serum lactate was significantly higher (4.1 [2.3, 13.0] vs. 2.2 [1.4, 4.0] mmol/L, p = 0.007) and a trend toward higher median CVP (24 [18, 31] vs. 19 [14, 24] mmHg, p = 0.052). In the multivariable logistic model, both serum lactate and CVP before RV-MCS placement were independent predictors of in-hospital mortality. Serum lactate had the highest predictive value. CONCLUSION: In our real-world cohort, 52% of patients treated with RV-MCS survived their index hospitalization. Serum lactate at presentation and CVP were the strongest predictors of in-hospital mortality.

Internal Medicine
Kalsi J, Suffredini J, Pickett JK, Alam M, Kayani W, and Jia X. Ischemic Evaluation and Revascularization in Patients Presenting With Advanced Atrioventricular Block Without Concomitant Acute Myocardial Infarction. *Tex Heart Inst J* 2024; 51(1). PMID: 38665004. Full Text

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Internal Medicine
Lohana AC, Gulati A, Kumar J, Shivani F, and **Kumar D**. The Silent Victims: How the Israel-Palestine War Impacts the Management of Chronic Kidney Disease and End-Stage Renal Disease Patients. *Cureus* 2024; 16(3):e55488. PMID: 38571837. Full Text

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This article discusses the multifaceted impact of wars and armed conflicts on healthcare systems, with a focus on the Israel-Palestine war and its consequences for individuals with chronic kidney disease (CKD) and end-stage renal disease (ESRD). The war has severely disrupted healthcare infrastructure, leading to damage or destruction of hospitals and clinics, shortages in medical supplies and staff, and interruptions in the delivery of essential services. This disruption poses significant challenges for the management of chronic conditions such as CKD and ESRD, where patients rely on regular and specialized care. The article highlights the logistical challenges and health risks faced by these patients, including the interruption of dialysis treatment, shortages of medications, and the impact of displacement on continuity of care. It also addresses the psychological toll on patients, emphasizing the increased stress, anxiety, and depression that can exacerbate their condition. The need for international aid and humanitarian efforts to support CKD and ESRD patients in conflict zones is underscored, along with the importance of addressing the root causes of the conflict to ensure the well-being of vulnerable populations.

Internal Medicine
Singh H, **Patel P**, **Mawari S**, and **Caliman N**. Cyclosporine-Associated Organizing Pneumonia. *Am J Ther* 2024; Epub ahead of print. PMID: 38563735. Full Text

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Nephrology

Bromberg JS, Bunnapradist S, **Samaniego-Picota M**, Anand S, Stites E, Gauthier P, Demko Z, Prewett A, Armer-Cabral M, Marshall K, Kaur N, Bloom MS, Tabriziani H, Bhorade S, and Cooper M. Elevation of Donor-derived Cell-free DNA Before Biopsy-proven Rejection in Kidney Transplant. *Transplantation* 2024; Epub ahead of print. PMID: 38595232. Full Text

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BACKGROUND: Standard-of-care biomarkers for renal allograft rejection are lagging indicators, signaling existing organ injury. This precludes early intervention, when immunological cascades leading to rejection are most susceptible. Donor-derived cell-free DNA (dd-cfDNA) shows promise as an early indicator of rejection, allowing earlier and possibly more effective treatment. This analysis was designed to assess this promise using real-world dd-cfDNA testing evidence. METHODS: This retrospective analysis of the prospective, observational ProActive registry study (NCT04091984) assessed dd-cfDNA and serum creatinine levels before biopsy in 424 patients with ≥1 dd-cfDNA test (n = 1013) in the 6 mo before biopsy. RESULTS: Of 4667 enrolled patients, 1631 patients had ≥18 mo of follow-up data, of which 424 had a biopsy and were included in this analysis. Twenty-six biopsies showed antibody-mediated rejection (ABMR), 62 showed T cell-mediated rejection, and 336 showed nonrejection; each from a unique patient. dd-cfDNA fractions were significantly elevated 5 mo before ABMR biopsies, and 2 mo before T cell-mediated rejection biopsies, compared with nonrejection biopsies. In contrast, serum creatinine did not discriminate between rejection and nonrejection in advance, or concurrent with biopsy. Among patients with nonrejection biopsies, estimated glomerular filtration rate was significantly lower in cases with ≥2 increased dd-cfDNA results (≥1%), compared with those with 0 or 1 increased dd-cfDNA result. CONCLUSIONS: These data indicate that dd-cfDNA is an early indicator of biopsy-proven rejection, especially ABMR, suggesting a greater role for dd-cfDNA in surveillance to identify patients at high risk of ongoing or future rejection, thus requiring closer monitoring, biopsy, or other management changes.

Nephrology

Garcia Valencia OA, Thongprayoon C, Jadlowiec CC, Mao SA, Leeaphorn N, Budhiraja P, **Khoury N**, Vaitla P, Suppadungsuk S, and Cheungpasitporn W. Evaluating Global and Temporal Trends in Pancreas and Islet Cell Transplantation: Public Awareness and Engagement. *Clin Pract* 2024; 14(2):590-601. PMID: 38666804. Full Text

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BACKGROUND: Pancreas transplantation is a crucial surgical intervention for managing diabetes, but it faces challenges such as its invasive nature, stringent patient selection criteria, organ scarcity, and centralized expertise. Despite the steadily increasing number of pancreas transplants in the United States, there is a need to understand global trends in interest to increase awareness of and participation in pancreas and islet cell transplantation. METHODS: We analyzed Google Search trends for "Pancreas Transplantation" and "Islet Cell Transplantation" from 2004 to 14 November 2023, assessing variations in

search interest over time and across geographical locations. The Augmented Dickey-Fuller (ADF) test was used to determine the stationarity of the trends ($p < 0.05$). RESULTS: Search interest for "Pancreas Transplantation" varied from its 2004 baseline, with a general decline in peak interest over time. The lowest interest was in December 2010, with a slight increase by November 2023. Ecuador, Kuwait, and Saudi Arabia showed the highest search interest. "Islet Cell Transplantation" had its lowest interest in December 2016 and a more pronounced decline over time, with Poland, China, and South Korea having the highest search volumes. In the U.S., "Pancreas Transplantation" ranked 4th in interest, while "Islet Cell Transplantation" ranked 11th. The ADF test confirmed the stationarity of the search trends for both procedures. CONCLUSIONS: "Pancreas Transplantation" and "Islet Cell Transplantation" showed initial peaks in search interest followed by a general downtrend. The stationary search trends suggest a lack of significant fluctuations or cyclical variations. These findings highlight the need for enhanced educational initiatives to increase the understanding and awareness of these critical transplant procedures among the public and professionals.

Nephrology

Nishio Lucar AG, Patel A, Mehta S, Yadav A, Doshi M, Urbanski MA, Concepcion BP, Singh N, Sanders ML, Basu A, Harding JL, Rossi A, Adebiyi OO, **Samaniego-Picota M**, Woodside KJ, and Parsons RF. Expanding the access to kidney transplantation: Strategies for kidney transplant programs. *Clin Transplant* 2024; 38(5):e15315. PMID: 38686443. Full Text

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Kidney transplantation is the most successful kidney replacement therapy available, resulting in improved recipient survival and societal cost savings. Yet, nearly 70 years after the first successful kidney transplant, there are still numerous barriers and untapped opportunities that constrain the access to transplant. The literature describing these barriers is extensive, but the practices and processes to solve them are less clear. Solutions must be multidisciplinary and be the product of strong partnerships among patients, their networks, health care providers, and transplant programs. Transparency in the referral, evaluation, and listing process as well as organ selection are paramount to build such partnerships. Providing early culturally congruent and patient-centered education as well as maximizing the use of local resources to facilitate the transplant work up should be prioritized. Every opportunity to facilitate pre-emptive kidney transplantation and living donation must be taken. Promoting the use of telemedicine and kidney paired donation as standards of care can positively impact the work up completion and maximize the chances of a living donor kidney transplant.

Neurology

Albanna AJ, **Jumah A**, **Agarwal U**, **Fana M**, **Kareem SA**, and **Miller D**. Anticoagulation Therapy in a Patient who had two Consecutive Strokes After Antibiotic Therapy for Infective Endocarditis: A Case Report. *Neurohospitalist* 2024; 14(2):204-207. PMID: 38666280. Full Text

Department of Neurology, Henry Ford Hospital, Detroit, MI, USA. RINGGOLD: 2971

A 77-year-old male presented with altered mentation and was diagnosed with infective endocarditis. Echocardiography revealed aortic valve vegetations. While receiving inpatient antibiotic therapy, the patient experienced an acute ischemic stroke. Magnetic resonance imaging of the brain showed punctate embolic-appearing infarcts in the right cerebellum and in the left occipital, frontal, and parietal lobes. Anticoagulation was not initiated due to a high risk of hemorrhagic transformation. He was readmitted after being discharged due to another episode of altered mentation. Repeat echocardiography indicated increased size of aortic valve vegetations. The patient was then transferred to our hospital for surgical intervention of enlarging vegetations, however was deemed unsuitable for surgery. During hospitalization, he suffered another embolic stroke in the right frontal lobe. By this time, the patient had completed a full course of antibiotics for infective endocarditis, and additional antibiotics were deemed unnecessary by our infectious disease specialists. Literature review highlighted that residual vegetations carry a higher risk for stroke, but no clear guidelines were found on how to intervene or assess the risk of hemorrhage with anticoagulation in this population. Consequently, a decision was made to initiate anticoagulation, Follow-up imaging revealed no evidence of hemorrhagic transformation. Subsequently, the patient remained stable and was discharged to a rehabilitation center, where he did not experience any further events.

Neurology
Chen L, **Xiong Y**, **Chopp M**, and **Zhang Y**. Engineered exosomes enriched with select microRNAs amplify their therapeutic efficacy for traumatic brain injury and stroke. *Front Cell Neurosci* 2024; 18:1376601. PMID: 38566841. Full Text

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Traumatic brain injury (TBI) and stroke stand as prominent causes of global disability and mortality. Treatment strategies for stroke and TBI are shifting from targeting neuroprotection toward cell-based neurorestorative strategy, aiming to augment endogenous brain remodeling, which holds considerable promise for the treatment of TBI and stroke. Compelling evidence underscores that the therapeutic effects of cell-based therapy are mediated by the active generation and release of exosomes from administered cells. Exosomes, endosomal derived and nano-sized extracellular vesicles, play a pivotal role in intercellular communication. Thus, we may independently employ exosomes to treat stroke and TBI. Systemic administration of mesenchymal stem cell (MSC) derived exosomes promotes neuroplasticity and neurological functional recovery in preclinical animal models of TBI and stroke. In this mini review, we describe the properties of exosomes and recent exosome-based therapies of TBI and stroke. It is noteworthy that the microRNA cargo within exosomes contributes to their therapeutic effects. Thus, we provide a brief introduction to microRNAs and insight into their key roles in mediating therapeutic effects. With the increasing knowledge of exosomes, researchers have "engineered" exosome microRNA content to amplify their therapeutic benefits. We therefore focus our discussion on the therapeutic benefits of recently employed microRNA-enriched engineered exosomes. We also discuss the current opportunities and challenges in translating exosome-based therapy to clinical applications.

Neurology
Jumah A, **Albanna AJ**, **Qureshi M**, and **Malik S**. Reversible Cerebral Vasoconstriction Syndrome Secondary to Loperamide Ingestion: A Case Report. *Neurohospitalist* 2024; 14(2):186-188. PMID: 38666269. Full Text

Department of Neurology, Henry Ford Hospital, Detroit, MI, USA. RINGGOLD: 24016

Reversible cerebral vasoconstriction syndrome (RCVS) is a cerebrovascular disorder highlighted by diffuse and multifocal vasoconstriction of the cerebral circulation. This syndrome has been reported to be associated with provoking vasoactive agents, and the identification of such offenders is quite challenging. In our case, the patient's RCVS was caused by the ingestion of loperamide. Although being reported in the cardiac literature, cerebral vasoconstriction due to loperamide has not been reported yet.

Neurology
Jumah A, **Fana M**, Aboul-Nour H, **Albanna AJ**, **AlSrouji OK**, and **Chebl A**. Guidezilla Catheter in Neuroendovascular Interventions: A Case Series Study. *World Neurosurg* 2024; Epub ahead of print. PMID: 38663737. Full Text

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BACKGROUND: Neuroendovascular procedures can be challenging due to severe angulation of the cervical and cranial vessels. Typical approaches for overcoming this tortuosity involve using multiple telescoping catheter systems to provide proximal support for therapeutic device delivery. While this approach can be effective, it does have limitations. METHODS: We describe the utility of the Guidezilla™ (Boston Scientific, Natick, MA) guide extension catheter, a device designed for coronary interventions, in the treatment of three patients undergoing neuroendovascular procedures. In the following cases, the decision to use a guide extension catheter had varied, but mainly were due to severe tortuosity, heavy calcifications, and failure to introduce stents into distal locations. CONCLUSION: Although helpful in overcoming challenging anatomy, the Guidezilla™ guide extension catheter should be used with caution when used as a bailout device.

Neurology
Kaur J, **Boyd ED**, **Ding G**, **Zhang L**, **Luo H**, **Li Q**, **Li L**, **Wei M**, **Landschoot-Ward J**, **Chopp M**, **Zhang Z**, and **Jiang Q**. The Association between Glymphatic System and Perivascular Macrophages in Brain Waste Clearance. *Diagnostics (Basel)* 2024; 14(7). PMID: 38611644. Full Text

Department of Neurology, Henry Ford Health System, Detroit, MI 48202, USA.
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The glymphatic system suggests the convective bulk flow of cerebrospinal fluid (CSF) through perivascular spaces and the interstitial spaces of the brain parenchyma for the rapid removal of toxic waste solutes from the brain. However, the presence of convective bulk flow within the brain interstitial spaces is still under debate. We first addressed this argument to determine the involvement of the glymphatic system in brain waste clearance utilizing contrast-enhanced 3D T1-weighted imaging (T1WI), diffusion tensor imaging (DTI), and confocal microscopy imaging. Furthermore, perivascular macrophages (PVMs), which are immune cells located within perivascular spaces, have not been thoroughly explored for their association with the glymphatic system. Therefore, we investigated tracer uptake by PVMs in the perivascular spaces of both the arteries/arterioles and veins/venules and the potential association of PVMs in assisting the glymphatic system for interstitial waste clearance. Our findings demonstrated that both convective bulk flow and diffusion are responsible for the clearance of interstitial waste solutes from the brain parenchyma. Furthermore, our results suggested that PVMs may play an important function in glymphatic system-mediated interstitial waste clearance. The glymphatic system and PVMs could be targeted to enhance interstitial waste clearance in patients with waste-associated neurological conditions and aging.

Neurosurgery
Chen L, **Xiong Y**, **Chopp M**, and **Zhang Y**. Engineered exosomes enriched with select microRNAs amplify their therapeutic efficacy for traumatic brain injury and stroke. *Front Cell Neurosci* 2024; 18:1376601. PMID: 38566841. Full Text

Department of Neurosurgery, Henry Ford Health, Detroit, MI, United States.
Department of Neurology, Henry Ford Health, Detroit, MI, United States.

Department of Physics, Oakland University, Rochester, MI, United States.

Traumatic brain injury (TBI) and stroke stand as prominent causes of global disability and mortality. Treatment strategies for stroke and TBI are shifting from targeting neuroprotection toward cell-based neurorestorative strategy, aiming to augment endogenous brain remodeling, which holds considerable promise for the treatment of TBI and stroke. Compelling evidence underscores that the therapeutic effects of cell-based therapy are mediated by the active generation and release of exosomes from administered cells. Exosomes, endosomal derived and nano-sized extracellular vesicles, play a pivotal role in intercellular communication. Thus, we may independently employ exosomes to treat stroke and TBI. Systemic administration of mesenchymal stem cell (MSC) derived exosomes promotes neuroplasticity and neurological functional recovery in preclinical animal models of TBI and stroke. In this mini review, we describe the properties of exosomes and recent exosome-based therapies of TBI and stroke. It is noteworthy that the microRNA cargo within exosomes contributes to their therapeutic effects. Thus, we provide a brief introduction to microRNAs and insight into their key roles in mediating therapeutic effects. With the increasing knowledge of exosomes, researchers have "engineered" exosome microRNA content to amplify their therapeutic benefits. We therefore focus our discussion on the therapeutic benefits of recently employed microRNA-enriched engineered exosomes. We also discuss the current opportunities and challenges in translating exosome-based therapy to clinical applications.

Neurosurgery

Hunt R, **Scarpace L**, and **Rock JP**. Intraoperative Augmented Reality for Complex Glioma Resection: A Case Report. *Cureus* 2024; 16(4):e57717. PMID: 38711731. Full Text

Neurosurgery, Henry Ford Health, Detroit, USA.
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Augmented reality (AR) is an emerging technology that can display three-dimensional patient anatomy in the surgeons' field of view. The use of this technology has grown considerably for both presurgical and intraoperative guidance. A patient diagnosed with breast cancer started to experience numbness in the left hand, which progressed to weakness in the left hand and arm. An MRI was performed demonstrating a 2.9 cm X 1.8 cm lesion with extensive surrounding edema in the posterior fronto-parietal lobes. Surgery was recommended for presumed metastatic disease. Preoperatively, an AR system and Brainlab navigation were registered to the patient. AR, traditional navigation, and ultrasound were all used to localize the lesion and determine the craniotomy site and size. The tumor was removed along the direction of the lesion. Intraoperatively, we used AR to reexamine the tumor details and could appreciate that we had to redirect our surgical trajectory anteriorly and laterally in order to follow along the main axis of the tumor. In doing this, we were able to more confidently remain with the tumor, which by this time was poorly defined by 2D navigation and by direct vision. Postoperative MRI confirmed gross total removal of the tumor. The patient had an uneventful postoperative course with resolution of preoperative symptoms and the final surgical pathology was grade 4 glioblastoma. Here, we describe the valuable use of AR for the resection of a glioma. The system has a seamless registration process and provides the surgeon with a unique view of 3D anatomy overlaid onto the patient's head. This exciting technology can add tremendous value to complex cranial surgeries.

Obstetrics, Gynecology and Women’s Health Services

Zaiem F, Bedi M, **Kheil M**, Abujamea A, Jain D, Rosen D, Alkaram W, Kim S, Ali-Fehmi R, and Gogoi R. Correlation between steroid receptor expression and response to progestational therapy in patients with atypical endometrial hyperplasia or cancer. *Gynecol Oncol Rep* 2024; 53:101402. PMID: 38699462. Full Text

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BACKGROUND: Conservative management of atypical endometrial hyperplasia (AEH) or endometrial cancer (EMCA) often relies on the treatment of synthetic progestins, which show varied success and response rates. We evaluate the correlation between steroid receptor expression and response to progestin therapy in patients with AEH and EMCA. METHODS: Retrospective cohort study collected data for patients with AEH or EMCA who had an endometrial sample after receiving conservative therapy utilizing either Megestrol acetate or Levonorgestrel Intrauterine device (IUD). Immunohistochemistry (IHC) was performed on pre- and post- treatment biopsy samples to assess androgen receptor (AR), estrogen receptor (ER), and progesterone receptor (PR) expression. IHC scores (1-12) were calculated based on staining intensity and percentage of positive cells. RESULTS AND ANALYSIS: We identified 15 patients with AEH and EMCA between 2015 and 2023 with the majority of African American ethnicity (53 %). Fourteen patients (93 %) received Megestrol acetate, and 1 patient received Levonorgestrel IUD alone. Three patients ultimately underwent hysterectomy. Seven (46.6 %) endometrial samples had strong positivity for AR, PR and ER expression on pre-treatment biopsies, and only 3 (20 %) of them maintained strong positivity for the 3 receptors in the post-treatment. Patients who successfully responded to the treatment demonstrated a significantly greater decrease in IHC scores after the treatment compared to those who did not respond ($p = 0.009$). CONCLUSION: Steroid receptor expression could be used as a possible biomarker for response to progestin therapy in patients undergoing conservative management for AEH and EMCA.

Ophthalmology and Eye Care Services

Frechie M, **Robbins C**, **Katz B**, and **Crandall D**. Advances in the Management of Dislocated Intraocular Lenses. *Advances in Ophthalmology and Optometry* 2024. Epub ahead of print. PMID: Not assigned. Full Text

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Orthopedics/Bone and Joint Center

Banks EM, **Braman JP**, Harrison AK, and Rao AJ. Anatomic shoulder arthroplasty in patients 40 years or younger. *Semin Arthroplasty* 2024. Epub ahead of print. PMID: Not assigned. Full Text

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Background: Glenohumeral arthritis in adults less than 40 years old represents a challenging clinical scenario to manage. While patients older than 55 have had reproducible success with current shoulder arthroplasty techniques, young patients have historically had less successful outcomes, possibly due to higher physical demands and more complex pathologies. Despite these concerns, anatomic total shoulder arthroplasty (TSA) remains the treatment of choice for young, active patients with severe glenohumeral arthritis and intact rotator cuff. We hypothesize that TSA provides significant relief in pain and functional outcomes in patients less than 40 years old. Methods: We performed a single-institution retrospective analysis of consecutive patients aged 40 years and younger who underwent TSA between 2007 and 2022. Demographic data included age, sex, body mass index, Charlson comorbidity index, and preoperative diagnosis. Outcome measures included the Single-Assessment Numerical Evaluation (SANE) score, final range of motion, complications, and revision rate. Statistically significant differences between variables were evaluated using a 2-sample t-test at an α level of $P < .05$. Results: Twenty-six TSAs were performed in 23 patients with an average final follow-up of 2 years after the procedure. The average age was 33.4 ± 5.3 years with a range of 19-39 years. The most common preoperative diagnosis was osteoarthritis (46%), followed by rheumatoid arthritis (27%) and osteonecrosis/avascular necrosis (19%). The most common glenoid morphology was type B (15) of which 14 were B2 glenoid, followed by type A (11). The SANE score, mean active forward elevation, abduction, external rotation, and internal rotation all improved significantly ($P < .05$) by the final follow-up. On average, patients in all groups were able to achieve minimal clinically important difference in SANE score after 1 year. There was 1 complication reported of an early postoperative infection treated with irrigation and débridement, and no

revision surgeries were performed during the follow-up period. Discussion/Conclusion: TSA significantly improved functional outcome measures in patients less than 40 years old with a low rate of complications and revisions in short-term outcomes. As the frequency of TSA continues to increase in adults less than 40 years old, additional studies recording long-term functional outcomes and implant survivorship in this population can be explored.

Orthopedics/Bone and Joint Center
Gaudiani MA, **Castle JP**, **Wolterink TD**, Sprys-Tellner TJ, **Haan JW**, and **Sean Lynch T**. Analysis of Player Performance and Financial Costs Associated With Implementation of an Updated National Hockey League Concussion Protocol: A Retrospective Comparative Study. *Orthop J Sports Med* 2024; 12(4):23259671241231757. PMID: 38665385. Full Text

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BACKGROUND: An updated National Hockey League (NHL) concussion protocol (NHLCP) was established in the 2016-2017 season to mitigate the negative outcomes of sport-related concussions. However, few studies on the effects of implementing the NHLCP have been performed. PURPOSE: To define concussion incidence and investigate differences in NHL player performance after a concussion during periods before and after NHLCP implementation and assess the financial impact on NHL teams associated with NHLCP implementation. STUDY DESIGN: Cohort study; Level of evidence, 3. METHODS: This was a retrospective review of NHL players who sustained a concussion before (2000-2001 to 2015-2016 seasons) and after (2016-2017 to 2020-2021 seasons) implementing the NHLCP (pre-NHLCP and post-NHLCP groups). For each group, multiple performance metrics-including 30 days, 1 season, and 3 seasons before and after concussion-were compared for both groups. Return to play, total concussion cost, and association of return to play with cost were investigated using regression analysis. RESULTS: A total of 452 players (423 skaters, 29 goalies) sustained concussions during the study period, including 331 players (315 skaters, 16 goalies) in the pre-NHLCP group and 121 players (108 skaters, 13 goalies) in the post-NHLCP group. For both groups, no significant differences in standard performance were observed during the 30-day and 1-season periods before and after concussion. The mean return to play was significantly higher in the pre-NHLCP group than in the post-NHLCP group (20.1 vs 15.7 days; P = .022). The mean adjusted player salary was not different between groups; nonetheless, the mean adjusted replacement player salary was significantly higher in the post-NHLCP group ($744,505 vs $896,942; P = .032). The mean cost of time missed did not differ between groups. The mean return to play time significantly decreased over the entire study period (R(2) = 0.33; P = .005), and the mean return to play time was positively associated with cost R(2) = 0.215; P = .030). CONCLUSION: Concussion incidence did not change after implementation of the updated NHLCP; nonetheless, players had significantly less missed time from injury after protocol implementation. Changes in player performance 30 days and 1 year before and after concussion injury were not different before and after NHLCP implementation. No differences were found in the financial cost of concussions between the pre- and post-NHLCP groups, and missed time was significantly correlated with mean cost from missed time.

Orthopedics/Bone and Joint Center
Guthrie ST, Dagher T, Essey-Stapleton J, and Balach T. Preference Signaling in the Orthopaedic Surgery Match: Applicant and Residency Program Attitudes, Behaviors, and Outcomes. *JB JS Open Access* 2024; 9(2). PMID: 38685965. Full Text

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INTRODUCTION: The orthopaedic surgery match has experienced a consistent increase in both the number of applicants and applications submitted per applicant. Preference signaling was implemented during the 2022 to 2023 application cycle in part to curtail the rising application burden on both applicants

and residency programs. Our aim was to explore the impact of the preference signaling system on applicant and residency program leader attitudes, behaviors, and outcomes. METHODS: We distributed surveys to American Orthopaedic Association/Council of Orthopaedic Residency Directors member program leaders (program directors, assistant program directors, and program coordinators) and applicants registered for the Electronic Standardized Letter of Recommendation after Universal Interview Offer Day 2022 (Fall Survey) and Match Day 2023 (Spring Survey). The surveys contained multiple-choice and numeric response questions on attitudes, behaviors, and outcomes that were analyzed and reported as percentages and medians, respectively. Open-text responses were reviewed for dominant themes. RESULTS: One hundred program leaders and 378 applicants (47%) completed the Fall Survey, and 146 program leaders and 290 applicants (36%) completed the Spring Survey. A majority of applicants (71%) and program leadership (91%) support the continued use of signaling. Applicants reported a 16% reduction in the number of programs to which they applied. Program directors largely used signaling as a tool for screening applications (75%), with few programs using signaling in the ranking process (20%). Applicants reported that 81% of their interviews were from programs they signaled. Slightly more than half of programs (53%) reported filling their last slot at a higher rank order position than the average of the previous 5 years. Qualitative analysis suggests a need for more transparency in the use of signals, consideration of application and/or interview caps, and reconsideration of the other components of the application. CONCLUSION: Preference signaling in the orthopaedic surgery match was met with positive feedback and led to a reduction in the number of applications. Future research will examine the continued impact of preference signaling and assess alterations for optimizing the match process.

Orthopedics/Bone and Joint Center

Huh J, Louis-Ugbo J, Sr., Hembree WC, Wagner E, Chodos MD, **Zingas CN**, Vopat BG, Dalal A, Alhadhoud M, and Sherman TI. 2023 Evidence-Based Medicine (EBM) Update. *Foot Ankle Int* 2024; Epub ahead of print. PMID: 38676415. Full Text

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Orthopedics/Bone and Joint Center

Khandare S, **Jalics A**, **Lawrence RL**, **Zauel R**, **Klochko C**, and **Bey MJ**. A novel 3D MRI-based approach for assessing supraspinatus muscle length. *J Biomech* 2024; 168:112110. PMID: 38677025. Full Text

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Rotator cuff (RC) tears are a common source of pain and decreased shoulder strength. Muscle length is known to affect muscle strength, and therefore evaluating changes in supraspinatus muscle length associated with RC pathology, surgical repair, and post-operative recovery may provide insights into

functional deficits. Our objective was to develop a reliable MRI-based approach for assessing supraspinatus muscle length. Using a new semi-automated approach for identifying 3D location of the muscle-tendon junction (MTJ), supraspinatus muscle length was calculated as the sum of MTJ distance (distance between 3D MTJ position and glenoid plane) and supraspinatus fossa length (distance between root of the scapular spine and glenoid plane). Inter- and intra-operator reliability of this technique were assessed with intraclass correlation coefficient (ICC) and found to be excellent (ICCs > 0.96). Muscle lengths of 6 patients were determined before RC repair surgery and at 3- and 12-months post-surgery. Changes in normalized muscle length (muscle length as a percentage of pre-surgical muscle length) at 3 months post-surgery varied considerably across patients (16.1 % increase to 7.0 % decrease) but decreased in all patients from 3- to 12-months post-surgery (0.3 % to 17.2 %). This study developed a novel and reliable approach for quantifying supraspinatus muscle length and provided preliminary demonstration of its utility by assessing muscle length changes associated with RC pathology and surgical repair. Future studies can use this technique to evaluate changes over time in supraspinatus muscle length in response to clinical intervention, and associations between muscle length and shoulder function.

Orthopedics/Bone and Joint Center
Prater AR, **McConnell JT**, **Yedulla NR**, **Peterson EL**, **Banka TR**, and **Day CS**. The Impact of Experience Versus Decision Aids on Patient Preference Toward Virtual Care. *Telemed Rep* 2024; 5(1):59-66. PMID: 38558954. Full Text

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INTRODUCTION: Virtual care utilization has increased in recent years bringing questions of how to best inform patients regarding their use. Decision aids (DAs) are tools created to assist patients in making informed decisions about their health care. This study seeks to determine whether a DA or previous experience could better educate and influence patient's preference on virtual care. METHODS: One hundred fifty participants from an orthopedic clinic of a multi-hospital system were divided into three groups. Group 1 (Virtual Care Cohort) had at least one previous virtual care visit and was surveyed with the Telemedicine Satisfaction Questionnaire (TSQ). Group 2 (In-person with Decision Aid) and Group 3 (In-person without Decision Aid) had no virtual care experience. Group 2 received a validated virtual care DA with a knowledge test. Both groups were also administered the TSQ. RESULTS: After the DA, patients improved their score on 3 of 4 virtual care knowledge questions. Each cohort demonstrated a positive perception of virtual care; however, the specific reasons for their favorable views varied. The DA cohort did not show increased preference toward virtual care compared with the non-DA group and only responded significantly higher regarding encounter comfort. Patients with previous experience in virtual care responded most favorably to the majority of survey questions regarding their virtual care preferences when compared with both virtual care naive cohorts. DISCUSSION AND CONCLUSION: We found that patient experience was the most important factor in influencing patient preference toward virtual care. Although the DA increased their virtual care knowledge it did not increase their preference; therefore, efforts should be placed at encouraging patient to experience virtual care.

Orthopedics/Bone and Joint Center
Schell LE, **Muh SJ**, Elwell JA, Jacobson S, Barfield WR, Roche CP, Eichinger JK, and Friedman RJ. Clinical outcomes based on planned glenoid baseplate retroversion in reverse total shoulder arthroplasty. *Semin Arthroplasty* 2024. Epub ahead of print. PMID: Not assigned. Full Text

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Background: While surgeons attempt to correct the baseplate version of a reverse total shoulder arthroplasty (rTSA), clinical outcomes based on the planned final version remain unknown. The purpose of this study is to determine the clinical and radiographic outcomes of rTSA based on the planned final version of the baseplate. Our hypothesis is that increasing component retroversion will not affect outcomes. Methods: All primary rTSA patients in a multicentered international registry with a 2-year

minimum follow-up implanted with computer navigation were included, except fracture and revision indications. A single medialized glenoid/lateralized humerus rTSA implant system was used with a standard or augmented baseplate. Patients were stratified by baseplate type and final planned baseplate version into 2 cohorts: 0°-5° (Group 1) or 6°-15° (Group 2) of retroversion. Demographics, radiographic outcomes, range of motion, and patient-reported outcome scores were compared between groups using Welch's t-test and Fisher's Exact test. Results: Five hundred and thirty-five patients (307 females/226 males/2 unknown) were identified, with a mean follow-up of 30 months. Demographics were similar between the cohorts. The mean native and final retroversion was 9.0° and 1.5° in Group 1 and 16.3° and 8.6° in Group 2, respectively. Preoperatively, 72% of patients were 6°-15° retroverted. Postoperatively, 73% of patients were 0°-5° retroverted and 27% were 6°-15°, with 97% of patients having less than or equal to 10° of planned baseplate retroversion. Without stratifying for baseplate types, there were no clinically significant differences between the cohorts with regards to postoperative pain, range of motion, or patient-reported outcome scores, except for abduction and internal rotation greater in the 6°-15° and 0°-5° cohorts, respectively. Scapular notching was low (7% vs. 8%) and less than reported without computer navigation. Complication and revision rates were similar between the 2 groups. Patient satisfaction was high (much better/better, 94% vs 95%) and not significantly different between the 2 groups. Discussion: There were no significant clinical differences between cohorts. This study demonstrates that favorable outcomes are achieved with a planned final baseplate version of less than 15° retroversion, with few differences between 0°-5° and 6°-15°. rTSA is forgiving enough such that one may plan to correct preoperative retroversion to less than 15° postoperatively in lieu of targeting postoperative version between 0°-5° for patients with higher native retroversion, potentially requiring less eccentric reaming especially when combined with other corrective measures.

Orthopedics/Bone and Joint Center

Williams AJ, **Malewicz JI**, **Pum JM**, Zurakowski D, and **Day CS**. How Did Black and Hispanic Orthopaedic Applicants and Residents Compare to General Surgery Between 2015 and 2022? *Clin Orthop Relat Res* 2024; Epub ahead of print. PMID: 38578021. Full Text

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BACKGROUND: Despite the heavy demand for and knowledge of the benefits of diversity, there is a persistent lack of racial, ethnic, and gender diversity in orthopaedic surgery. Since the implementation of diversity initiatives, data have shown that general surgery has been one of the top competitive surgical fields and has demonstrated growth in racial, ethnic, and gender diversity, making general surgery a good point of reference and comparison when analyzing racial and ethnic growth in orthopaedic surgery. QUESTIONS/PURPOSES: (1) What were the growth rates for Black and Hispanic orthopaedic residency applicants and residents between 2015 and 2022? (2) How did the growth rates of Black and Hispanic individuals in orthopaedic surgery compare with those of general surgery? (3) How did applicant recruitment and resident acceptance differ between Black and Hispanic people in orthopaedic surgery? METHODS: Applicant data were obtained from historical specialty-specific data from the Association of American Medical Colleges Electronic Residency Application Service Statistics database between 2018 and 2022, and resident data were obtained from the Accreditation Council of Graduate Medical Education Data Resource Book between 2015 and 2021. Between 2018 and 2022, the number of residency applicants totaled 216,677, with 17,912 Black residency applicants and 20,413 Hispanic residency applicants. Between 2015 and 2021, the number of active residents totaled 977,877, with 48,600 Black residents and 62,605 Hispanic residents. Because the applicant and resident data do not overlap throughout all years of observation, a sensitivity analysis of overlapping years (between 2018 and 2021) was conducted to ensure observed trends were consistent and valid throughout the study. All datasets obtained were used to establish the different racial and ethnic proportions of Black and Hispanic residency applicants and residents in four nonsurgical primary care specialties and four surgical subspecialties. A reference slope was created using data from the Association of American Medical

Colleges and Accreditation Council of Graduate Medical Education to represent the growth rate for total residency applicants and residents, independently, across all residency specialties reported in each database. This slope was used for comparison among the resident and applicant growth rates for all eight selected specialties. Datapoints were placed into a scatterplot with regression lines, using slope equations to depict rate of growth and R2 values to depict linear fit. Applicant growth corresponded to applicant recruitment and resident growth corresponded to resident acceptance. Chi-square tests were used to compare residents and residency applicants for the Black and Hispanic populations, separately. Two-way analysis of variance with a time-by-specialty interaction term (F-test) was conducted to determine differences between growth slopes. RESULTS: There was no difference in the growth rate of Black orthopaedic surgery applicants between 2018 and 2022, and there was no difference in the growth rate of Hispanic orthopaedic surgery applicants (R2 = 0.43; p = 0.23 and R2 = 0.63; p = 0.11, respectively). However, there was a very slight increase in the growth rate of Black orthopaedic surgery residents between 2015 and 2021, and a very slight increase in the growth rate of Hispanic orthopaedic surgery residents (R2 = 0.73; p = 0.02 and R2 = 0.79; p = 0.01, respectively). There were no differences in orthopaedic and general surgery rates of growth for Black applicants between 2018 and 2022 (0.004 applicants/year versus -0.001 applicants/year; p = 0.22), and no differences were found in orthopaedic and general surgery rates of growth for Black residents between 2015 and 2021 (0.003 residents/year versus 0.002 residents/year; p = 0.59). Likewise, Hispanic orthopaedic applicant growth rates did not differ between 2018 and 2022 from the rates of general surgery (0.004 applicants/year versus 0.005 applicants/year; p = 0.68), and there were no differences in orthopaedic and general surgery rates of growth for Hispanic residents (0.007 residents/year versus 0.01 residents/year; p = 0.35). Furthermore, growth rate comparisons between Black orthopaedic applicants and residents between 2018 and 2021 showed applicant growth was larger than resident growth, illustrating that the recruitment of Black applicants increased slightly more rapidly than resident acceptance. Growth rate comparisons between Hispanic applicants and residents showed a larger rate of resident growth, illustrating Hispanic resident acceptance increased slightly faster than applicant recruitment during that time. CONCLUSION: We found low acceptance of Black residents compared with the higher recruitment of Black applicants, as well as overall low proportions of Black and Hispanic applicants and residents. Future studies might explore the factors contributing to the higher acceptances of Hispanic orthopaedic residents than Black orthopaedic residents. CLINICAL RELEVANCE: We recommend that more emphasis should be placed on increasing Black and Hispanic representation at the department level to ensure cultural considerations remain at the forefront of applicant recruitment. Internal or external reviews of residency selection processes should be considered, and more immersive, longitudinal orthopaedic surgery clerkships and research mentorship experiences should be targeted toward Black and Hispanic students. Holistic reviews of applications and selection processes should be implemented to produce an increased racially and ethnically diverse applicant pool and a diverse residency work force, and implicit bias training should be implemented to address potential biases and diversity barriers that are present in residency programs and leadership.

Otolaryngology – Head and Neck Surgery

Eide JG, Kshirsagar RS, Wen C, Qatanani A, Harris J, **Sellers L**, Abello EH, Douglas JE, Palmer JN, Adappa ND, and Kuan EC. Endoscopic Repair of Anterior Skull Base Cerebrospinal Fluid Leaks is Successful in Frail Patients. *Laryngoscope* 2024; Epub ahead of print. PMID: 38581362. Full Text

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OBJECTIVE: Surgical frailty estimates a patient's ability to withstand the physiologic stress of an intervention. There is limited data regarding the impact of frailty on endoscopic cerebrospinal fluid (CSF) leak repair. METHODS: Patients undergoing CSF leak repair at two tertiary academic skull base

programs were retrospectively reviewed. Demographic, treatment, and postoperative outcomes data were recorded. Frailty was calculated using validated indices, including the American Society of Anesthesiologists (ASA) classification, Charlson Comorbidity Index (CCI), and the Modified 5-Item Frailty Index (mFI-5). Outcomes included 30-day medical and surgical complications and readmission. RESULTS: A total of 185 patients were included with 128 (69.2%) female patients and average age of 54 ± 14 years. The average body mass index was 34.6 ± 8.5. The most common identified etiology was idiopathic intracranial hypertension (IIH) in 64 patients (34.6%). A total of 125 patients (68%) underwent perioperative lumbar drain placement (primarily to measure intracranial pressures and diagnose IIH). Most patients were ASA class 3 (48.6%) with mean CCI 2.14 ± 2.23 and mFI-5 0.97 ± 0.90. Three patients had postoperative CSF leaks, with an overall repair success rate of 98.4%. There was no association between increased frailty and 30-day medical outcomes, surgical outcomes, or readmission (all $p > 0.05$). CONCLUSIONS: Endoscopic CSF leak repair in a frail population, including lumbar drain placement and bed rest, was not associated with an increased rate of complications. Previous data suggests increased complications in open craniotomy procedures in patients with significant comorbidities. This study suggests that the endoscopic approach to CSF leak repair is well tolerated in the frail population. LEVEL OF EVIDENCE: IV Laryngoscope, 2024.

Otolaryngology – Head and Neck Surgery

Graboyes EM, Cagle JL, Ramadan S, Prasad K, Yan F, Pearce J, Mazul AL, Anoma JS, Hill EG, Chera BS, Puram SV, Jackson R, Sandulache VC, **Tam S**, Topf MC, Kahmke R, Osazuwa-Peters N, Nussenbaum B, Alberg AJ, Sterba KR, and Halbert CH. Neighborhood-Level Disadvantage and Delayed Adjuvant Therapy in Head and Neck Cancer. *JAMA Otolaryngol Head Neck Surg* 2024; Epub ahead of print. PMID: 38662392. Full Text

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IMPORTANCE: For patients with head and neck squamous cell carcinoma (HNSCC), initiation of postoperative radiation therapy (PORT) within 6 weeks of surgery is recommended by the National Comprehensive Cancer Network Guidelines and the Commission on Cancer. Although individual-level measures of socioeconomic status are associated with receipt of timely, guideline-adherent PORT, the role of neighborhood-level disadvantage has not been examined. OBJECTIVE: To characterize the

association of neighborhood-level disadvantage with delays in receiving PORT. DESIGN, SETTING, AND PARTICIPANTS: This retrospective cohort study included 681 adult patients with HNSCC undergoing curative-intent surgery and PORT from 2018 to 2020 at 4 US academic medical centers. The data were analyzed between June 21, 2023, and March 5, 2024. MAIN OUTCOME MEASURES AND MEASURES: The primary outcome was delay in initiating guideline-adherent PORT (ie, >6 weeks after surgery). Time-to-PORT (TTP) was a secondary outcome. Census block-level Area Deprivation Index (ADI) scores were calculated and reported as national percentiles (0-100); higher scores indicate greater deprivation. The association of ADI scores with PORT delay was assessed using multivariable logistic regression adjusted for demographic, clinical, and institutional characteristics. PORT initiation across ADI score population quartiles was evaluated with cumulative incidence plots and Cox models. RESULTS: Among 681 patients with HNSCC undergoing surgery and PORT (mean [SD] age, 61.5 [11.2] years; 487 [71.5%] men, 194 [29.5%] women) the PORT delay rate was 60.8% (414/681) and median (IQR) TTP was 46 (40-56) days. The median (IQR) ADI score was 62.0 (44.0-83.0). Each 25-point increase in ADI score was associated with a corresponding 32% increase in the adjusted odds ratio (aOR) of PORT delay (aOR, 1.32; 95% CI, 1.07-1.63) on multivariable regression adjusted for institution, age, race and ethnicity, insurance, comorbidity, cancer subsite, stage, postoperative complications, care fragmentation, travel distance, and rurality. Increasing ADI score population quartiles were associated with increasing TTP (hazard ratio of PORT initiation, 0.71; 95% CI, 0.53-0.96; 0.59; 95% CI, 0.44-0.77; and 0.54; 95% CI, 0.41-0.72; for ADI quartiles 2, 3, and 4 vs ADI quartile 1, respectively). CONCLUSIONS AND RELEVANCE: Increasing neighborhood-level disadvantage was independently associated with a greater likelihood of PORT delay and longer TTP in a dose-dependent manner. These findings indicate a critical need for the development of multilevel strategies to improve the equitable delivery of timely, guideline-adherent PORT.

Otolaryngology – Head and Neck Surgery

Kaffenberger TM, **Plawecki A**, Kaki P, Boon M, and Huntley C. Troubleshooting Upper Airway Stimulation Therapy Using Drug-Induced Sleep Endoscopy. *Otolaryngol Head Neck Surg* 2024; Epub ahead of print. PMID: 38643409. Full Text

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OBJECTIVE: This study assesses the utility of drug-induced sleep endoscopy (DISE) in guiding further treatment for patients with obstructive sleep apnea (OSA) who have difficulty tolerating upper airway stimulation (UAS) or have inadequate response to therapy. STUDY DESIGN: We conducted a retrospective analysis of UAS patients at our institution who underwent DISE, post-UAS, and evaluated the efficacy of different electrode configurations and maneuvers. SETTING: A tertiary care hospital. METHODS: Out of 379 patients who received UAS therapy, 34 patients who underwent DISE post-UAS (DISE-UAS) were included. Palatal coupling (PC) was assessed with UAS stimulation alone, jaw thrust alone, and both simultaneously during DISE. RESULTS: Among 34 patients, 5 had suboptimal adherence to UAS therapy, 19 had suboptimal therapy efficacy with residual OSA burden, and 10 had both. During DISE-UAS, PC was observed in 7 patients (21%) with UAS stimulation alone, 9 patients (26%) with jaw thrust alone, and 8 patients (24%) with both maneuvers combined. Notably, 10 patients (29%) did not exhibit PC with any maneuver. Based on DISE-UAS findings, 13 patients were recommended oral appliance therapy (OAT), and 8 patients underwent further surgical interventions. CONCLUSION: DISE-UAS is a valuable adjunct in troubleshooting UAS therapy for patients intolerant to CPAP or with suboptimal therapy efficacy. This study provides an algorithm for targeted multimodality therapy based on DISE findings, facilitating personalized management approaches.

Otolaryngology – Head and Neck Surgery

Moreno MA, Wax MK, Gardner JR, Cannady SB, Graboyes EM, Bewley AF, Dziegielewski PT, Khaja SF, Bayon R, Ryan J, Al-Khudari S, El-Deiry MW, **Ghanem TA**, Huang A, Patel R, Higgins KM, Jackson RS, and Patel UA. Reconstruction for Salvage Laryngectomy With Limited Pharyngectomy. *JAMA Otolaryngol Head Neck Surg* 2024; Epub ahead of print. PMID: 38635282. Full Text

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IMPORTANCE: Closure technique for optimization of postoperative and functional outcomes following salvage laryngectomy remains an area of debate among head and neck surgeons. OBJECTIVE: To investigate the association of salvage laryngectomy closure technique with early postoperative and functional outcomes. DESIGN, SETTING, AND PARTICIPANTS: This retrospective cohort study included patients from 17 academic, tertiary care centers who underwent total laryngectomy with no or limited pharyngectomy after completing a course of definitive radiotherapy or chemoradiotherapy with curative intent between January 2011 and December 2016. Patients with defects not amenable to primary closure were excluded. Data were analyzed from February 14, 2021, to January 29, 2024. EXPOSURES: Total laryngectomy with and without limited pharyngectomy, reconstructed by primary mucosal closure (PC), regional closure (RC), or free tissue transfer (FTT). MAIN OUTCOMES AND MEASURES: Patients were stratified on the basis of the pharyngeal closure technique. Perioperative and long-term functional outcomes were evaluated with bivariate analyses. A multivariable regression model adjusted for historical risk factors for pharyngocutaneous fistula (PCF) was used to assess risk associated with closure technique. Relative risks (RRs) with 95% CIs were determined. RESULTS: The study included 309 patients (256 [82.8%] male; mean age, 64.7 [range, 58.0-72.0] years). Defects were reconstructed as follows: FTT (161 patients [52.1%]), RC (64 [20.7%]), and PC (84 [27.2%]). A PCF was noted in 36 of 161 patients in the FTT group (22.4%), 25 of 64 in the RC group (39.1%), and 29 of 84 in the PC group (34.5%). On multivariable analysis, patients undergoing PC or RC had a higher risk of PCF compared with those undergoing FTT (PC: RR, 2.2 [95% CI, 1.1-4.4]; RC: RR, 2.5 [95% CI, 1.3-4.8]). Undergoing FTT was associated with a clinically meaningful reduction in risk of PCF (RR, 0.6; 95% CI, 0.4-0.9; number needed to treat, 7). Subgroup analysis comparing inset techniques for the RC group showed a

higher risk of PCF associated with PC (RR, 1.8; 95% CI, 1.1-3.0) and predominately pectoralis myofascial flap with onlay technique (RR, 1.9; 95% CI, 1.2-3.2), but there was no association of pectoralis myocutaneous flap with cutaneous paddle interposition with PCF (RR, 1.2; 95% CI, 0.5-2.8) compared with FTT with cutaneous inset. There were no clinically significant differences in functional outcomes between the groups. CONCLUSION AND RELEVANCE: In this study of patients with limited pharyngeal defects, interpositional fasciocutaneous closure technique was associated with reduced risk of PCF in the salvage setting, which is most commonly achieved by FTT in academic practices. Closure technique was not associated with functional outcomes at 1 and 2 years postoperatively.

Otolaryngology – Head and Neck Surgery

Sikorskii A, **Tam S**, Given B, Given CW, **Adjei Boakye E**, **Zatirka T**, **Nair M**, **Su WK**, **Jogunoori S**, **Watson P**, **Movsas B**, and **Chang S**. Thresholds in PROMIS Scores Anchored to Subsequent Unscheduled Health Service Use Among People Diagnosed With Cancer. *JCO Oncol Pract* 2024; Epub ahead of print. PMID: 38564704. Full Text

Department of Psychiatry, College of Osteopathic Medicine, Michigan State University, East Lansing, MI.
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PURPOSE: To establish thresholds in the Patient-Reported Outcomes Measurement Information System (PROMIS) pain interference, physical function, fatigue, and depression scores on the basis of their association with subsequent use of the emergency department (ED) or urgent care by people diagnosed with cancer. METHODS: Retrospective data from 952 people seen at Henry Ford Cancer and insured through the Health Alliance Plan were analyzed using generalized linear mixed-effects models. The log odds of ED or urgent care use during 14 or 30 days after each patient-reported outcome (PRO) assessment were related to PRO scores, while adjusting for comorbidity, sociodemographic, and tumor characteristics. RESULTS: Pain interference and physical function were associated with subsequent ED or urgent care visits, but fatigue and depression were not, and the results for 14- and 30-day visits were similar. Thresholds anchored in the likelihood of these visits differed according to cancer stage. For people with advanced cancer, a pain interference score of 60 or higher (odds ratio [OR] 3.75, [95% CI, 1.53 to 7.87]) and a physical function score lower than 40 (OR 2.94, [95% CI, 1.22 to 7.06]) produced the largest ORs with narrowest CIs for 30-day visits. For people with nonadvanced cancer, the thresholds of 65 for pain interference (OR 2.64, [95% CI, 1.40 to 5.01]) and 35 for physical function (OR 1.87, [95% CI, 1.01 to 3.45]) produced largest ORs with narrowest CIs for 30-day visits. CONCLUSION: These anchor-based thresholds in PROMIS scores can inform clinicians' actions with the goal of preventing ED or urgent care visits.

Pathology and Laboratory Medicine

Danagoulian S, **Miller J**, **Cook B**, **Gunaga S**, **Fadel R**, **Gandolfo C**, Mills NL, **Modi S**, Mahler SA, Levy PD, **Parikh S**, **Krupp S**, **Abdul-Nour K**, **Klausner H**, **Rockoff S**, **Gindi R**, **Lewandowski A**, **Hudson M**, **Perrotta G**, **Zweig B**, **Lanfear D**, **Kim H**, **Shaheen E**, **Darnell G**, **Nassereddine H**, **Hawatian K**, **Tang A**, Keerie C, and **McCord J**. Is rapid acute coronary syndrome evaluation with high-sensitivity cardiac troponin less costly? An economic evaluation. *J Am Coll Emerg Physicians Open* 2024; 5(2):e13140. PMID: 38567033. Full Text

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OBJECTIVE: Protocols to evaluate for myocardial infarction (MI) using high-sensitivity cardiac troponin (hs-cTn) have the potential to drive costs upward due to the added sensitivity. We performed an economic evaluation of an accelerated protocol (AP) to evaluate for MI using hs-cTn to identify changes in costs of treatment and length of stay compared with conventional testing. METHODS: We performed a planned secondary economic analysis of a large, cluster randomized trial across nine emergency departments (EDs) from July 2020 to April 2021. Patients were included if they were 18 years or older with clinical suspicion for MI. In the AP, patients could be discharged without further testing at 0 h if they had a hs-cTnI < 4 ng/L and at 1 h if the initial value were 4 ng/L and the 1-h value ≤7 ng/L. Patients in the standard of care (SC) protocol used conventional cTn testing at 0 and 3 h. The primary outcome was the total cost of treatment, and the secondary outcome was ED length of stay. RESULTS: Among 32,450 included patients, an AP had no significant differences in cost (+$89, CI: -$714, $893 hospital cost, +$362, CI: -$414, $1138 health system cost) or ED length of stay (+46, CI: -28, 120 min) compared with the SC protocol. In lower acuity, free-standing EDs, patients under the AP experienced shorter length of stay (-37 min, CI: -62, 12 min) and reduced health system cost (-$112, CI: -$250, $25). CONCLUSION: Overall, the implementation of AP using hs-cTn does not result in higher costs.

Pathology and Laboratory Medicine

Potterveld SK, Williamson SR, **Al-Obaidy KI**, Akgul M, Chan E, Giannico GA, and Sangoi AR. GATA3 Expression in Prostatic Adenosquamous Carcinoma: A Potential Diagnostic Pitfall. *Int J Surg Pathol* 2024; Epub ahead of print. PMID: 38562047. Full Text

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Urothelial carcinoma and prostatic adenocarcinoma can have overlapping histologic features and in some instances pose challenges to pathologists. GATA binding protein 3 (GATA3) immunohistochemistry (IHC) is a well-established tool to aid in this specific diagnostic dilemma as it has been shown to be a sensitive marker for urothelial carcinoma and a putatively specific marker in excluding prostatic adenocarcinoma. However, in encountering an index tumor of prostatic adenosquamous carcinoma positive for GATA3, herein we sought to investigate this potential diagnostic pitfall in a larger series of tumors. In this study, we retrospectively reviewed prostatic adenosquamous carcinomas diagnosed in 17 patients across the authors' institutions and personal consult collections in the past 10 years. GATA3 IHC was either reviewed or performed on tumors not previously tested. We also recorded other immunostains that were performed at initial diagnosis. Positivity for GATA3 was found in 9 of 17 (53%) tumors, all within squamous regions (2 tumors also showed concomitant moderate GATA3 positivity within glandular elements). The GATA3 positive tumors were all positive for p63 in the 7 tumors where p63 was also performed. Of all tumors tested, NKX3.1 was positive in 100% (13/13) of the glandular elements (3 tumors also showed NKX3.1 concomitant positivity within squamous regions). In summary, when encountering a carcinoma with mixed glandular/squamous features in which prostatic origin is being

considered, awareness of GATA3 immunoreactivity in a subset of prostatic adenosquamous carcinoma is critical to avoid diagnostic pitfalls.

Pathology and Laboratory Medicine
Singh H, **Patel P**, **Mawari S**, and **Caliman N**. Cyclosporine-Associated Organizing Pneumonia. *Am J Ther* 2024; Epub ahead of print. PMID: 38563735. Full Text

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Pharmacy
Mohammad I, **Lobkovich A**, **Martirosov AL**, Lipari M, Garwood CL, Salinitri FD, Gortney JS, and Berlie HD. The Struggle is Real: Facilitating Pharmacy Student Success on Rotations When Challenges Arise. *J Am Pharm Assoc (2003)* 2024; 102086. Epub ahead of print. PMID: 38582382. Full Text

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Pharmacy preceptors are pivotal to facilitating and maximizing student learning on experiential rotations. However, preceptors may encounter a variety of behaviors or barriers that can hinder student success. Although some guidance exists for preceptors, emerging learner challenges along with new educational outcomes call for an updated practical approach to promoting student success on rotations. This paper provides preceptors with a structured approach to facilitate success for students who exhibit challenges on rotations. Four categories that preceptors can use to identify behaviors and barriers to learning are outlined - knowledge, skills, professional attitudes and behaviors, and external factors including the Social Determinants of Learning™. We describe strategies to help preceptors identify and categorize these challenges and provide a stepwise approach to facilitate student success.

Pharmacy
Vandervelde R, **Mlynarek ME**, **Ramesh M**, Patel N, **Veve MP**, and **August BA**. Impact of time to treatment in first occurrence, non-severe Clostridioides difficile infection for elderly patients: are we waiting too long to treat? *Antimicrob Steward Healthc Epidemiol* 2024; 4(1):e59. PMID: 38698948. Full Text

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OBJECTIVE: Data evaluating timeliness of antibiotic therapy in Clostridioides difficile infections (CDI) are not well established. The study's purpose was to evaluate the impact of time-to-CDI treatment on disease

progression. METHODS: A case-control study was performed among hospitalized patients with CDI from 1/2018 to 2/2022. Inclusion criteria were age ≥65 years, first occurrence, non-severe CDI at symptom onset, and CDI treatment for ≥72 hours. Cases included patients who progressed to severe or fulminant CDI; controls were patients without CDI progression. Time to CDI treatment was evaluated in three ways: a classification and regression tree (CART)-defined threshold, time as a continuous variable, and time as a categorical variable. RESULTS: 272 patients were included; 136 with CDI progression, 136 patients without. The median (IQR) age was 74 (69-81) years, 167 (61%) were women, and 108 (40%) were immunosuppressed. CDI progression patients more commonly were toxin positive (66 [49%] vs 52 [38%], P = .087) with hospital-acquired disease (57 [42%] vs 29 [21%], P < 0.001). A CART-derived breakpoint for optimal time-to-CDI treatment of 64 hours established early (184, 68%) and delayed treatment (88, 32%). When accounting for confounding variables, delayed CDI treatment was associated with disease progression (adjOR, 4.6; 95%CI, 2.6-8.2); this was observed regardless of how time-to-CDI-active therapy was evaluated (continuous adjOR, 1.02; categorical adjOR, 2.11). CONCLUSION: Delayed CDI treatment was associated with disease progression and could represent an important antimicrobial stewardship measure with future evaluation.

Public Health Sciences

Arkhipov SN, **Liao TS**, **Potter DL**, **Bobbitt KR**, **Ivanov V**, **Ortiz PA**, and **Pavlov TS**. Dissociation of Hypertension and Renal Damage After Cessation of High-Salt Diet in Dahl Rats. *Hypertension* 2024; Epub ahead of print. PMID: 38618734. Full Text

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BACKGROUND: Every year, thousands of patients with hypertension reduce salt consumption in the efforts to control their blood pressure. However, hypertension has a self-sustaining character in a significant part of the population. We hypothesized that chronic hypertension leads to irreversible renal damage that remains after removing the trigger, causing an elevation of the initial blood pressure. METHODS: Dahl salt-sensitive rat model was used for chronic, continuous observation of blood pressure. Rats were fed a high salt diet to induce hypertension, and then the diet was switched back to normal sodium content. RESULTS: We found that developed hypertension was irreversible by salt cessation: after a short period of reduction, blood pressure grew even higher than in the high-salt phase. Notably, the self-sustaining phase of hypertension was sensitive to benzamil treatment due to sustaining epithelial sodium channel hyperactivity, as shown with patch-clamp analysis. Glomerular damage and proteinuria were also irreversible. In contrast, some mechanisms, contributing to the development of salt-sensitive hypertension, normalized after salt restriction. Thus, flow cytometry demonstrated that dietary salt reduction in hypertensive animals decreased the number of total CD45(+), CD3(+)CD4(+), and CD3(+)CD8(+) cells in renal tissues. Also, we found tubular recovery and improvement of glomerular filtration rate in the postsalt period versus a high-salt diet. CONCLUSIONS: Based on earlier publications and current data, poor response to salt restriction is due to the differential contribution of the factors recognized in the developmental phase of hypertension. We suggest that proteinuria or electrolyte transport can be prioritized over therapeutic targets of inflammatory response.

Public Health Sciences

Chai W, and **Tao MH**. Overall and Sex-Specific Associations of Serum Lipid-Soluble Micronutrients with Metabolic Dysfunction-Associated Steatotic Liver Disease among Adults in the United States. *Nutrients* 2024; 16(8). PMID: 38674932. Full Text

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This study examined overall and sex-specific associations of serum lipid-soluble micronutrients including α- and γ-tocopherols, 25-hydroxy-vitamin D (25(OH)D), retinol, and six major carotenoids with metabolic dysfunction-associated steatotic lever disease (MASLD) using the 2017-2018 National Health and Nutrition Examination Survey. This analysis included 3956 adults (1991 men, 1965 women) aged ≥ 20 years. Steatotic liver disease was determined through transient elastography examination. Odds ratios (ORs) and 95% confidence intervals (95% CIs) for MASLD associated with micronutrients were estimated using logistic regressions. Higher serum α-tocopherol (highest vs. lowest quartile: OR = 1.53, 95% CI = 1.05-2.22, p = 0.03) and γ-tocopherol (highest vs. lowest quartile: OR = 4.15, 95% CI = 3.00-5.74, p < 0.0001) levels were associated with increased odds of MASLD. Higher serum 25(OH)D levels were associated with reduced odds of MASLD (highest vs. lowest quartile: OR = 0.41, 95% CI = 0.27-0.61, p = 0.0001). Inverse associations with the condition were also observed for carotenoids (α-carotene, β-carotene, α-cryptoxanthin, β-cryptoxanthin, combined lutein and zeaxanthin, and lycopene) in the serum (Ps < 0.05). The results were comparable between men and women, except for those on α-tocopherol, for which a positive association was only observed for men (p = 0.01). Our results suggest potential protective associations of serum 25(OH)D and carotenoids with MASLD. The positive associations between tocopherols and MASLD may reflect pathophysiological conditions associated with the condition.

Public Health Sciences

Chiarelli G, **Stephens A**, **Finati M**, **Cirulli GO**, Beatrici E, Filipas DK, **Arora S**, **Tinsley S**, **Bhandari M**, Carrieri G, Trinh QD, Briganti A, Montorsi F, Lughezzani G, Buffi N, **Rogers C**, and **Abdollah F**. Adequacy of prostate cancer prevention and screening recommendations provided by an artificial intelligence-powered large language model. *Int Urol Nephrol* 2024; Epub ahead of print. PMID: 38564079. Full Text

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PURPOSE: We aimed to assess the appropriateness of ChatGPT in providing answers related to prostate cancer (PCa) screening, comparing GPT-3.5 and GPT-4. METHODS: A committee of five reviewers designed 30 questions related to PCa screening, categorized into three difficulty levels. The questions were formulated identically for both GPTs three times, varying the prompts. Each reviewer assigned a score for accuracy, clarity, and conciseness. The readability was assessed by the Flesch Kincaid Grade (FKG) and Flesch Reading Ease (FRE). The mean scores were extracted and compared using the Wilcoxon test. We compared the readability across the three different prompts by ANOVA. RESULTS: In GPT-3.5 the mean score (SD) for accuracy, clarity, and conciseness was 1.5 (0.59), 1.7 (0.45), 1.7 (0.49), respectively for easy questions; 1.3 (0.67), 1.6 (0.69), 1.3 (0.65) for medium; 1.3 (0.62), 1.6 (0.56), 1.4 (0.56) for hard. In GPT-4 was 2.0 (0), 2.0 (0), 2.0 (0.14), respectively for easy questions; 1.7 (0.66), 1.8 (0.61), 1.7 (0.64) for medium; 2.0 (0.24), 1.8 (0.37), 1.9 (0.27) for hard. GPT-4 performed better for all three qualities and difficulty levels than GPT-3.5. The FKG mean for GPT-3.5 and GPT-4 answers were 12.8 (1.75) and 10.8 (1.72), respectively; the FRE for GPT-3.5 and GPT-4 was 37.3 (9.65) and 47.6 (9.88), respectively. The 2nd prompt has achieved better results in terms of clarity (all p < 0.05). CONCLUSIONS: GPT-4 displayed superior accuracy, clarity, conciseness, and readability than GPT-3.5. Though prompts influenced the quality response in both GPTs, their impact was significant only for clarity.

Public Health Sciences

Danagoulian S, **Miller J**, **Cook B**, **Gunaga S**, **Fadel R**, **Gandolfo C**, Mills NL, **Modi S**, Mahler SA, Levy PD, **Parikh S**, **Krupp S**, **Abdul-Nour K**, **Klausner H**, **Rockoff S**, **Gindi R**, **Lewandowski A**, **Hudson M**, **Perrotta G**, **Zweig B**, **Lanfear D**, **Kim H**, **Shaheen E**, **Darnell G**, **Nassereddine H**, **Hawatian K**, **Tang A**, Keerie C, and **McCord J**. Is rapid acute coronary syndrome evaluation with high-sensitivity cardiac troponin less costly? An economic evaluation. *J Am Coll Emerg Physicians Open* 2024; 5(2):e13140. PMID: 38567033. Full Text

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OBJECTIVE: Protocols to evaluate for myocardial infarction (MI) using high-sensitivity cardiac troponin (hs-cTn) have the potential to drive costs upward due to the added sensitivity. We performed an economic evaluation of an accelerated protocol (AP) to evaluate for MI using hs-cTn to identify changes in costs of treatment and length of stay compared with conventional testing. METHODS: We performed a planned secondary economic analysis of a large, cluster randomized trial across nine emergency departments (EDs) from July 2020 to April 2021. Patients were included if they were 18 years or older with clinical suspicion for MI. In the AP, patients could be discharged without further testing at 0 h if they had a hs-cTnI < 4 ng/L and at 1 h if the initial value were 4 ng/L and the 1-h value ≤7 ng/L. Patients in the standard of care (SC) protocol used conventional cTn testing at 0 and 3 h. The primary outcome was the total cost of treatment, and the secondary outcome was ED length of stay. RESULTS: Among 32,450 included patients, an AP had no significant differences in cost (+$89, CI: -$714, $893 hospital cost, +$362, CI: -$414, $1138 health system cost) or ED length of stay (+46, CI: -28, 120 min) compared with the SC protocol. In lower acuity, free-standing EDs, patients under the AP experienced shorter length of stay (-37 min, CI: -62, 12 min) and reduced health system cost (-$112, CI: -$250, $25). CONCLUSION: Overall, the implementation of AP using hs-cTn does not result in higher costs.

Public Health Sciences

Fruh V, Wesselink AK, Schildroth S, Bethea TN, Geller RJ, Calafat AM, Coull BA, **Wegienka G**, Harmon QE, Baird DD, Wise LA, and Claus Henn B. Non-persistent endocrine disrupting chemical mixtures and uterine leiomyomata in the study of environment, lifestyle and fibroids (SELF). *Chemosphere* 2024; 357:142050. PMID: 38631496. Request Article

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BACKGROUND: Results of studies investigating associations between individual endocrine-disrupting chemicals (EDCs) and incidence of uterine leiomyomata (UL), a hormone-dependent gynecological condition, have been inconsistent. However, few studies have evaluated simultaneous exposure to a mixture of EDCs with UL incidence. METHODS: We conducted a case-cohort analysis (n = 708) of data from the Study of the Environment, Lifestyle and Fibroids (SELF), a prospective cohort study. Participants were aged 23-35 years at enrollment, had an intact uterus, and identified as Black or African American. We measured biomarker concentrations of 21 non-persistent EDCs, including phthalates, phenols, parabens, and triclocarban, in urine collected at baseline, 20-month, and 40-month clinic visits. We ascertained UL incidence and characteristics using ultrasounds at baseline and approximately every 20 months through 60 months. We used probit Bayesian Kernel Machine Regression (BKMR-P) to evaluate joint associations between EDC mixtures with cumulative UL incidence. We estimated the mean difference in the probit of UL incidence over the study period, adjusting for baseline age, education, years since last birth, parity, smoking status and body mass index. We converted probit estimates to odds ratios for ease of interpretation. RESULTS: We observed that urinary concentrations of the overall EDC mixture were inversely associated with UL incidence in the overall mixtures model, with the strongest inverse associations at the 70th percentile of all biomarkers compared with their 50th percentile (odds ratio = 0.59; 95% confidence interval: 0.36, 0.96). Strongest contributors to the joint association for the mixture were bisphenol S (BPS), ethyl paraben (EPB), bisphenol F (BPF) and mono (2-ethyl-5-carboxypentyl) phthalate (MECPP), which each demonstrated inverse associations except for MECPP. There was suggestive evidence of an interaction between MECPP and EPB. CONCLUSION: In this prospective ultrasound study, we observed evidence of an inverse association between the overall mixture of urinary biomarker concentrations of non-persistent EDCs with UL incidence.

Public Health Sciences

Gamallat Y, Felipe Lima J, Seyedi S, Li Q, Rokne JG, Alhajj R, **Ghosh S**, and Bismar TA. Exploring The Prognostic Significance of SET-Domain Containing 2 (SETD2) Expression in Advanced and Castrate-Resistant Prostate Cancer. *Cancers (Basel)* 2024; 16(7). PMID: 38611113. Full Text

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SET-domain containing 2 (SETD2) is a histone methyltransferase and an epigenetic modifier with oncogenic functionality. In the current study, we investigated the potential prognostic role of SETD2 in prostate cancer. A cohort of 202 patients' samples was assembled on tissue microarrays (TMAs) containing incidental, advanced, and castrate-resistant CRPCa cases. Our data showed significant elevated SETD2 expression in advanced and castrate-resistant disease (CRPCa) compared to incidental cases (2.53 ± 0.58 and 2.21 ± 0.63 vs. 1.9 ± 0.68; $p < 0.001$, respectively). Interestingly, the mean intensity of SETD2 expression in deceased vs. alive patients was also significantly different (2.31 ± 0.66 vs. 2 ± 0.68; $p = 0.003$, respectively). Overall, high SETD2 expression was found to be considered high risk and was significantly associated with poor prognosis and worse overall survival (OS) (HR 1.80; 95% CI: 1.28-2.53, $p = 0.001$) and lower cause specific survival (CSS) (HR 3.14; 95% CI: 1.94-5.08, $p < 0.0001$). Moreover, combining high-intensity SETD2 with PTEN loss resulted in lower OS (HR 2.12; 95%

CI: 1.22-3.69, p = 0.008) and unfavorable CSS (HR 3.74; 95% CI: 1.67-8.34, p = 0.001). Additionally, high SETD2 intensity with ERG positive expression showed worse prognosis for both OS (HR 1.99, 95% CI 0.87-4.59; p = 0.015) and CSS (HR 2.14, 95% CI 0.98-4.68, p = 0.058). We also investigated the protein expression database TCPA, and our results showed that high SETD2 expression is associated with a poor prognosis. Finally, we performed TCGA PRAD gene set enrichment analysis (GSEA) data for SETD2 overexpression, and our data revealed a potential association with pathways involved in tumor progression such as the AMPK signaling pathway, the cAMP signaling pathway, and the PI3K-Akt signaling pathway, which are potentially associated with tumor progression, chemoresistance, and a poor prognosis.

Public Health Sciences

Gongala S, Garcia JA, Korakavi N, Patil N, Akbari H, Sloan A, Barnholtz-Sloan JS, Sun J, **Griffith B**, **Poisson LM**, Booth TC, Jain R, Mohan S, Nasralla MP, Bakas S, Tippareddy C, Puig J, Palmer JD, Shi W, Colen RR, Sotiras A, Ahn SS, Park YW, Davatzikos C, and Badve C. Sex-specific Differences in IDH1-Wildtype Glioblastoma patients in the ReSPOND Consortium. *AJNR Am J Neuroradiol* 2024; Epub ahead of print. PMID: 38684319. Full Text

BACKGROUND: Understanding sex-based differences in glioblastoma patients is necessary for accurate personalized treatment planning to improve patient outcomes. PURPOSE: To investigate sex-specific differences in molecular, clinical and radiological tumor parameters, as well as survival outcomes in glioblastoma, isocitrate dehydrogenase-1 wildtype (IDH1-WT), grade 4 patients. METHODS: Retrospective data of 1832 glioblastoma, IDH1-WT patients with comprehensive information on tumor parameters was acquired from the Radiomics Signatures for Precision Oncology in Glioblastoma (ReSPOND) consortium. Data imputation was performed for missing values. Sex-based differences in tumor parameters, such as, age, molecular parameters, pre-operative KPS score, tumor volumes, epicenter and laterality were assessed through non-parametric tests. Spatial atlases were generated using pre-operative MRI maps to visualize tumor characteristics. Survival time analysis was performed through log-rank tests and Cox proportional hazard analyses. RESULTS: GBM was diagnosed at a median age of 64 years in females compared to 61.9 years in males (FDR = 0.003). Males had a higher Karnofsky Performance Score (above 80) as compared to females (60.4% females Vs 69.7% males, FDR = 0.044). Females had lower tumor volumes in enhancing (16.7 cm(3) Vs. 20.6 cm(3) in males, FDR = 0.001), necrotic core (6.18 cm(3) Vs. 7.76 cm(3) in males, FDR = 0.001) and edema regions (46.9 cm(3) Vs. 59.2 cm(3) in males, FDR = 0.0001). Right temporal region was the most common tumor epicenter in the overall population. Right as well as left temporal lobes were more frequently involved in males. There were no significant differences in survival outcomes and mortality ratios. Higher age, unmethylated O6-methylguanine-DNAmethyltransferase (MGMT) promoter and undergoing subtotal resection increased the mortality risk in both males and females. CONCLUSIONS: Our study demonstrates significant sex-based differences in clinical and radiological tumor parameters of glioblastoma, IDH1-WT, grade 4 patients. Sex is not an independent prognostic factor for survival outcomes and the tumor parameters influencing patient outcomes are identical for males and females. ABBREVIATIONS: IDH1-WT = isocitrate dehydrogenase-1 wildtype; MGMTp = O6-methylguanine-DNA-methyltransferase promoter; KPS = Karnofsky performance score; EOR = extent of resection; WHO = world health organization; FDR = false discovery rate.

Public Health Sciences

Ober C, **Joseph CLM**, and Novembre J. Population descriptors in asthma and allergy research: Time to re-group. *J Allergy Clin Immunol* 2024; Epub ahead of print. PMID: 38642714. Full Text

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Public Health Sciences

Olson J, Ko A, **Nowak KA**, **Latack K**, and Bozimowsky G. Using Simulation Training to Reduce Skill Decay Among Certified Registered Nurse Anesthetists. *J Contin Educ Nurs* 2024; 55(4):187-194. PMID: 38063801. Full Text

BACKGROUND: Skill decay refers to the loss of skills and knowledge resulting from lack of consistent use. Among certified registered nurse anesthetists (CRNAs), skill decay can lead to negative results. One method that has been shown to mitigate skill decay is low-dose, high-frequency (LDHF) simulation. There is a gap in the LDHF simulation literature regarding CRNAs to determine its effectiveness in reducing skill decay or increasing confidence levels. METHOD: This study used a quasi-experimental pretest-posttest follow-up design. The pretests and posttests were evaluated using a Wilcoxon signed rank test to determine CRNAs' proficiency and confidence in central venous catheter (CVC) insertion before and after a simulated refresher training course. RESULTS: The CRNAs showed a significant improvement in CVC insertion proficiency, from a 50% pretest average to a 94% posttest average ($p < .0001$), and they retained proficiency 6 months later (91%, $p = .0109$). There was no significant change in CRNAs' confidence level following the training ($p = .4486$). CONCLUSION: A program of LDHF simulation training is an important activity in meeting the continuing education/training needs of CRNAs in improving and retaining CVC insertion proficiency. This study demonstrates the efficacy of a LDHF simulation program for CRNAs and helps to bridge the gap in the literature on the use of LDHF simulation among CRNAs. [J Contin Educ Nurs. 2024;55(4):187-194.].

Public Health Sciences

Prater AR, **McConnell JT**, **Yedulla NR**, **Peterson EL**, **Banka TR**, and **Day CS**. The Impact of Experience Versus Decision Aids on Patient Preference Toward Virtual Care. *Telemed Rep* 2024; 5(1):59-66. PMID: 38558954. Full Text

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INTRODUCTION: Virtual care utilization has increased in recent years bringing questions of how to best inform patients regarding their use. Decision aids (DAs) are tools created to assist patients in making informed decisions about their health care. This study seeks to determine whether a DA or previous experience could better educate and influence patient's preference on virtual care. METHODS: One hundred fifty participants from an orthopedic clinic of a multi-hospital system were divided into three groups. Group 1 (Virtual Care Cohort) had at least one previous virtual care visit and was surveyed with the Telemedicine Satisfaction Questionnaire (TSQ). Group 2 (In-person with Decision Aid) and Group 3 (In-person without Decision Aid) had no virtual care experience. Group 2 received a validated virtual care DA with a knowledge test. Both groups were also administered the TSQ. RESULTS: After the DA, patients improved their score on 3 of 4 virtual care knowledge questions. Each cohort demonstrated a positive perception of virtual care; however, the specific reasons for their favorable views varied. The DA cohort did not show increased preference toward virtual care compared with the non-DA group and only responded significantly higher regarding encounter comfort. Patients with previous experience in virtual care responded most favorably to the majority of survey questions regarding their virtual care preferences when compared with both virtual care naive cohorts. DISCUSSION AND CONCLUSION: We found that patient experience was the most important factor in influencing patient preference toward virtual care. Although the DA increased their virtual care knowledge it did not increase their preference; therefore, efforts should be placed at encouraging patient to experience virtual care.

Public Health Sciences

Schildroth S, Claus Henn B, Vines AI, Geller RJ, Lovett SM, Coleman CM, Bethea TN, Botelho JC, Calafat AM, Milando C, Baird DD, **Wegienka G**, and Wise LA. Per- and polyfluoroalkyl substances (PFAS), perceived stress, and depressive symptoms in a prospective cohort study of black women. *Sci Total Environ* 2024; 929:172445. PMID: 38642767. Request Article

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BACKGROUND: Per- and polyfluoroalkyl substances (PFAS) are endocrine-disrupting chemicals with neurotoxic properties. PFAS have been associated with depressive symptoms among women in some studies, but little research has evaluated the effects of PFAS mixtures. Further, no study has investigated interactions of PFAS-depression associations by perceived stress, which has been shown to modify the effects of PFAS on other health outcomes. OBJECTIVE: In a prospective cohort study of reproductive-aged Black women, we investigated associations between PFAS and depressive symptoms and the extent to which perceived stress modified these associations. METHODS: We analyzed data from 1499 participants (23-35 years) in the Study of Environment, Lifestyle, and Fibroids. We quantified concentrations of nine PFAS in baseline plasma samples using online solid-phase extraction-liquid chromatography-isotope dilution tandem mass spectrometry. Participants reported perceived stress via the Perceived Stress Scale (PSS-4; range = 0-16) at baseline and depressive symptoms via the Center for Epidemiologic Studies Depression Scale (CESD; range = 0-44) at the 20-month follow-up visit. We used Bayesian Kernel Machine Regression to estimate associations between PFAS concentrations, individually and as a mixture, and depressive symptoms, and to assess effect modification by PSS-4 scores, adjusting for confounders. RESULTS: Baseline perfluorodecanoic acid concentrations were associated with greater depressive symptoms at the 20-month follow-up, but associations for other PFAS were null. The PFAS were not associated with depressive symptoms when evaluated as a mixture. The association between the 90th percentile (vs. 50th percentile) of the PFAS mixture with CES-D scores was null at the 10th (β = 0.03; 95 % CrI = 0.20, 0.25), 50th (β = 0.02; 95 % CrI = -0.16, 0.19), and 90th (β = 0.01; 95 % CrI = 0.18, 0.20) percentiles of PSS-4 scores, suggesting perceived stress did not modify the PFAS mixture. CONCLUSION: In this prospective cohort study, PFAS concentrations-assessed individually or as a mixture-were not appreciably associated with depressive symptoms, and there was no evidence of effect modification by perceived stress.

Public Health Sciences

Sikorskii A, **Tam S**, Given B, Given CW, **Adjei Boakye E**, **Zatirka T**, **Nair M**, **Su WK**, **Jogunoori S**, **Watson P**, **Movsas B**, and **Chang S**. Thresholds in PROMIS Scores Anchored to Subsequent Unscheduled Health Service Use Among People Diagnosed With Cancer. *JCO Oncol Pract* 2024; Epub ahead of print. PMID: 38564704. Full Text

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PURPOSE: To establish thresholds in the Patient-Reported Outcomes Measurement Information System (PROMIS) pain interference, physical function, fatigue, and depression scores on the basis of their

association with subsequent use of the emergency department (ED) or urgent care by people diagnosed with cancer. METHODS: Retrospective data from 952 people seen at Henry Ford Cancer and insured through the Health Alliance Plan were analyzed using generalized linear mixed-effects models. The log odds of ED or urgent care use during 14 or 30 days after each patient-reported outcome (PRO) assessment were related to PRO scores, while adjusting for comorbidity, sociodemographic, and tumor characteristics. RESULTS: Pain interference and physical function were associated with subsequent ED or urgent care visits, but fatigue and depression were not, and the results for 14- and 30-day visits were similar. Thresholds anchored in the likelihood of these visits differed according to cancer stage. For people with advanced cancer, a pain interference score of 60 or higher (odds ratio [OR] 3.75, [95% CI, 1.53 to 7.87]) and a physical function score lower than 40 (OR 2.94, [95% CI, 1.22 to 7.06]) produced the largest ORs with narrowest CIs for 30-day visits. For people with nonadvanced cancer, the thresholds of 65 for pain interference (OR 2.64, [95% CI, 1.40 to 5.01]) and 35 for physical function (OR 1.87, [95% CI, 1.01 to 3.45]) produced largest ORs with narrowest CIs for 30-day visits. CONCLUSION: These anchor-based thresholds in PROMIS scores can inform clinicians' actions with the goal of preventing ED or urgent care visits.

Public Health Sciences

Surie D, Yuengling KA, DeCuir J, Zhu Y, Lauring AS, Gaglani M, Ghamande S, Peltan ID, Brown SM, Ginde AA, Martinez A, Mohr NM, Gibbs KW, Hager DN, Ali H, Prekker ME, Gong MN, Mohamed A, Johnson NJ, Srinivasan V, Steingrub JS, Leis AM, Khan A, Hough CL, Bender WS, Duggal A, Bendall EE, Wilson JG, Qadir N, Chang SY, Mallow C, Kwon JH, Exline MC, Shapiro NI, Columbus C, **Vaughn IA**, **Ramesh M**, Mosier JM, Safdar B, Casey JD, Talbot HK, Rice TW, Halasa N, Chappell JD, Grijalva CG, Baughman A, Womack KN, Swan SA, Johnson CA, Lwin CT, Lewis NM, Ellington S, McMorrow ML, Martin ET, and Self WH. Severity of Respiratory Syncytial Virus vs COVID-19 and Influenza Among Hospitalized US Adults. *JAMA Netw Open* 2024; 7(4):e244954. PMID: 38573635. Full Text

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IMPORTANCE: On June 21, 2023, the Centers for Disease Control and Prevention recommended the first respiratory syncytial virus (RSV) vaccines for adults aged 60 years and older using shared clinical decision-making. Understanding the severity of RSV disease in adults can help guide this clinical decision-making. OBJECTIVE: To describe disease severity among adults hospitalized with RSV and compare it with the severity of COVID-19 and influenza disease by vaccination status. DESIGN, SETTING, AND PARTICIPANTS: In this cohort study, adults aged 18 years and older admitted to the hospital with acute respiratory illness and laboratory-confirmed RSV, SARS-CoV-2, or influenza infection were prospectively enrolled from 25 hospitals in 20 US states from February 1, 2022, to May 31, 2023. Clinical data during each patient's hospitalization were collected using standardized forms. Data were analyzed from August to October 2023. EXPOSURES: RSV, SARS-CoV-2, or influenza infection. MAIN OUTCOMES AND MEASURES: Using multivariable logistic regression, severity of RSV disease was compared with COVID-19 and influenza severity, by COVID-19 and influenza vaccination status, for a range of clinical outcomes, including the composite of invasive mechanical ventilation (IMV) and in-hospital death. RESULTS: Of 7998 adults (median [IQR] age, 67 [54-78] years; 4047 [50.6%] female) included, 484 (6.1%) were hospitalized with RSV, 6422 (80.3%) were hospitalized with COVID-19, and 1092 (13.7%) were hospitalized with influenza. Among patients with RSV, 58 (12.0%) experienced IMV or death, compared with 201 of 1422 unvaccinated patients with COVID-19 (14.1%) and 458 of 5000 vaccinated patients with COVID-19 (9.2%), as well as 72 of 699 unvaccinated patients with influenza (10.3%) and 20 of 393 vaccinated patients with influenza (5.1%). In adjusted analyses, the odds of IMV or in-hospital death were not significantly different among patients hospitalized with RSV and unvaccinated patients hospitalized with COVID-19 (adjusted odds ratio [aOR], 0.82; 95% CI, 0.59-1.13; P = .22) or influenza (aOR, 1.20; 95% CI, 0.82-1.76; P = .35); however, the odds of IMV or death were significantly higher among patients hospitalized with RSV compared with vaccinated patients hospitalized with COVID-19 (aOR, 1.38; 95% CI, 1.02-1.86; P = .03) or influenza disease (aOR, 2.81; 95% CI, 1.62-4.86; P < .001). CONCLUSIONS AND RELEVANCE: Among adults hospitalized in this US cohort during the 16 months before the first RSV vaccine recommendations, RSV disease was less common but similar in severity compared with COVID-19 or influenza disease among unvaccinated patients and more severe than COVID-19 or influenza disease among vaccinated patients for the most serious outcomes of IMV or death.

Public Health Sciences

Tesfaye S, Cronin RM, Lopez-Class M, Chen Q, Foster CS, Gu CA, Guide A, Hiatt RA, Johnson AS, **Joseph CLM**, Khatri P, Lim S, Litwin TR, Munoz FA, Ramirez AH, Sansbury H, Schlundt DG, Viera EN, Dede-Yildirim E, and Clark CR. Measuring social determinants of health in the All of Us Research Program. *Sci Rep* 2024; 14(1):8815. PMID: 38627404. Full Text

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To accelerate medical breakthroughs, the All of Us Research Program aims to collect data from over one million participants. This report outlines processes used to construct the All of Us Social Determinants of Health (SDOH) survey and presents the psychometric characteristics of SDOH survey measures in All of Us. A consensus process was used to select SDOH measures, prioritizing concepts validated in diverse populations and other national cohort surveys. Survey item non-response was calculated, and Cronbach's alpha was used to analyze psychometric properties of scales. Multivariable logistic regression models were used to examine associations between demographic categories and item non-response. Twenty-nine percent (N = 117,783) of eligible All of Us participants submitted SDOH survey data for these analyses. Most scales had less than 5% incalculable scores due to item non-response. Patterns of item non-response were seen by racial identity, educational attainment, income level, survey language, and age. Internal consistency reliability was greater than 0.80 for almost all scales and most demographic groups. The SDOH survey demonstrated good to excellent reliability across several measures and within multiple populations underrepresented in biomedical research. Bias due to survey non-response and item non-response will be monitored and addressed as the survey is fielded more completely.

Pulmonary and Critical Care Medicine

Khan SL, Danoff SK, Kulkarni T, Reichuber J, Shifren A, Shlobin OA, **Thavarajah K**, Warrior K, and Case AH. Practice Patterns for Screening and Treating Interstitial Lung Disease-related Pulmonary Hypertension at Specialty Care Centers in the United States. *Ann Am Thorac Soc* 2024; Epub ahead of print. PMID: 38626420. Full Text

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Pulmonary and Critical Care Medicine

Koster TD, Shah PL, Valipour A, Criner GJ, Herth FJF, Sue R, Hogarth DK, Martin RT, Mahajan AK, Alalawi R, Kopas L, **Cohen A**, Wood DE, Kurman J, Shargill NS, Dransfield M, Slebos DJ, and Perch M.

Optimizing clinical outcomes for bronchoscopic lung volume reduction with Zephyr® valves. *Respir Med* 2024; 227:107639. PMID: 38642906. Full Text

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Bronchoscopic lung volume reduction treatment with Zephyr one-way valves is an effective guideline-based treatment option for patients with severe emphysema and hyperinflation. However, in some cases the treatment response is less than anticipated or there might be a loss of initial treatment effect. Reasons for the lack of response can include incorrect assessment of collateral ventilation, improper valve placement, or patient related factors. Loss of initial benefit can be due to granulation tissue formation and subsequent valve dysfunction, or there may be side effects such as excessive coughing or infectious problems. Careful follow-up after treatment with valves is important and evaluation with a CT scan and/or bronchoscopy is helpful if there is no improvement after treatment or loss of initial benefit. This paper aims to describe the most important causes and provide a strategy of how to approach and manage these patients.

Pulmonary and Critical Care Medicine

Maligireddy A, **Jabri A**, Zghouzi M, Rojulpote C, VanAken G, Janga C, **Radjef R**, **Aronow H**, **Awdish R**, **Kelly B**, **Grafton G**, Paul TK, Lin CJ, Mikhalkova D, Alaswad K, **Franco-Palacios D**, **Villablanca P**, and **Aggarwal V**. Maternal and Fetal Outcomes in Pulmonary Hypertension During Pregnancy: A Contemporary Nationwide Analysis. *Am J Cardiol* 2024; Epub ahead of print. PMID: 38663575. Full Text

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Pulmonary hypertension (PH) disproportionately affects women, presenting challenges during pregnancy. Historically, patients with PH are advised to avoid pregnancy; however, recent reports have indicated that the incidence of adverse events in pregnant patients with PH may be lower than previously reported. We conducted a retrospective cohort study in pregnant patients with PH using the National Readmission Database from January 1, 2016, to December 31, 2020. PH was categorized according to the World Health Organization classification. Primary end points include maternal mortality and 30-day nonelective readmission rate. Other adverse short-term maternal (cardiovascular and obstetric) and fetal outcomes were also analyzed. Of 9,922,142 pregnant women, 3,532 (0.04%) had PH, with Group 1 PH noted in 1,833 (51.9%), Group 2 PH in 676 (19.1%), Group 3 PH in 604 (17.1%), Group 4 PH in 23 (0.7%), Group 5 PH in 98 (2.8%), and multifactorial PH in 298 (8.4%). PH patients exhibited higher rates of adverse cardiovascular events (15.7% vs 0.3% without PH, p <0.001) and mortality (0.9% vs 0.01% without PH, p <0.001). Mixed PH and Group 2 PH had the highest prevalence of adverse cardiovascular events in the World Health Organization PH groups. Patients with PH had a significantly higher nonelective 30-day readmission rate (10.4% vs 2.3%) and maternal adverse obstetric events (24.2% vs 9.1%) compared with those without PH (p <0.001) (Figure 1). In conclusion, pregnant women with PH had significantly higher adverse event rates, including in-hospital maternal mortality (85-fold), compared with those without PH.

Pulmonary and Critical Care Medicine

Singh H, **Patel P**, **Mawari S**, and **Caliman N**. Cyclosporine-Associated Organizing Pneumonia. *Am J Ther* 2024; Epub ahead of print. PMID: 38563735. Full Text

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Radiation Oncology

Hobson MA, Hu Y, Caldwell B, Cohen GN, Glide-Hurst C, Huang L, **Jackson PD**, Jang S, Langner U, Lee HJ, Levesque IR, Narayanan S, Park JC, Steffen J, Wu QJ, and Zhou Y. AAPM Task Group 334: A guidance document to using radiotherapy immobilization devices and accessories in an MR environment. *Med Phys* 2024; Epub ahead of print. PMID: 38648857. Full Text

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Use of magnetic resonance (MR) imaging in radiation therapy has increased substantially in recent years as more radiotherapy centers are having MR simulators installed, requesting more time on clinical diagnostic MR systems, or even treating with combination MR linear accelerator (MR-linac) systems. With this increased use, to ensure the most accurate integration of images into radiotherapy (RT), RT immobilization devices and accessories must be able to be used safely in the MR environment and produce minimal perturbations. The determination of the safety profile and considerations often falls to the medical physicist or other support staff members who at a minimum should be a Level 2 personnel as per the ACR. The purpose of this guidance document will be to help guide the user in making determinations on MR Safety labeling (i.e., MR Safe, Conditional, or Unsafe) including standard testing, and verification of image quality, when using RT immobilization devices and accessories in an MR environment.

Radiation Oncology
Lombardo J, Castillo E, Castillo R, Miller R, Jones B, Miften M, Kavanagh B, Dicker A, Boyle C, Leiby B, Banks J, Simone NL, **Movsas B**, Grills I, Guerrero T, Rusthoven CG, and Vinogradskiy Y. Prospective trial of Functional Lung Avoidance Radiation Therapy for Lung Cancer: Quality of Life Report. *Int J Radiat Oncol Biol Phys* 2024; Epub ahead of print. PMID: 38614278. Full Text

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PURPOSE: A novel form of lung function imaging has been developed that uses 4DCT data to generate lung ventilation images (4DCT-ventilation). Functional avoidance uses 4DCT-ventilation to reduce doses to functional lung with the aim of reducing pulmonary side-effects. A 4DCT-ventilation functional avoidance, phase II, multi-center clinical trial was completed. The purpose of this work is to quantify patient reported outcomes (PRO) changes for patients treated with functional avoidance and to determine which metrics are predictive of PRO changes. MATERIALS AND METHODS: Patients with locally advanced lung cancer receiving curative intent radiotherapy were accrued. Each patient had a 4DCT-ventilation image generated using 4DCT data and image processing. PRO instruments included the Functional Assessment of Cancer Therapy-Lung (FACT-L) questionnaire, administered pre-treatment, 3, 6, and 12 months post-treatment. FACT-TOI (Trial Outcome Index) and the FACT-LCS (Lung Cancer Subscale) percentage of clinically meaningful declines (CMD) were determined. A linear mixed-effects model was used to determine which patient, clinical, dose, and dose-function metrics were predictive of PRO decline. RESULTS: 59 patients completed baseline PRO surveys. 83% of patients had non-small-cell lung cancer, with 75% having stage III disease. The median dose was 60 Gy in 30 fractions. CMD FACT-TOI decline was 46.3%, 38.5%, and 26.8%, at 3, 6, and 12 months, respectively. CMD FACT-LCS

decline was 33.3%, 33.3%, and 29.3%, at 3, 6, and 12 months, respectively. While an increase in most dose and dose-function parameters was associated with a modest decline in PROs, none of the results were significant (all p>0.053). CONCLUSION: The current work provides an innovative combination of functional avoidance and PROs and is the first report of PROs for patients treated with prospective 4DCT-ventilation functional avoidance. Approximately 30% of patients had clinically significant decline in PROs at 12 months. The study provides additional data on outcomes with 4DCT-ventilation functional avoidance.

Radiation Oncology
Parikh PJ, Chuong MD, and Lee P. In Reply to Cellini and Fiore. *Int J Radiat Oncol Biol Phys* 2024; 119(1):309-310. PMID: 38631746. Full Text

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Radiation Oncology
Rodrigues G, Higgins KA, Rimner A, Amini A, Chang JY, Chun SG, Donington J, Edelman MJ, Gubens MA, Iyengar P, **Movsas B**, Ning MS, Park HS, Wolf A, and Simone CB, 2nd. American Radium Society Appropriate Use Criteria for Unresectable Locally Advanced Non-Small Cell Lung Cancer. *JAMA Oncol* 2024; Epub ahead of print. PMID: 38602670. Full Text

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IMPORTANCE: The treatment of locally advanced non-small cell lung cancer (LA-NSCLC) has been informed by more than 5 decades of clinical trials and other relevant literature. However, controversies remain regarding the application of various radiation and systemic therapies in commonly encountered clinical scenarios. OBJECTIVE: To develop case-referenced consensus and evidence-based guidelines to inform clinical practice in unresectable LA-NSCLC. EVIDENCE REVIEW: The American Radium Society (ARS) Appropriate Use Criteria (AUC) Thoracic Committee guideline is an evidence-based consensus document assessing various clinical scenarios associated with LA-NSCLC. A systematic review of the literature with evidence ratings was conducted to inform the appropriateness of treatment recommendations by the ARS AUC Thoracic Committee for the management of unresectable LA-NSCLC. FINDINGS: Treatment appropriateness of a variety of LA-NSCLC scenarios was assessed by a consensus-based modified Delphi approach using a range of 3 points to 9 points to denote consensus agreement. Committee recommendations were vetted by the ARS AUC Executive Committee and a 2-week public comment period before official approval and adoption. Standard of care management of good prognosis LA-NSCLC consists of combined concurrent radical (60-70 Gy) platinum-based chemoradiation followed by consolidation durvalumab immunotherapy (for patients without progression). Planning and delivery of locally advanced lung cancer radiotherapy usually should be performed using intensity-modulated radiotherapy techniques. A variety of palliative and radical fractionation schedules are available to treat patients with poor performance and/or pulmonary status. The salvage therapy for a local recurrence after successful primary management is complex and likely requires both multidisciplinary input and shared decision-making with the patient. CONCLUSIONS AND RELEVANCE: Evidence-based

guidance on the management of various unresectable LA-NSCLC scenarios is provided by the ARS AUC to optimize multidisciplinary patient care for this challenging patient population.

Radiation Oncology
Roumeliotis M, **Thind K**, Morrison H, Burke B, Martell K, van Dyke L, Barbera L, and Quirk S. The impact of advancing the standard of care in radiotherapy on operational treatment resources. *J Appl Clin Med Phys* 2024; e14363. Epub ahead of print. PMID: 38634814. Full Text

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PURPOSE: To demonstrate the impact of implementing hypofractionated prescription regimens and advanced treatment techniques on institutional operational hours and radiotherapy personnel resources in a multi-institutional setting. The study may be used to describe the impact of advancing the standard of care with modern radiotherapy techniques on patient and staff resources. METHODS: This study uses radiation therapy data extracted from the radiotherapy information system from two tertiary care, university-affiliated cancer centers from 2012 to 2021. Across all patients in the analysis, the average fraction number for curative and palliative patients was reported each year in the decade. Also, the institutional operational treatment hours are reported for both centers. A sub-analysis for curative intent breast and lung radiotherapy patients was performed to contextualize the impact of changes to imaging, motion management, and treatment technique. RESULTS: From 2012 to 2021, Center 1 had 42 214 patient plans and Center 2 had 43 252 patient plans included in the analysis. Averaged over both centers across the decade, the average fraction number per patient decreased from 6.9 to 5.2 (25%) and 21.8 to 17.2 (21%) for palliative and curative patients, respectively. The operational treatment hours for both institutions increased from 8 h 15 min to 9 h 45 min (18%), despite a patient population increase of 45%. CONCLUSION: The clinical implementation of hypofractionated treatment regimens has successfully reduced the radiotherapy workload and operational treatment hours required to treat patients. This analysis describes the impact of changes to the standard of care on institutional resources.

Radiation Oncology
Sikorskii A, **Tam S**, Given B, Given CW, **Adjei Boakye E**, **Zatirka T**, **Nair M**, **Su WK**, **Jogunoori S**, **Watson P**, **Movsas B**, and **Chang S**. Thresholds in PROMIS Scores Anchored to Subsequent Unscheduled Health Service Use Among People Diagnosed With Cancer. *JCO Oncol Pract* 2024; Epub ahead of print. PMID: 38564704. Full Text

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PURPOSE: To establish thresholds in the Patient-Reported Outcomes Measurement Information System (PROMIS) pain interference, physical function, fatigue, and depression scores on the basis of their association with subsequent use of the emergency department (ED) or urgent care by people diagnosed with cancer. METHODS: Retrospective data from 952 people seen at Henry Ford Cancer and insured through the Health Alliance Plan were analyzed using generalized linear mixed-effects models. The log odds of ED or urgent care use during 14 or 30 days after each patient-reported outcome (PRO) assessment were related to PRO scores, while adjusting for comorbidity, sociodemographic, and tumor characteristics. RESULTS: Pain interference and physical function were associated with subsequent ED or urgent care visits, but fatigue and depression were not, and the results for 14- and 30-day visits were similar. Thresholds anchored in the likelihood of these visits differed according to cancer stage. For people with advanced cancer, a pain interference score of 60 or higher (odds ratio [OR] 3.75, [95% CI, 1.53 to 7.87]) and a physical function score lower than 40 (OR 2.94, [95% CI, 1.22 to 7.06]) produced the largest ORs with narrowest CIs for 30-day visits. For people with nonadvanced cancer, the thresholds of 65 for pain interference (OR 2.64, [95% CI, 1.40 to 5.01]) and 35 for physical function (OR 1.87, [95% CI, 1.01 to 3.45]) produced largest ORs with narrowest CIs for 30-day visits. CONCLUSION: These anchor-based thresholds in PROMIS scores can inform clinicians' actions with the goal of preventing ED or urgent care visits.

Sleep Medicine

Valente V, Machado D, Jorge S, **Drake CL**, and Marques DR. Reply to the comment on "Does valerian work for insomnia? An umbrella review of the evidence". *Eur Neuropsychopharmacol* 2024; 83:55. PMID: 38643636. Full Text

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Surgery

Brubaker AL, Sellers MT, Abt PL, Croome KP, Merani S, Wall A, Abreu P, Alebrahim M, Baskin R, Bohorquez H, Cannon RM, Cederquist K, Edwards J, Huerter BG, Hobeika MJ, Kautzman L, Langnas AN, Lee DD, Manzi J, **Nassar A**, Neidlinger N, Nydam TL, Schnickel GT, Siddiqui F, Suah A, Taj R, Taner CB, Testa G, Vianna R, Vyas F, and Montenovo MI. US Liver Transplant Outcomes After Normothermic Regional Perfusion vs Standard Super Rapid Recovery. *JAMA Surg* 2024; Epub ahead of print. PMID: 38568597. Full Text

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IMPORTANCE: Normothermic regional perfusion (NRP) is an emerging recovery modality for transplantable allografts from controlled donation after circulatory death (cDCD) donors. In the US, only 11.4% of liver recipients who are transplanted from a deceased donor receive a cDCD liver. NRP has the potential to safely expand the US donor pool with improved transplant outcomes as compared with standard super rapid recovery (SRR). OBJECTIVE: To assess outcomes of US liver transplants using controlled donation after circulatory death livers recovered with normothermic regional perfusion vs standard super rapid recovery. DESIGN, SETTING, AND PARTICIPANTS: This was a retrospective, observational cohort study comparing liver transplant outcomes from cDCD donors recovered by NRP vs SRR. Outcomes of cDCD liver transplant from January 2017 to May 2023 were collated from 17 US transplant centers and included livers recovered by SRR and NRP (thoracoabdominal NRP [TA-NRP] and abdominal NRP [A-NRP]). Seven transplant centers used NRP, allowing for liver allografts to be transplanted at 17 centers; 10 centers imported livers recovered via NRP from other centers. EXPOSURES: cDCD livers were recovered by either NRP or SRR. MAIN OUTCOMES AND MEASURES: The primary outcome was ischemic cholangiopathy (IC). Secondary end points included primary nonfunction (PNF), early allograft dysfunction (EAD), biliary anastomotic strictures, posttransplant length of stay (LOS), and patient and graft survival. RESULTS: A total of 242 cDCD livers were included in this study: 136 recovered by SRR and 106 recovered by NRP (TA-NRP, 79 and A-NRP, 27). Median (IQR) NRP and SRR donor age was 30.5 (22-44) years and 36 (27-49) years, respectively. Median (IQR) posttransplant LOS was significantly shorter in the NRP cohort (7 [5-11] days vs 10 [7-16] days; P < .001). PNF occurred only in the SRR allografts group (n = 2). EAD was more common in the SRR cohort (123 of 136 [56.1%] vs 77 of 106 [36.4%]; P = .007). Biliary anastomotic strictures were increased 2.8-fold in SRR recipients (7 of 105 [6.7%] vs 30 of 134 [22.4%]; P = .001). Only SRR recipients had IC (0 vs 12 of 133 [9.0%]; P = .002); IC-free survival by Kaplan-Meier was significantly improved in NRP recipients. Patient and graft survival were comparable between cohorts. CONCLUSION AND RELEVANCE: There was comparable patient and graft survival in liver transplant recipients of cDCD donors recovered by NRP vs SRR, with reduced rates of IC, biliary complications, and EAD in NRP recipients. The feasibility of A-NRP and TA-NRP implementation across multiple US transplant centers supports increasing adoption of NRP to improve organ use, access to transplant, and risk of wait-list mortality.

Surgery
Bryce K, and Vierecke JK. Me Versus Not Me: Assimilating to a Left Ventricular Assist Device Implant. *J Heart Lung Transplant* 2024; Epub ahead of print. PMID: 38685445. Full Text

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Surgery
Jones O, Claasen MP, **Ivanics T**, Choi WJ, Gavaria F, Rajendran L, Ghanekar A, Hirschfield G, Gulamhusein A, Shwaartz C, Reichman T, Sayed BA, Selzner M, Bhat M, Tsien C, Jaeckel E, Lilly L, McGilvray ID, Cattral MS, Selzner N, and Sapisochin G. Pursuing living donor liver transplantation improves outcomes of patients with autoimmune liver diseases - An intention-to-treat analysis. *Liver Transpl* 2024; Epub ahead of print. PMID: 38619393. Full Text

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Background Living donor liver transplantation (LDLT) offers the opportunity to decrease waitlist time and mortality for patients with AILD; autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC). We compared the survival of patients with a potential live donor (pLDLT) on the waitlist vs. no potential live donor (pDDLT), on an intention-to-treat (ITT) basis. Methods Our retrospective cohort study investigated adults with AILD listed for liver transplant at our program between 2000 and 2021. The pLDLT group comprised recipients with a potential live donor. Otherwise, they were included in the pDDLT group. ITT survival was assessed from the time of listing. Results Of the 533 patients included, 244(43.8%) had a potential living donor. Waitlist dropout was higher for the pDDLT groups among all AILDs (pDDLT 85[29.4%] vs. pLDLT 9[3.7], p<0.001). The 1-, 3- and 5-year ITT survival rates were higher for pLDLT vs. pDDLT among all AILDs (95.7%vs.78.1%, 89.0%vs.70.1%, and 87.1%vs.65.5%, p<0.001). After adjusting for covariates, pLDLT was associated with a 38% reduction in the risk of death among the AILD cohort (HR:0.62, 95%CI:0.42-0.93[p<0.05]), and 60% among the PSC cohort (HR:0.40, 95%CI:0.22-0.74[p<0.05]). There were no differences in the 1-, 3- and 5-year post-transplant survival between LDLT and DDLT (AILD: 95.6%vs.92.1%, 89.9%vs.89.4%, and 89.1%vs. 87.1%, p=0.41). This was consistent after adjusting for covariates (HR: 0.97, 95%CI:0.56-1.68[p>0.9]). Conclusion Our study suggests that having a potential live donor could decrease the risk of death in patients with PSC on the waitlist. Importantly, the post-transplant outcomes in this population are similar between the LDLT and DDLT groups.

Surgery

Shen MR, Hammoud MM, Bonham AJ, Aaron B, Ghaferi AA, **Varban OA**, **Carlin AM**, Ehlers AP, and Finks JF. Conversion of sleeve gastrectomy to Roux-en-Y gastric bypass: impact on reflux and weight loss. *Surg Obes Relat Dis* 2024; Epub ahead of print. PMID: 38704333. Full Text

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BACKGROUND: Sleeve gastrectomy (SG) is the most commonly performed weight loss operation, and its 2 most common complications are postoperative reflux and weight recurrence. There is limited evidence to guide decision-making in treating these conditions. OBJECTIVES: To determine the efficacy of conversion of SG to Roux-en-Y gastric bypass (RYGB) for GERD management and weight loss. SETTING: Forty-one hospitals in Michigan. METHODS: We conducted a retrospective cohort study examining patients who underwent conversion of SG to RYGB from 2014 to 2022. The primary outcomes were changes in GERD-HRQL scores, anti-reflux medication use, and weight from baseline to 1 year after conversion. Secondary outcomes included 30-day postoperative complications and resource utilization. RESULTS: Among 2133 patients undergoing conversion, 279 (13%) patients had baseline and 1-year GERD-HRQL survey data and anti-reflux medication data. GERD-HRQL scores decreased significantly from 24.6 to 6.6 (P < .01). Among these, 207 patients (74%) required anti-reflux medication at baseline, with only 76 patients (27%) requiring anti-reflux medication at 1 year postoperatively (P < .01). Of the 380 patients (18%) with weight loss data, mean weight decreased by 68.4lbs, with a 24.3% decline in total body weight and 51.5% decline in excess body weight. In terms of 30-day complications, 308 (14%) patients experienced any complication and 89 (4%) experienced a serious complication, but there were no leaks, perforations, or deaths. Three-hundred and fifty-five (17%) patients presented to the emergency department and 64 (3%) patients underwent reoperation. CONCLUSIONS: This study represents the largest reported experience with conversion from SG to RYGB. We found that conversion to RYGB is associated with significant improvement in GERD symptoms, reduction in anti-reflux medication use, and significant weight loss and is therefore an effective treatment for GERD and weight

regain after SG. However, the risks and benefits of conversion surgery should be carefully considered, especially in patients with significant comorbidity burden.

Urology
Atiemo HO, and Stoffel JT. A Primer for Primary Care Physicians Managing Neurogenic Bladder Patients. *Urol Clin North Am* 2024; 51(2):305-311. PMID: 38609202. Full Text

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Primary care plays an important role in caring for neurogenic bladder patients. Clinicians should assess neurogenic bladder patients for common urologic symptoms/signs and refer to urology if refractory or safety issues are identified.

Urology
Bulusu A, Ferrante S, Wu RC, Qi J, Montie J, Ginsburg KB, Semerjian A, Raman JD, Ginzburg S, **Patel A**, **Rogers CG**, George VK, Stork B, and George AK. Current Perceptions, Practice Patterns, and Barriers to Adoption of Transperineal Prostate Biopsy under local anesthesia. *Urology* 2024; Epub ahead of print. PMID: 38679295. Full Text

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OBJECTIVES: To assess perceptions, practice patterns, and barriers to adoption of Transperineal prostate biopsy (TPBx) under local anesthesia. METHODS: Providers from Michigan Urological Surgery Improvement Collaborative (MUSIC) and Pennsylvania Urologic Regional Collaborative (PURC) were administered an online survey to assess beliefs and educational needs regarding TPBx. Providers were divided into those who performed or did not perform TPBx. The MUSIC and PURC registry were queried to assess TPBx utilization. Descriptive analytics and bivariate analysis determined associations between provider/practice demographics and attitudes. RESULTS: Since 2019, TPBx adoption has increased more than 2-fold to 7.0% and 16% across MUSIC and PURC practices, respectively. Of 350 urologists invited to participate in a survey, a total of 91 complete responses were obtained with 21 respondents (23%) reported performing TPBx. Participants estimated the learning curve was <10 procedure for TPBx performers and non-performers. No significant association was observed between learning curve and provider age/practice setting. The major perceived benefits of TPBx were decreased risk of sepsis, improved cancer detection rate and antibiotic stewardship. The most commonly cited challenges to implementation included access to equipment and patient experience. Urologists performing TPBx reported learning curve as an additional barrier, while those not performing TPBx reported duration of procedure. CONCLUSIONS: Access to equipment and patient experience concerns remain substantial barriers to adoption of TPBx. Dissemination of techniques utilizing existing equipment and optimization of local anesthetic protocols for TPBx may help facilitate the continued adoption of TPBx.

Urology

Chiarelli G, **Stephens A**, **Finati M**, **Cirulli GO**, Beatrici E, Filipas DK, **Arora S**, **Tinsley S**, **Bhandari M**, Carrieri G, Trinh QD, Briganti A, Montorsi F, Lughezzani G, Buffi N, **Rogers C**, and **Abdollah F**. Adequacy of prostate cancer prevention and screening recommendations provided by an artificial intelligence-powered large language model. *Int Urol Nephrol* 2024; Epub ahead of print. PMID: 38564079. Full Text

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PURPOSE: We aimed to assess the appropriateness of ChatGPT in providing answers related to prostate cancer (PCa) screening, comparing GPT-3.5 and GPT-4. METHODS: A committee of five reviewers designed 30 questions related to PCa screening, categorized into three difficulty levels. The questions were formulated identically for both GPTs three times, varying the prompts. Each reviewer assigned a score for accuracy, clarity, and conciseness. The readability was assessed by the Flesch Kincaid Grade (FKG) and Flesch Reading Ease (FRE). The mean scores were extracted and compared using the Wilcoxon test. We compared the readability across the three different prompts by ANOVA. RESULTS: In GPT-3.5 the mean score (SD) for accuracy, clarity, and conciseness was 1.5 (0.59), 1.7 (0.45), 1.7 (0.49), respectively for easy questions; 1.3 (0.67), 1.6 (0.69), 1.3 (0.65) for medium; 1.3 (0.62), 1.6 (0.56), 1.4 (0.56) for hard. In GPT-4 was 2.0 (0), 2.0 (0), 2.0 (0.14), respectively for easy questions; 1.7 (0.66), 1.8 (0.61), 1.7 (0.64) for medium; 2.0 (0.24), 1.8 (0.37), 1.9 (0.27) for hard. GPT-4 performed better for all three qualities and difficulty levels than GPT-3.5. The FKG mean for GPT-3.5 and GPT-4 answers were 12.8 (1.75) and 10.8 (1.72), respectively; the FRE for GPT-3.5 and GPT-4 was 37.3 (9.65) and 47.6 (9.88), respectively. The 2nd prompt has achieved better results in terms of clarity (all $p < 0.05$). CONCLUSIONS: GPT-4 displayed superior accuracy, clarity, conciseness, and readability than GPT-3.5. Though prompts influenced the quality response in both GPTs, their impact was significant only for clarity.

Urology

Ditonno F, Franco A, Manfredi C, Sturgis MR, Feng CL, Roadman DF, Mossak SM, Bologna E, Licari LC, De Nunzio C, **Corsi NJ**, **Rogers C**, **Abdollah F**, Antonelli A, Cherullo EE, Olweny E, and Autorino R. Trends and costs of minimally invasive surgery for kidney cancer in the US: A population-based study. *Urology* 2024; Epub ahead of print. PMID: 38670274. Full Text

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OBJECTIVE: To analyze temporal trends and costs associated with the use of minimally invasive surgery (MIS) for kidney cancer in the US over the past decade. To examine the impact of social determinants of health (SDOH) on perioperative outcomes. METHODS: The PearlDiver Mariner, a national database of insurance billing records, was queried for this retrospective observational cohort analysis. The MIS population was identified and stratified according to treatment modality, using International Classification of Diseases (ICD) and current procedural terminology (CPT) codes. SDOH were assessed using ICD codes. Negative binomial regression was used to evaluate the overall number of renal MIS and Cochran-Armitage tests to compare the utilization of different treatment modalities, over the study period. Multivariable logistic regression analysis identified predictors of perioperative complications. RESULTS: A total of 80,821 MIS for kidney cancer were included. Minimally invasive partial nephrectomy (MIPN) adoption as a fraction of total MIS increased significantly (slope of regression line, reg. = 0.026, p<.001). Minimally invasive radical nephrectomy (MIRN) ($26,9k±40,9k) and renal ablation (RA) ($18,9k±31,6k) were the most expensive and the cheapest procedure, respectively. No statistically significant difference was observed in terms of number of complications (p=.06) and presence of SDOH (p=.07) among the treatment groups. At multivariable analysis, patients with SDOH undergoing MIRN had higher odds of perioperative complications, while RA had a significantly lower probability of perioperative complications. CONCLUSIONS: This study describes the current management of kidney cancer in the US, offering a socioeconomic perspective on the impact of this disease in everyday clinical practice. DATA AVAILABILITY: Raw data generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Urology

Rambhatla A, Shah R, Ziouziou I, et al. Global Practice Patterns and Variations in the Medical and Surgical Management of Non-Obstructive Azoospermia: Results of a World-Wide Survey, Guidelines and Expert Recommendations. *World J Mens Health* 2024; Epub ahead of print. PMID: 38606867. Full Text

PURPOSE: Non-obstructive azoospermia (NOA) is a common, but complex problem, with multiple therapeutic options and a lack of clear guidelines. Hence, there is considerable controversy and marked variation in the management of NOA. This survey evaluates contemporary global practices related to medical and surgical management for patients with NOA. MATERIALS AND METHODS: A 56-question online survey covering various aspects of the evaluation and management of NOA was sent to specialists around the globe. This paper analyzes the results of the second half of the survey dealing with the management of NOA. Results have been compared to current guidelines, and expert recommendations have been provided using a Delphi process. RESULTS: Participants from 49 countries submitted 336 valid responses. Hormonal therapy for 3 to 6 months was suggested before surgical sperm retrieval (SSR) by 29.6% and 23.6% of participants for normogonadotropic hypogonadism and hypergonadotropic hypogonadism respectively. The SSR rate was reported as 50.0% by 26.0% to 50.0% of participants. Interestingly, 46.0% reported successful SSR in <10% of men with Klinefelter syndrome and 41.3% routinely recommended preimplantation genetic testing. Varicocele repair prior to SSR is recommended by 57.7%. Half of the respondents (57.4%) reported using ultrasound to identify the most vascularized areas in the testis for SSR. One-third proceed directly to microdissection testicular sperm extraction (mTESE) in every case of NOA while others use a staged approach. After a failed conventional TESE, 23.8% wait for 3 months, while 33.1% wait for 6 months before proceeding to mTESE. The cut-off of follicle-stimulating hormone for positive SSR was reported to be 12-19 IU/mL by 22.5% of participants and 20-40 IU/mL by 27.8%, while 31.8% reported no upper limit. CONCLUSIONS: This is the largest survey to date on the real-world medical and surgical management of NOA by reproductive experts. It demonstrates a diverse practice pattern and highlights the need for evidence-based international consensus guidelines.

Urology

Shah R, **Rambhatla A**, Atmoko W, et al. Global Practice Patterns in the Evaluation of Non-Obstructive Azoospermia: Results of a World-Wide Survey and Expert Recommendations. *World J Mens Health* 2024; Epub ahead of print. PMID: 38606865. Full Text

PURPOSE: Non-obstructive azoospermia (NOA) represents the persistent absence of sperm in ejaculate without obstruction, stemming from diverse disease processes. This survey explores global practices in NOA diagnosis, comparing them with guidelines and offering expert recommendations. MATERIALS AND METHODS: A 56-item questionnaire survey on NOA diagnosis and management was conducted globally from July to September 2022. This paper focuses on part 1, evaluating NOA diagnosis. Data from 367 participants across 49 countries were analyzed descriptively, with a Delphi process used for expert recommendations. RESULTS: Of 336 eligible responses, most participants were experienced attending physicians (70.93%). To diagnose azoospermia definitively, 81.7% requested two semen samples. Commonly ordered hormone tests included serum follicle-stimulating hormone (FSH) (97.0%), total testosterone (92.9%), and luteinizing hormone (86.9%). Genetic testing was requested by 66.6%, with karyotype analysis (86.2%) and Y chromosome microdeletions (88.3%) prevalent. Diagnostic testicular biopsy, distinguishing obstructive azoospermia (OA) from NOA, was not performed by 45.1%, while 34.6% did it selectively. Differentiation relied on physical examination (76.1%), serum hormone profiles (69.6%), and semen tests (68.1%). Expectations of finding sperm surgically were higher in men with normal FSH, larger testes, and a history of sperm in ejaculate. CONCLUSIONS: This expert survey, encompassing 367 participants from 49 countries, unveils congruence with recommended guidelines in NOA diagnosis. However, noteworthy disparities in practices suggest a need for evidence-based, international consensus guidelines to standardize NOA evaluation, addressing existing gaps in professional recommendations.

Urology

Wang Y, **Wilder S**, **Butaney M**, Hijazi M, Gandham D, Van Til M, Goldman B, Qi J, Mirza M, Johnson A, Rudoff M, Wenzler D, **Rogers CG**, and Lane BR. Conversion to Radical Nephrectomy From Robotic Partial Nephrectomy Is Most Commonly Due to Anatomic and Oncologic Complexity. *J Urol* 2024; 211(5):669-676. PMID: 38591701. Full Text

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PURPOSE: Partial nephrectomy is standard-of-care treatment for small renal masses. As utilization of partial nephrectomy increases and includes larger and complex tumors, the risk of conversion to radical nephrectomy likely increases. We evaluated incidence and reason for conversion to radical nephrectomy in patients scheduled for partial nephrectomy by surgeons participating in MUSIC (the Michigan Urologic Surgery Improvement Collaborative). MATERIALS AND METHODS: All patients in whom robotic partial nephrectomy was planned were stratified by completed procedure (robotic partial nephrectomy vs radical nephrectomy). Preoperative and intraoperative records were reviewed for preoperative assessment of difficulty and reason for conversion. Patient, tumor, pathologic, and practice variables were compared between cohorts. RESULTS: Of 650 patients scheduled for robotic partial nephrectomy, conversion to radical nephrectomy occurred in 27 (4.2%) patients. No conversions to open were reported. Preoperative documentation indicated a plan for possible conversion in 18 (67%) patients including partial with possible radical (n = 8), partial vs radical (n = 6), or likely radical nephrectomy (n = 4). Intraoperative documentation indicated that only 5 (19%) conversions were secondary to bleeding, with the remaining conversions due to tumor complexity and/or oncologic concerns. Patients undergoing conversion had larger (4.7 vs 2.8 cm, P < .001) and higher-complexity tumors (64% vs 6%, P < .001) with R.E.N.A.L. (for radius, exophytic/endophytic, nearness of tumor to collecting system, anterior/posterior, location relative to polar line) nephrometry score ≥ 10. The converted cases had a higher rate of ≥ pT3 (27% vs 8.4%, P = .008). CONCLUSIONS: There was a low rate of conversion from robotic partial to radical nephrectomy in the MUSIC-KIDNEY (Kidney mass: Identifying and Defining Necessary Evaluation and therapY) collaborative, and an even lower risk of conversion due to uncontrolled bleeding. Targeted review of each conversion identified appropriate decision-making based on oncologic risk in most cases.

Conference Abstracts

Cardiology/Cardiovascular Research

Ayyad A, **Fadel R**, and **Alqarqaz M**. 100.76 Assessing Mortality Risk in Cardiogenic Shock Patients on VA-ECMO: The Role of SAVE Score, SOFA Score, and 8-Hour Lactate Clearance. *JACC Cardiovasc Interv* 2024; 17(4):S23-S24. Full Text

Background: Cardiogenic shock (CS) is a life-threatening perfusion impairment due to cardiac dysfunction. Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) can provide robust hemodynamic support in patients unresponsive to medical therapy. However, predicting outcomes in patients requiring ECMO support has proved challenging. This study sought to examine in-hospital mortality rates in patients with refractory CS undergoing VA-ECMO and evaluate the association of Survival After VA-ECMO (SAVE) score, Sequential Organ Failure Assessment (SOFA) score, and post-cannulation lactate levels with inpatient mortality. Methods: A retrospective review of adult patients who underwent peripheral VA-ECMO cannulation from January 2018 to September 2022 at a quaternary care center. In-hospital mortality was assessed and compared to predicted mortality by SAVE and SOFA scores, with adjusted odds ratio of risk factors for mortality identified by multivariate logistic regression analysis. Additionally, the prognostic value of 8-hour 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. In-hospital mortality was 70%, and 54% of patients died while on ECMO or within 24 hours of decannulation. SAVE score (OR 0.93 per unit increase, 95% CI 0.86 - 0.99, p=0.008), SOFA score (OR 1.53 per unit increase, 95% CI 1.32 - 1.75), and 8-hour post-cannulation lactate level (OR 1.20 per mmol/L increase, 95% CI 1.04 - 1.36, p=0.012) and clearance (OR 0.98 per % decrease, 95% CI 0.97 - 0.99, p=0.026) were independently associated with in-hospital mortality. An 8-hour post-cannulation lactate level above 7.8 mmol/L was associated with high specificity for in-hospital mortality (91.1%). Patients with 8-hour post-cannulation lactate levels above the cutoff of 7.3 mmol/L demonstrated significantly higher 30-day mortality across the entire follow-up period. Conclusion: SAVE and SOFA scores are useful tools in determining prognosis of patients with CS on VA-ECMO. 8-hour post-cannulation serum lactate levels are a pragmatic biomarker which can further assist in prognostication of patients requiring VA-ECMO, and the cutoff of 7.3 mmol/L at 8-hours appears to be a reliable measure. The development of accurate prognostic tools is critical in managing and optimizing care for patients with CS.

Cardiology/Cardiovascular Research

Lampert B, **Williams C**, Montfort JH, Obrien RK, Aggarwal-Gupta C, Ravichandran A, Rao R, Campbell PT, Yaranov D, Carey S, Olymbios M, Armer-Cabral M, Zhang Z, and Hall S. Outcomes in Patients with Acute Cellular Rejection Grade 1R: Is the Debate Over? *J Heart Lung Transplant* 2024; 43(4):S377. Full Text

Purpose: Acute Cellular Rejection (ACR) grade 1R is usually untreated; however, recurrent 1Rs are associated with negative long-term outcomes. Donor-derived cell-free DNA (dd-cfDNA) is a biomarker for heart allograft injury and rejection. We hypothesize that ACR 1R concurrent with elevated dd-cfDNA may be indicative of clinically relevant rejection. We analyzed outcomes in an interim sub-analysis of patients with ACR 1R enrolled in the multicenter Prospera Test Evaluation in Cardiac Transplant (ProTECT) study, a registry of adult heart transplant (HTx) recipients in the US undergoing dd-cfDNA monitoring with the Prospera™ test (Natera, Austin, TX). Methods: Patients with biopsy-graded ACR 1R and a matched (i.e. within two weeks of biopsy) dd-cfDNA result were stratified by dd-cfDNA level: high (≥0.15%) and low (<0.15%). Time from ACR 1R diagnosis to the first instance of a composite endpoint (death, retransplantation, biopsy-proven rejection, treated rejection and graft dysfunction) was calculated. Kaplan-Meier curves were implemented using right-censoring techniques and differences in proportion of events between groups were assessed using Fisher's exact test. Results: Of the first 100 patients enrolled in ProTECT, 48 had an ACR 1R episode and matched dd-cfDNA result. The median follow-up time after the initial ACR 1R diagnosis was 10.4 mos (IQR: 7.3, 12.4 mos). 13/48 patients had a high dd-cfDNA result (median: 0.25%; IQR: 0.2%, 0.71%) and 35/48 had a low dd-cfDNA result (median: 0.04%; IQR: 0.02%, 0.07%). Significantly more of the high dd-cfDNA cohort (76.9%; [10/13]) met the composite endpoint than the low dd-cfDNA cohort (17.1% [6/35]; p<0.001; Figure 1). Conclusion: Elevated dd-cfDNA

was associated with lower freedom from subsequent adverse outcomes in HTx recipients with an episode of ACR 1R. These findings suggest that not all ACR 1R cases are benign. More data are needed to validate these findings, however, the use of dd-cfDNA could help discern ACR 1R rejections needing closer monitoring or treatment. [Formula presented]

Cardiology/Cardiovascular Research
Maneta E, Taleb I, Kyriakopoulos CP, Dranow E, Wever-Pinzon O, Selzman CH, Singh R, Psotka MA, Birks EJ, Slaughter MS, Koenig SC, Hoffman K, Guglin M, Silvestry SC, Vidic A, Raval NY, Mehra MR, **Cowger JA**, Parker L, Tseliou E, Stehlik J, Alharethi R, Kfoury AG, Hanff TC, Fang JC, Sideris K, Goldstein J, Nelson M, Karra R, Kanwar MK, Shah P, and Drakos SG. Derivation and Validation of a Multicenter Model to Identify Candidates for Advanced HF Therapies with High Potential to Achieve Post-LVAD Reverse Cardiac Remodeling. *J Heart Lung Transplant* 2024; 43(4):S83. Full Text

Purpose: We sought to develop and validate a predictive personalized tool to identify candidates for advanced HF therapies with a high potential to achieve significant improvement in myocardial structure and function post-LVAD. This tool can aid clinicians and patients considering advanced HF therapies options. Methods: A total of 759 consecutive LVAD patients were enrolled. The derivation and validation cohorts included 509 patients (Allegheny, Inova, Louisville, Utah) and 250 patients (Advent, Duke, Kentucky), respectively. The primary outcome was “significant reverse remodeling”, defined as LVEF ≥40% and LV end-diastolic diameter ≤6 cm within one year on LVAD support. Bootstrap imputation and LASSO variable selection were used to derive a predictive model which was externally validated. Results: Patients were predominantly white (78%), male (80.1%), 57±14 years old. Overall, 12.8% patients were identified as responders. Four variables associated with reverse remodeling were included in the multivariable model achieving a C-statistic of 0.72 (95% CI: 0.66-0.79) in the derivation and 0.83 (95% CI: 0.73-0.93) in the validation cohort (Figure). We created a calculator for individualized prediction of the probability of cardiac recovery and when applied to the studied population, we identified patients with 0.2%-67.6% chance of significant reverse remodeling (see Figure for patient example). Conclusion: The Multicenter Recovery Calculator is a predictive tool that provides individualized probability of significant reverse remodeling. This tool may help clinicians and patients to maximize the benefits of both heart transplant and LVAD. Specifically, it may serve to (a) improve patient selection for LVAD as bridge to recovery and (b) benefit transplant waitlist outcomes by prioritizing allocation of donor allografts to patients without a high potential for cardiac reverse remodeling. [Formula presented]

Cardiology/Cardiovascular Research
Nassif G, **Oulabi K**, **Boules T**, **Savage K**, **Kavousi Y**, Mansour M, **Osinbowale O**, **Jackson M**, **Daley B**, and **Kabbani L**. The Utility of Chat GPT in Venous Education. *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 2024; 12(3). Full Text

Objectives: Chat GPT is an artificial intelligence-powered language model that is being increasingly used in the medical setting. Although quick access to large amounts of information is promising for vascular surgical education, the quality and depth of information provided by the current Chat GPT model is not well-understood. We aimed to study the utility of Chat GPT in teaching medical students and vascular surgery residents about varicose veins. We hypothesized that Chat GPT can provide a basic overview to medical students’ and possibly residents’ education. Methods: We generated two learning documents using Chat GPT, one for medical students and one for residents. We asked Chat GPT 3.5 to produce a document for “varicose veins explained to a medical student” and another for “varicose veins explained to a vascular surgery resident.” We asked it to “include background, anatomy, pathophysiology, risk factors, clinical presentation, complications, diagnostic evaluation, and management.” Texts generated for students and residents were compared and reviewed by seven academic vascular surgeons practicing in a teaching hospital. Five-point Likert scales were used to rate the accuracy, completeness, complexity, and applicability of each text (Table I). Average values of each survey question were compared using Mann-Whitney U tests. Results: Aside from increased use of more advanced medical terminology in residents’ texts, content was similar in the two texts. Overall, the scores were slightly higher for the text generated for the residents (average, 3.91) vs the students (average, 3.71) (Table II). All surgeons believed that information was accurate (average, 4.5), although more accurate for residents (average, 4.71) vs students (average, 4.29). Most surgeons believed that information was not advanced enough

(average, 3.21), albeit slightly more advanced for residents (average, 3.29 vs 3.14 for students). Most surgeons were on the fence on whether they would use the text to teach medical students (average, 3.43) or residents (average, 3.57). Conclusions: Although Chat GPT offers promising prospects in venous education, the current Chat GPT is not up to standards when used for medical education. Although the information was accurate and concise, it was not advanced enough for medical education, and most surgeons were not very enthusiastic about using it to teach students or residents. Optimizing Chat GPT-generated searches and expanding its applicability to specialized education is subject to future development and research. [Formula presented] [Formula presented]

Cardiology/Cardiovascular Research

Nichol G, Dickert N, Adams K, Morse D, Morse S, Facemire C, Shah K, Dasari S, Bodnar J, Kapur N, **O'Neill W**, and Stone GW. Methods and Preliminary Results of Implementation of Multi-Center Earlyimpella® Support in Patients with St-Segment Elevation Myocardial Infarction Complicated by Cardiogenic Shock (RECOVER IV) Trial Under Exception from Informed Consent. *J Heart Lung Transplant* 2024; 43(4):S126-S127. Full Text

Purpose: Cardiogenic shock (CS) is end-organ hypoperfusion due to reduced cardiac output (CO). ~50% of patients with CS and acute myocardial infarction die before discharge. Drugs or devices can improve CO. We do not know if temporary mechanical circulatory support (MCS) improves long-term survival. Few trials have enrolled patients with CS in the United States (US) in part due to difficulties obtaining informed consent. The prognosis of patients with CS who are able to consent for research differs from those who are not, so consent-based trials may bias estimates of treatment. Exception from informed consent (EFIC) for emergency research is allowed in the US if certain conditions are met a priori. Prior EFIC studies required more than nine months to meet these conditions due to local site variation in implementation. We are implementing and evaluating a centralized, standardized EFIC framework in the RECOVER IV trial of standard care with Impella (Abiomed, Danvers, MA) MCS vs. standard care alone in patients who present with CS. Methods: Over five years, 560 patients (280 per group) will be randomized to intervention (Impella and standard care) vs. control for 90% power to detect a 13.5% difference in 30-day survival. Community consultation (CC) and public disclosure (PD) in candidate sites is required before starting enrollment. CC seeks community feedback about the study. PD gives information about the study for transparency and trustworthiness. We will centrally-coordinate CC and PD across up to 40 US sites, with localized study-specific websites, social media, focus groups, community events, radio ads, print media, and a single IRB to increase efficiency of site start up. Participants enrolled under EFIC will be notified of enrollment as soon as feasible, and consent will be sought for ongoing participation. Ten European sites will enroll patients using deferred consent. Results: The first site to complete CC and PD required three months from initiation of activities to IRB approval using our centralized framework. Conclusion: Effectively studying interventions in patients with CS requires EFIC in the US. Centrally-coordinated EFIC may improve the efficiency of study initiation to facilitate rapid advancement of evidence-based care.

Cardiology/Cardiovascular Research

Pienta M, Pegues J, Cascino T, **Cowger J**, Rosenbaum A, Hawkins RB, Colvin M, Aaronson K, Yang J, Likosky D, Pagani F, and Tang PC. Intermacs Analysis of Impact of Significant Post-LVAD Mitral Regurgitation on Outcomes. *J Heart Lung Transplant* 2024; 43(4):S136-S137. Full Text

Purpose: Impact of significant post-implant mitral regurgitation (PI-MR) on left ventricular assist device (LVAD) outcomes remains controversial. We investigated the effect of PI-MR from a real-world experience. Methods: Intermacs Database was queried to identify 7,385 patients receiving primary HeartMate 3 implant from 2014-2021. Patients undergoing concomitant mitral valve procedures were excluded. Significant PI-MR following LVAD implant was defined as moderate/severe MR post-implant on 1 or 3-month echocardiogram. Those not surviving 3 months (n=682) and/or without echocardiogram results available (n=781) were excluded. Survival and readmission analysis using log-rank statistics were conditional on 3 month survival. Results: The study cohort consisted of 363 patients with significant PI-MR and 2,744 patients without significant PI-MR. Those with significant PI-MR were younger (53 vs 57 years, P<0.001), more likely to be African American (39% vs 31%, P<0.01), have a higher pre-implant total bilirubin (1.5 vs 1.2 mg/dL) and more likely to have an intra-aortic balloon pump at the time of LVAD implant (35% vs 28%, P<0.01) compared to patients with no PI-MR. Of those with preop significant MR,

17% (n=292) had persistent significant PI-MR. For those with mild or less pre-implant MR, 5% (n=71) developed new significant PI-MR. Patients with significant PI-MR had worse survival at 2 years, conditional upon surviving 3 months (80% vs 87%, P=0.024) and freedom from all-cause readmissions (27% vs 36%, P=0.03). Significant PI-MR also predicted worse conditional mortality based on log-rank statistics (P=0.012, Figure A) and increased readmissions (P=0.004, Figure B). Those patients with significant PI-MR were more likely to have received concomitant tricuspid valve surgery (17% vs 10%, P<0.001). Conclusion: Significant residual MR following LVAD adversely impacts 2-year survival and all-cause readmissions. These data suggest that strategies to reduce the occurrence of PI-MR may improve durable LVAD outcomes. [Formula presented]

Cardiology/Cardiovascular Research
Shapiro S, Pienta M, Zhou S, Swaminathan S, Chandanabhumma P, Chenoweth C, Hawkins R, Cascino T, Aaronson K, **Cowger J**, Malani P, Cabrera L, Likosky D, and Pagani F. Effectiveness of Pump Exchange for Major Device Related Infection in Patients Receiving a Durable Left Ventricular Assist Device. *J Heart Lung Transplant* 2024; 43(4):S447. Full Text

Purpose: Purpose: Device-related infection (DRI) remains a major cause of morbidity and mortality following durable left ventricular assist device (dLVAD) implantation. Given limited data that informs the long term effectiveness of pump exchange for treatment of DRI, this study evaluated outcomes following pump exchange for DRI following dLVAD implantation. Methods: Methods: In this single center analysis, 49 patients were identified with DRI leading to dLVAD exchange (1/2007 - 12/2022). Major outcomes include survival, incidence of reinfection and proportion of patients free from reinfection 1-year following pump exchange. Results: Results: Median age was 49 years with 71% male and 57% White with 28.6% HeartMate 3, 57.1% HeartMate II, and 16.3% HVAD pumps. Median time from primary dLVAD implant to DRI diagnosis was 26 [7.8, 33.5] months. Time from DRI diagnosis to pump exchange was 4.1 [1.4, 10.1] months. Of the DRIs, 31 (63%) were localized to the percutaneous lead and 18 (37%) involved the pump pocket/component. The most common organism was Staphylococcus aureus (methicillin sensitive, N=17, 35%; methicillin resistant, N=5, 10%). Thirty (61%) patients underwent pump exchange alone and 19 (39%) underwent pump exchange with omental flap. Overall survival was 62.5+/-7.4% at 2-years following pump exchange. Freedom from reinfection at 1-year was 76% (N=37). The median time to DRI recurrence (N=18) was 5.8 [2.6, 14.7] months with 33% experiencing DRI after 12 months. Freedom from reinfection was obtained in 22/23 (96%) of patient whose time to pump exchange from DRI diagnosis was </= 3 months and 15/26 (58%) if > 3 months. Conclusion: Conclusion: While most patients achieve early success following pump exchange for DRI, the risk of DRI recurrence and mortality remains high. Early (</= 3 months) pump exchange following DRI diagnosis increases the likelihood of success while reducing the rate of DRI recurrence. Further studies are needed to optimize the strategy of pump exchange for DRI.

Cardiology/Cardiovascular Research
Steinberg RS, **Cowger J**, Hsi B, Morris A, Nohria A, Hall S, and Nayak A. Clinician Assessed Versus Objective Measures of Frailty in Left Ventricular Assist Device Patients. *J Heart Lung Transplant* 2024; 43(4):S500-S501. Full Text

Purpose: Society guidelines recommend frailty assessment in Left Ventricular Assist Device (LVAD) candidates. Frailty is a multi-domain syndrome that includes compromised mobility and nutritional status. While often assessed via the “eyeball test,” there is a need to identify objective frailty measures that correlate with patient outcomes, allowing for standardization of candidacy assessment. We studied 1) the association of clinician assessed frailty with objective measures of mobility (6-minute walk distance, 6MWD) and nutritional status (prealbumin), and 2) the association of these factors with outcomes. Methods: We included LVAD patients from 2007-17 from the Intermacs registry who had frailty status reported. Objective frailty measures were compared between patients with and without clinician assessed frailty. Multivariable models were used to study the association between objective frailty measures and post-LVAD mortality. The association of clinician assessed frailty with mortality was studied via a propensity score-matched analysis, matching for disease severity and objective frailty measures. Results: Of 15,371 patients (age: 56.9 13.0 yrs, 21% female, 24% Black), 1015 (6.6%) were clinician assessed as frail. Clinician assessed frailty correlated with objective frailty measures. (Table 1) Patients too sick to

complete testing or those with 6MWD <300 m, and prealbumin<16 mg/dL had significantly worse mortality than those with values above these thresholds, independent of clinician assessed frailty. (Table 2) Clinician assessed frailty remained associated with mortality in the propensity-matched analysis (n=932, HR: 1.25 [1.01-1.55], p=0.04). Conclusion: In this analysis, we demonstrate that routinely obtained, objective measures of frailty can be used to identify patients at risk for increased events after LVAD. Utilization of objective measures may allow for improved frailty comparisons over time, between centers, and amongst different patient populations. [Formula presented]

Emergency Medicine

Fagan T, **Miller ME**, and **Henkin D**. Use of Buprenorphine for Cancer Related Pain in Pregnancy. *J Pain Symptom Manage* 2024; 67(5):e755. Full Text

Outcomes: 1. Participants will be able to recognize buprenorphine as a safe and effective analgesic for cancer pain in pregnancy 2. Participants will be able to integrate buprenorphine into more facets of clinical practice in treatment of cancer-related pain. Key Message: There is paucity of literature describing the treatment of cancer associated pain in pregnancy. Buprenorphine is an increasingly recognized analgesic used to treat cancer pain with an established safety profile studied in maternal opioid use disorder (OUD). We present a case demonstrating the safe and efficacious use of buprenorphine for cancer-related pain in a pregnant woman with a pancreatic neoplasm. Opioids often are utilized for the optimization of cancer related pain; however, managing cancer-related pain in pregnancy can present challenges, particularly due to opioid-related risks to the fetus in utero. In addition, there is a paucity of literature with regard to treating cancer related pain in pregnancy. Here we present a case where buprenorphine was successfully used to manage cancer related pain for a pregnant female. We present a case of a 36-year-old G3P2 female diagnosed with metastatic solid pseudopapillary epithelial neoplasm (SPEN) of the pancreas at 27 weeks gestation. She began experiencing severe nociceptive visceral abdominal pain, which impaired her ability to perform activities of daily living and even sleep throughout the night. She was started on very low doses of buprenorphine (partial Suboxone SL films), three times a day with improved pain control, physical functioning and sleep with minimal to no side effects. Labor was induced at 34 weeks secondary to intrauterine growth restriction and oligohydramnios, with APGAR scores 8/8 at birth. Buprenorphine was continued for pain control postpartum at varying doses, compatible with patient's wish to continue to breastfeed with appropriate analgesia. Buprenorphine is becoming increasingly more recognized for its efficacy in treating cancer-related pain. The literature describing buprenorphine for pain management in pregnancy is limited; however, its use in treating opioid use disorder in pregnancy and fetal safety profile is well understood. In presenting this case, we demonstrate the safe and efficacious utility of buprenorphine for cancer-related pain during pregnancy Keywords: Disease specific management / Pharmacotherapeutics / Pharmacopalliation

Emergency Medicine

Gunaga S, **Al-Hage A**, **Welchans M**, **Buchheister A**, **Corcoran J**, **Meeker K**, **Buckley B**, Egbe-Etu E, **Miller J**, and Banerjee C. Emergency Departments as the Portal of Entry for Inpatient Geriatric Hospice and Palliative Medicine Consults. *J Pain Symptom Manage* 2024; 67(5):e714. Full Text

Outcomes: 1. Recognize the Emergency Department as a primary portal of hospital entry for downstream Hospice and Palliative Medicine Consults in Geriatric patients. 2. Recognize that one out of eleven geriatric ED patients in this sample received a Hospice and/or Palliative medicine consult during their hospitalization. Key Message: At the crossroads of acute care and palliative medicine, Emergency Departments (ED) play a defining role in providing end-of-life geriatric care. This study specifically explores geriatric ED visits and subsequent Hospice and Palliative Medicine (HPM) needs, uncovering a rising annual trend of HPM consults and identifying the ED as the portal of hospital entry for 84.4% of all these patients. Introduction: At the crossroads of acute care and palliative medicine, Emergency Departments (ED) play a defining role in providing end-of-life geriatric care. Objective: This study aims to quantify the prevalence and trends of geriatric (Age > 65) ED visits and subsequent downstream hospice and palliative medicine (HPM) needs. Methods: We conducted a multi-center retrospective cohort study of electronic health records from five hospitals within a large metropolitan health system, from January 1st, 2018, to December 31st, 2022. Data included all ED visits and inpatient hospital admissions in adult patients with a HPM consult ordered during their encounter. A variety of patient specific demographic,

clinical, and outcome variables were collected. The yearly number of HPM consults ordered in each hospital were also obtained and compared by year and site. Across years, we compared the incidence of geriatric ED visits, hospitalizations and HPM consults per every 1,000 geriatric ED visits. Data analysis included descriptive statistics, chi-square testing, and regression analysis. Results: A total of 27,100 HPM consults were ordered for 23,555 unique patients meeting inclusion criteria. In 2018, 4,229 unique patients received HPM consults, and this number grew by 24.1% to 5,247 consults in 2022 (p <.001). Among patients who received HPM consults, 84.4% (19,870) were admitted to the hospital through the ED. Of all HPM consults, 74.8% (17,622) involved geriatric patients. Geriatric patients accounted for 23.2% (503,249) of all ED encounters, of which 42.3% (231,036) resulted in an inpatient hospitalization or observation stay. Of these geriatric admissions, 7.8% (16,698) ultimately received a HPM consult. The calculated prevalence of HPM consults for geriatric patients was 33 downstream consults for every 1,000 geriatric ED visits. Keywords: Emergencies / Refractory Symptom ManagementScientific Research

Endocrinology and Metabolism

Davydov E, **Davydov E**, **Gomes K**, and **Athimulam S**. #1704446 Bilateral Adrenal Hemorrhage Causing Acute Adrenal Insufficiency. *Endocr Pract* 2024; 30(5):S8-S9. Full Text

Introduction: Adrenal hemorrhage is an under-recognized condition often found incidentally on imaging in acutely ill patients. Unilateral adrenal hemorrhage is usually clinically silent however bilateral adrenal hemorrhage can cause acute primary adrenal insufficiency which can be life threatening. This is a case of acute adrenal insufficiency secondary to bilateral adrenal hemorrhage. Case(s) Description: A 79 year old male with a history of chronic obstructive pulmonary disease presented to the emergency department with a chief complaint of altered mental status. He initially presented to an outside hospital one day prior with abdominal pain and computed tomography (CT) with contrast demonstrated no discrete adrenal nodules. On repeat imaging, CT abdomen/pelvis without contrast demonstrated new bilateral adrenal masses concerning for bilateral adrenal hemorrhage and possible enteritis. He was started on antibiotics for presumed infection of abdominal source and was transferred to our facility for higher level of care. Repeat CT abdomen and pelvis with and without contrast two days later demonstrated bilateral adrenal masses, 2.9 cm on the left and 3.8 cm on the right, with heterogeneous attenuation consistent with bilateral adrenal hemorrhage which was stable from prior but new from the initial imaging study. Three days after admission he was transferred to the medical intensive care unit due to hypotension requiring pressors. Morning cortisol was 6.6 ug/dL. He was started on hydrocortisone 100 mg every 8 hours and fludrocortisone 0.05 mg daily with improvement in blood pressure. Blood cultures were negative and antibiotics were discontinued. He was discharged home on oral hydrocortisone and fludrocortisone with plans for further workup outpatient. Sick day rules were provided. Discussion: This case illustrates a presentation of acute adrenal insufficiency due to bilateral adrenal hemorrhage. Most signs and symptoms are nonspecific but the most commonly reported are hypotension, mental status changes, and nausea and vomiting which can all be attributed to adrenal insufficiency. Abdominal pain can also occur. On non-contrast cross sectional CT imaging, acute adrenal hemorrhage is seen by the development of high or mixed attenuated adrenal lesion within hours or days, as seen in this patient. Predisposing factors for adrenal hemorrhage that should be considered are adrenal tumors, sepsis, coagulopathies, surgeries, or trauma. Further work up will need to be done to try to determine the etiology of the adrenal hemorrhage as it can be the initial presentation of underlying hematologic disorder or adrenal lesion.

Endocrinology and Metabolism

Gomes K, **Rothstein-Costris A**, and **Bhan A**. #1703236 Hyperthyroidism As an Initial Presentation of Thyroid Metastasis from Lung Adenocarcinoma. *Endocr Pract* 2024; 30(5):S148-S149. Full Text

Introduction: Metastases to the thyroid have a low reported incidence, with a frequency of 2-4% among all thyroid malignancies. In autopsy series, lung cancer is reported to be the most common primary tumor, while clinically, renal cell cancer is the most common. Most thyroid metastases present as unifocal nodules; however, diffuse metastases are less often seen. Patients are euthyroid at presentation, and hyperthyroidism is very rarely reported. Case(s) Description: A 74-year-old man was referred for evaluation of hyperthyroidism. Initial symptoms included palpitations and weight loss. TSH was < 0.01 uIU/mL (0.40 - 7.50), free T4 3.08 ng/dL (0.61 - 1.44), total T3 125 ng/dL (87 - 178). TSI was negative. Evaluation of weight loss prompted a CT chest which revealed several lung nodules and enlarged

mediastinal and hilar lymph nodes. Incidental finding of punctate calcification was reported in the left thyroid lobe with no distinct thyroid nodules. Staging 18F-FDG-PET CT revealed intense uptake in bilateral thyroid lobes, initially thought to be related to active hyperthyroidism. Biopsy of a right supraclavicular lymph node was performed, and pathological evaluation revealed metastatic lung cancer. Given intense uptake in the thyroid on PET, neck ultrasound was performed and revealed bilateral heterogeneous appearing thyroid gland with numerous diffuse punctate echogenic foci with no discrete nodules and several morphologically abnormal lymph nodes. Random fine needle aspiration of bilateral thyroid lobes and left cervical lymph node was performed and was positive for lung adenocarcinoma. Core needle biopsy of right lung mass revealed adenocarcinoma. On follow up, thyroid labs spontaneously normalized, consistent with thyroiditis. Molecular testing guided treatment with Capmatinib. Discussion: Hyperthyroidism as an initial presentation of thyroid malignancy is rare as most patients are euthyroid. In this case, we speculate that aggressive invasion of tumor cells into the thyroid resulted in thyroiditis. Additionally, diffuse echogenic foci in the thyroid are uncommonly seen in metastatic thyroid disease, which usually presents as single or multiple nodules. Diffuse uptake on PET CT has been shown to be associated with benign autoimmune thyroid disease while malignant lesions usually have focal uptake. However, in the setting of an underlying malignancy, this case highlights that a diffuse uptake should not be regarded as a benign finding. Random bilateral thyroid biopsies should be performed in patients who have positive diffuse FDG-PET uptake, without a discrete nodule, in patients known to have an underlying non-thyroidal malignancy.

Family Medicine

Liaqat H, Liaqat H, Chavez L, and **Pasha F**. #1706859 Localizing The Source of Androgens. *Endocr Pract* 2024; 30(5):S129-S130. Full Text

Introduction: There are multiple etiologies of excess testosterone in a female of childbearing age. Over 95% cases are due to PCOS but this is a diagnosis of exclusion after other pathologies like Cushing's, nonclassical congenital adrenal hyperplasia, ovarian and adrenal tumors have been ruled out. Case(s) Description: We present a case of a 22-year-old female evaluated for hyperandrogenic symptoms including hirsutism across all areas of body, secondary amenorrhea for 2 years, balding in a male pattern and deepening of her voice. Physical exam revealed frontal balding, absence of clitoromegaly and excessive hair on chin and upper lip. Initial evaluation showed elevated total testosterone of 235 ng/dL and a free testosterone of 7.99 ng/dL. Repeat testing showed similar results. Other testing revealed normal DHEA-S, estradiol, 17 hydroxyprogesterone, 24-hour urine cortisol and adequate suppression with 1 mg dexamethasone suppression testing. Ultrasound of the ovaries revealed multi follicular ovaries. An initial diagnosis of PCOS was made. Given her elevated testosterone level above 150, we proceeded to rule out an adrenal or ovarian source of excess androgens. 2-day dexamethasone androgen suppression test showed adequate suppression of DHEA-S and cortisol but no suppression of total and free testosterone, which pointed towards an ovarian source. Further evaluation included MRI of the pelvis which did not reveal any pelvic masses and tumor markers including beta hCG, CA125 and alpha-fetoprotein were all normal. This was deemed as a case of PCOS with excessively elevated testosterone with hyperandrogenic symptoms. Once other pathologies were ruled out, she was treated along PCOS guidelines. Discussion: Testosterone above 150 ng/dl is normally not seen in PCOS, and guidelines recommend ruling out other sources of hyperandrogenism. Initial lab testing includes total and free testosterone, 17-hydroxyprogesterone, TSH, prolactin and DHEA-S. Elevated 17-hydroxyprogresterone points towards nonclassical CAH. If labs show normal 17-OH progesterone, the next step involves a 2-day dexamethasone-androgen suppression test which helps differentiate adrenal from ovarian sources depending on cortisol, testosterone and DHEA-S levels post suppression. If the testosterone level fails to be suppressed but DHEA-S and cortisol respond, the source of testosterone is primarily the ovaries. Lack of suppression of androgens and cortisol points to adrenal hyperfunction, like Cushing's. If the high level of testosterone is suppressed more than 40% and DHEAS is suppressed more than 60% after administration of dexamethasone, the source of the increased androgen is most likely the adrenal glands. Although not outlined in the guidelines, ruling out an ovarian tumor with a transvaginal ultrasound or MRI pelvis with or without tumor markers of ovarian origin can be undertaken if suspicion is high. Other testing like GnRH analogues for androgen suppression or ovarian vein sampling can be undertaken on a case-by-case basis but not always needed. Treatment depends on underlying etiology.

Internal Medicine

Ayyad A, **Fadel R**, and **Alqarqaz M**. 100.76 Assessing Mortality Risk in Cardiogenic Shock Patients on VA-ECMO: The Role of SAVE Score, SOFA Score, and 8-Hour Lactate Clearance. *JACC Cardiovasc Interv* 2024; 17(4):S23-S24. Full Text

Background: Cardiogenic shock (CS) is a life-threatening perfusion impairment due to cardiac dysfunction. Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) can provide robust hemodynamic support in patients unresponsive to medical therapy. However, predicting outcomes in patients requiring ECMO support has proved challenging. This study sought to examine in-hospital mortality rates in patients with refractory CS undergoing VA-ECMO and evaluate the association of Survival After VA-ECMO (SAVE) score, Sequential Organ Failure Assessment (SOFA) score, and post-cannulation lactate levels with inpatient mortality. Methods: A retrospective review of adult patients who underwent peripheral VA-ECMO cannulation from January 2018 to September 2022 at a quaternary care center. In-hospital mortality was assessed and compared to predicted mortality by SAVE and SOFA scores, with adjusted odds ratio of risk factors for mortality identified by multivariate logistic regression analysis. Additionally, the prognostic value of 8-hour 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. In-hospital mortality was 70%, and 54% of patients died while on ECMO or within 24 hours of decannulation. SAVE score (OR 0.93 per unit increase, 95% CI 0.86 - 0.99, p=0.008), SOFA score (OR 1.53 per unit increase, 95% CI 1.32 - 1.75), and 8-hour post-cannulation lactate level (OR 1.20 per mmol/L increase, 95% CI 1.04 - 1.36, p=0.012) and clearance (OR 0.98 per % decrease, 95% CI 0.97 - 0.99, p=0.026) were independently associated with in-hospital mortality. An 8-hour post-cannulation lactate level above 7.8 mmol/L was associated with high specificity for in-hospital mortality (91.1%). Patients with 8-hour post-cannulation lactate levels above the cutoff of 7.3 mmol/L demonstrated significantly higher 30-day mortality across the entire follow-up period. Conclusion: SAVE and SOFA scores are useful tools in determining prognosis of patients with CS on VA-ECMO. 8-hour post-cannulation serum lactate levels are a pragmatic biomarker which can further assist in prognostication of patients requiring VA-ECMO, and the cutoff of 7.3 mmol/L at 8-hours appears to be a reliable measure. The development of accurate prognostic tools is critical in managing and optimizing care for patients with CS.

Internal Medicine

Gomes K, **Rothstein-Costris A**, and **Bhan A**. #1703236 Hyperthyroidism As an Initial Presentation of Thyroid Metastasis from Lung Adenocarcinoma. *Endocr Pract* 2024; 30(5):S148-S149. Full Text

Introduction: Metastases to the thyroid have a low reported incidence, with a frequency of 2-4% among all thyroid malignancies. In autopsy series, lung cancer is reported to be the most common primary tumor, while clinically, renal cell cancer is the most common. Most thyroid metastases present as unifocal nodules; however, diffuse metastases are less often seen. Patients are euthyroid at presentation, and hyperthyroidism is very rarely reported. Case(s) Description: A 74-year-old man was referred for evaluation of hyperthyroidism. Initial symptoms included palpitations and weight loss. TSH was < 0.01 uIU/mL (0.40 - 7.50), free T4 3.08 ng/dL (0.61 - 1.44), total T3 125 ng/dL (87 - 178). TSI was negative. Evaluation of weight loss prompted a CT chest which revealed several lung nodules and enlarged mediastinal and hilar lymph nodes. Incidental finding of punctate calcification was reported in the left thyroid lobe with no distinct thyroid nodules. Staging 18F-FDG-PET CT revealed intense uptake in bilateral thyroid lobes, initially thought to be related to active hyperthyroidism. Biopsy of a right supraclavicular lymph node was performed, and pathological evaluation revealed metastatic lung cancer. Given intense uptake in the thyroid on PET, neck ultrasound was performed and revealed bilateral heterogeneous appearing thyroid gland with numerous diffuse punctate echogenic foci with no discrete nodules and several morphologically abnormal lymph nodes. Random fine needle aspiration of bilateral thyroid lobes and left cervical lymph node was performed and was positive for lung adenocarcinoma. Core needle biopsy of right lung mass revealed adenocarcinoma. On follow up, thyroid labs spontaneously normalized, consistent with thyroiditis. Molecular testing guided treatment with Capmatinib. Discussion: Hyperthyroidism as an initial presentation of thyroid malignancy is rare as most patients are euthyroid. In this case, we speculate that aggressive invasion of tumor cells into the thyroid resulted in thyroiditis. Additionally, diffuse echogenic foci in the thyroid are uncommonly seen in

metastatic thyroid disease, which usually presents as single or multiple nodules. Diffuse uptake on PET CT has been shown to be associated with benign autoimmune thyroid disease while malignant lesions usually have focal uptake. However, in the setting of an underlying malignancy, this case highlights that a diffuse uptake should not be regarded as a benign finding. Random bilateral thyroid biopsies should be performed in patients who have positive diffuse FDG-PET uptake, without a discrete nodule, in patients known to have an underlying non-thyroidal malignancy.

Internal Medicine

Qureshi AA, Munir L, **Qureshi MA**, Alvi Z, Kashif T, Muhammad A, Khalid A, and Shahid A. TEMPORAL TRENDS IN SUDDEN CARDIAC DEATH MORTALITY RATES IN UNITED STATES FROM 1999 TO 2020 - AN ANALYSIS OF EPIDEMIOLOGICAL DISPARITIES. *J Am Coll Cardiol* 2024; 83(13):703. Full Text

Background Sudden cardiac death (SCD) mortality is on the decline in the United States. This study explores SCD trends from 1999 to 2020, using age-adjusted mortality rates (AAMR) to identify disparities within specific epidemiological groups. Methods We analyzed SCD mortality trends using the Centers for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiological Research database. AAMR per 100,000 people and annual percent changes (APC) with 95% confidence intervals were calculated. Joinpoint regression analysis was used to assess overall trends and variations among key demographic (gender, race, age, urban/rural), and regional groups. Results Between 1999 and 2020, 281,330 sudden cardiac deaths were reported. The overall AAMR for SCD decreased from 4.5 in 1999 to 3.6 in 2020. Higher mortality rates were observed in males, African Americans, individuals over 85 years old and residents of nonmetropolitan areas. From 1999 to 2018, the AAMR decreased significantly with an annual percent change (APC) of -1.92. However, an increase occurred between 2018 (AAMR 3.1) and 2020 (AAMR 3.6) with an APC of 4.16. Conclusion Over the past two decades, SCD mortality has declined in the United States, but recent data suggests a concerning upturn. Persistent demographic and geographic disparities in SCD mortality underscore the need for further investigation and intervention.

Nephrology

Tennant T, **Grech A**, and **Shaban H**. Ease and Efficacy of Subcutaneous Ketamine for Depression in Home Hospice Patients: 2 Case Reports. *J Pain Symptom Manage* 2024; 67(5):e623-e624. Full Text

Outcomes: 1. Identify hospice patients that would benefit from the use of ketamine in the home setting. 2. List the acceptable routes of administration and starting dose of Ketamine. Key Message: Patients suffering from depression at the end of life often do not have weeks to wait for antidepressants to take effect. Ketamine is a promising treatment as it offers rapid and durable response; however, often requires infusion in a clinic or inpatient setting. These two cases demonstrate the safety and feasibility of administering subcutaneous ketamine in the home hospice setting. Background: Ketamine is known to relieve treatment-resistant depression and opioid refractory pain. While antidepressants take several weeks, ketamine has a rapid onset, making it a promising therapy for depression in patients at end of life (EOL). Literature demonstrates that cancer patients may experience rapid and sustained improvement in depression and anxiety. These studies largely use compounded oral or intravenous (IV) formulations of ketamine which are barriers to widespread implementation. Hospices may not have access to compounding pharmacies and the IV route may not be feasible for patients at EOL, especially in the home setting. Case Description: Mrs. C was an 80-year-old female with metastatic cervical cancer, severe pulmonary hypertension, and depression. She experienced severe major depression after home hospice enrollment. She was administered intravenous ketamine 0.5 mg/kg over 40 minutes in her home under physician and nurse supervision. She experienced rapid improvement in mood within an hour and no significant side effects or changes in vital signs. Her son stated, “I got my mom back.” Due to difficulty obtaining IV access two subsequent infusions were administered subcutaneously (SQ) over 45 minutes on weeks 2 and 3 following the initial. Effects on mood were sustained for the following 20 weeks until death. In case #2, Mrs. B was a 74-year-old female with congestive heart failure and depression. Her depression was poorly controlled on five agents. Subcutaneous ketamine was administered at the same dose and supervision as the first case while rotating her oral antidepressant regimen. She did not experience improvement in mood, but tolerated the injection without significant side effect or change in vital signs. Conclusion: These cases suggest SQ ketamine administration is safe and feasible in the

home hospice setting. Treatment response was mixed and highlights need for further research in dosing intervals and titration for apparent ketamine non-responders. Keywords: Managing Suffering and Distress; Models of Palliative Care Delivery

Neurology

Stocchi F, Espay A, Albanese A, Ellenbogen A, Ferreira JJ, Giladi N, Gurevich T, Hassin-Baer S, Hernandez-Vara J, Isaacson S, Kieburtz K, **LeWitt P**, Lopez-Manzanares L, Olanow CW, Pahwa R, Poewe W, Sarva H, Yardeni T, Adar L, Lopes N, Sasson N, Case R, and Rascol O. Continuous subcutaneous levodopa/carbidopa infusion (ND0612) for patients with Parkinson's disease and motor fluctuations: A Phase 3, active-controlled study (BouNDless). *Parkinsonism and Related Disorders* 2024; 122. Full Text

Background: We determined the efficacy, safety, and tolerability of ND0612, an investigational, continuous 24-hours/day subcutaneous infusion of levodopa/carbidopa (LD/CD), versus oral immediate-release (IR) LD/CD in people with Parkinson's disease (PwP) experiencing motor fluctuations. Methods: This is a phase 3, double-blind, double-dummy (DBDD) trial (NCT04006210). PwP on ≥4 oral LD/CD doses/day (≥400mg/day LD) and experiencing ≥2.5h of daily OFF-time underwent 4-6 weeks of open-label IR-LD/CD dose adjustment followed by 4-6 weeks of open-label ND0612 conversion (+ IR-LD/CD as needed). Patients were randomized (1:1) to 12-week DBDD treatment with either their optimized ND0612 or IR-LD/CD regimens. Results: In the open-label adjustment/conversion phases, mean ON-time without troublesome dyskinesia (OTwoTD) increased from 9.4h (both arms) at enrollment to 11.8h (ND0612) and 12.1h (IR-LD/CD) following optimization of the ND0612 regimen. During the 12-week DBDD treatment OTwoTD was maintained in the ND0612 group (11.5h at endpoint) but decreased in the IR-LD/CD group who had their ND0612 infusion withdrawn (9.8h at endpoint). The study met its primary endpoint, with the ND0612 regimen providing an additional 1.72h [95%CI: 1.08h, 2.36h] of OTwoTD compared with IR-LD/CD ($p<0.0001$). Significant treatment effects (TE) vs. IR-LD/CD were also seen in the hierarchical secondary endpoints: OFF-time (TE: -1.40 [-1.99, -0.80]h, $p<0.0001$), MDS-UPDRS Part II (TE: -3.05 [-4.28, -1.81], $p<0.0001$) and global impressions by patients (Odds ratio [OR] of improvement: 5.31 [2.67, 10.58], $p<0.0001$) and clinicians (OR: 7.23 [3.57, 14.64], $p<0.0001$). Infusion site reactions were the most reported adverse events (82.6% during open-label conversion to infusion, during the DBDD period the rates were 57.0% for ND0612 vs. 42.7% for IR-LD/CD). Discontinuation rates after randomization (DBDD phase; ND0612 vs IR-LD/CD) were 6.3% vs 6.1% overall, and 5.5% vs 3.1% due to adverse events. Conclusions: ND0612 treatment led to clinically meaningful improvement in motor fluctuations and functional endpoints vs oral IR-LD/CD and was generally well tolerated.

Neurosurgery

Wilson TG, **Baghel M**, **Kaur N**, **Loveless I**, **Datta I**, Potla P, **Mendez D**, **Hansen L**, **Baker K**, **Lynch TS**, **Moutzouros V**, **Davis J**, and **Ali SA**. IDENTIFICATION AND CHARACTERIZATION OF MIR-126-3P AS A DIAGNOSTIC BIOMARKER, MECHANISTIC DRIVER, AND THERAPEUTIC TARGET FOR KNEE OSTEOARTHRITIS. *Osteoarthritis Cartilage* 2024; 32:S52-S53. Full Text

Purpose (the aim of the study): To reduce the immense burden of disease associated with knee osteoarthritis (OA), there is an urgent need for molecular biomarkers for earlier diagnosis and therapeutic targets for effective intervention. MicroRNAs (miRNAs) are small non-coding RNAs with the potential to meet both these needs given their specificity and stability in liquid biopsies as well as their ability to regulate key biological processes through direct inhibition of gene targets. Found across tissues, miRNAs are expressed as primary transcripts (pri-miRNAs) that are processed into precursor transcripts (pre-miRNAs) then mature miRNAs. To identify important miRNAs in knee OA, we performed secondary analysis of two miRNA-sequencing datasets and discovered circulating miR-126-3p to be elevated compared to non-OA controls, a finding we validated in our Henry Ford Health OA cohort. Existing literature indicates miR-126-3p is primarily expressed by endothelial cells and regulates angiogenesis through inhibition of its gene target SPRED1. In a rat model of OA, exosomes carrying miR-126-3p were shown to attenuate the severity of disease. Based on these findings, the objectives of this study are to assess miR-126-3p as a diagnostic biomarker, mechanistic driver, and therapeutic target for knee OA. Methods: To investigate the biomarker potential of miR-126-3p, we assessed its predictive ability with area under the receiver operating characteristic curve (AUC) analysis and explored correlations with

common confounding variables. To investigate the mechanistic potential of miR-126-3p, we collected subchondral bone, infrapatellar fat pad, synovium, anterior cruciate ligament, meniscus and articular cartilage from N=20 OA patients undergoing knee replacement. We measured pri-mir-126, pre-mir-126, and miR-126-3p in each tissue by real-time PCR and quantified miR-126-3p secretion from tissue explants into culture medium over time. We transfected bone, fat pad and synovium explants and cells with 100nM miR-126-3p mimic, inhibitor, or controls and measured candidate gene expression changes. To investigate the therapeutic potential of miR-126-3p, we performed medial meniscectomy or sham surgery in right knees of 12-week-old mice and delivered 4 weekly injections of miR-126-3p mimic, inhibitor, or controls. At 20 weeks, harvested knee joints were assessed by OARSI grading in a blinded manner. Results: Exploring its potential as a biomarker for radiographic knee OA, we found that circulating miR-126-3p showed greater accuracy for predicting knee OA (AUC = 0.83) compared to age, sex, and BMI alone (AUC = 0.52), and importantly showed no association with age, sex, or BMI. Exploring miR-126-3p in knee OA tissues, we found the highest levels in bone, fat pad and synovium versus cartilage which showed the lowest levels (Figure 1). Fat pad had high levels of both pri- and pre-mir-126, and exhibited the highest rate of miR-126-3p secretion over time, suggesting it may be a source of circulating miR-126-3p. Prioritizing bone, fat pad and synovium, we treated explants with miR-126-3p mimic and found reduced expression of OSX and OCN in bone, ADIPOQ and LEP in fat pad, and IL1b, IL6 and TNF in fat pad and synovium; we also found reduced NGF in all three tissues. For canonical functions of miR-126-3p, we found reduced SPRED1 and increased angiogenesis in endothelial cells isolated from bone, fat pad and synovium. Exploring the therapeutic potential of miR-126-3p in a mouse model, treatment with miR-126-3p mimic reduced the severity of knee OA, while inhibitor increased the severity. Conclusions: Our data-driven strategy identified circulating miR-126-3p in radiographic knee OA and further characterization revealed its potential as a candidate diagnostic biomarker. Systematic profiling of primary human knee OA tissues suggests miR-126-3p impacts specific mechanisms in bone, fat pad and synovium, reducing markers of osteogenesis, adipogenesis, inflammation and pain, with a concomitant increase in angiogenesis potentially indicating anabolism. Ta en together, our findings suggest that miR-126-3p may become elevated during OA as a mechanism to mitigate disease processes and therefore should be further evaluated as a therapeutic target for OA, where delivery at earlier stages may prevent progression to later stages. [Formula presented]

Nursing

Gunaga S, **Al-Hage A**, **Welchans M**, **Buchheister A**, **Corcoran J**, **Meeker K**, **Buckley B**, Egbe-Etu E, **Miller J**, and Banerjee C. Emergency Departments as the Portal of Entry for Inpatient Geriatric Hospice and Palliative Medicine Consults. *J Pain Symptom Manage* 2024; 67(5):e714. Full Text

Outcomes: 1. Recognize the Emergency Department as a primary portal of hospital entry for downstream Hospice and Palliative Medicine Consults in Geriatric patients. 2. Recognize that one out of eleven geriatric ED patients in this sample received a Hospice and/or Palliative medicine consult during their hospitalization. Key Message: At the crossroads of acute care and palliative medicine, Emergency Departments (ED) play a defining role in providing end-of-life geriatric care. This study specifically explores geriatric ED visits and subsequent Hospice and Palliative Medicine (HPM) needs, uncovering a rising annual trend of HPM consults and identifying the ED as the portal of hospital entry for 84.4% of all these patients. Introduction: At the crossroads of acute care and palliative medicine, Emergency Departments (ED) play a defining role in providing end-of-life geriatric care. Objective: This study aims to quantify the prevalence and trends of geriatric (Age > 65) ED visits and subsequent downstream hospice and palliative medicine (HPM) needs. Methods: We conducted a multi-center retrospective cohort study of electronic health records from five hospitals within a large metropolitan health system, from January 1st, 2018, to December 31st, 2022. Data included all ED visits and inpatient hospital admissions in adult patients with a HPM consult ordered during their encounter. A variety of patient specific demographic, clinical, and outcome variables were collected. The yearly number of HPM consults ordered in each hospital were also obtained and compared by year and site. Across years, we compared the incidence of geriatric ED visits, hospitalizations and HPM consults per every 1,000 geriatric ED visits. Data analysis included descriptive statistics, chi-square testing, and regression analysis. Results: A total of 27,100 HPM consults were ordered for 23,555 unique patients meeting inclusion criteria. In 2018, 4,229 unique patients received HPM consults, and this number grew by 24.1% to 5,247 consults in 2022 (p <.001). Among patients who received HPM consults, 84.4% (19,870) were admitted to the hospital through the

ED. Of all HPM consults, 74.8% (17,622) involved geriatric patients. Geriatric patients accounted for 23.2% (503,249) of all ED encounters, of which 42.3% (231,036) resulted in an inpatient hospitalization or observation stay. Of these geriatric admissions, 7.8% (16,698) ultimately received a HPM consult. The calculated prevalence of HPM consults for geriatric patients was 33 downstream consults for every 1,000 geriatric ED visits. Keywords: Emergencies / Refractory Symptom ManagementScientific Research

Orthopedics/Bone and Joint Center

Baghel M, **Wilson TG**, **Davis J**, **Moutzouros V**, Ormseth M, **Yousif P**, **Alkhatib A**, **Meysami A**, and **Ali SA**. PROFILING CIRCULATING MICRORNAS IN EARLY OSTEOARTHRITIS AND EARLY RHEUMATOID ARTHRITIS. *Osteoarthritis Cartilage* 2024; 32:S140. Full Text

Purpose (the aim of the study): In clinical settings, osteoarthritis (OA) and rheumatoid arthritis (RA) can present similarly and therefore can be difficult to distinguish, especially at early stages of single-joint disease when symptoms overlap. OA is most often assessed through radiography [e.g., Kellgren-Lawrence (KL) grading] by changes in bone (e.g., osteophytes) and joint space narrowing, features that are less obvious in early stages. Meanwhile, RA is diagnosed through symptom duration and serological factors which can overlap with other inflammatory conditions, especially in early stages. These limitations in current diagnostic methods for early stages of OA and RA can lead to delays in timely diagnosis and management, which is particularly problematic for RA since treatments are available. Accordingly, there is a need to identify biomarkers that can reliably differentiate early OA from early RA. A promising group of candidate biomarkers are circulating microRNAs (miRNAs) given their specificity, stability, and ease of detection in liquid biopsies. Here we aim to use microRNA-sequencing (miRNA-seq) to profile circulating miRNAs that can distinguish early OA patients from early RA patients. Methods: We collected plasma samples that were carefully matched for sex, age, and BMI, utilizing our Henry Ford Health Arthritis Biobank and the Nashville VA Medical Center Biobank. Early OA was defined as individuals with knee pain and radiographic KL 0 or 1, and early RA was defined as treatment-naïve individuals with <6 months of symptoms and anti-citrullinated protein antibodies within 24-2613.5 U/mL. We subjected these samples to miRNA-seq according to our previously published protocols. Briefly, RNA isolated from plasma was sequenced on an Illumina NextSeq2000 system using a 75-bp single-end read protocol at a depth of approximately 12 million reads/sample. Analysis through our previously optimized pipeline involved alignment to reference databases (miRBase v22.1 and human genome vGRCh38), filtering out low count miRNAs, and principal component analysis (PCA) to assess potential confounding variables. Following normalization by total counts, differentially expressed (DE) miRNAs were identified using a quasi-likelihood F-test with trended dispersion. The list of DE miRNAs was filtered by FDR <0.05 to identify statistically significant miRNAs in early OA versus early RA. Results: We performed miRNA-seq on plasma samples obtained from N=12 early OA individuals [6 female, 49 years (SD 11), BMI 28 kg/m2(SD 5)] and N=6 early RA individuals [2 female, 56 years (SD 8), BMI 27 kg/m2 (SD 5)]. Following initial filtering for abundance (miRNAs with >10 counts/million in more than 2 samples), we identified 285 miRNAs that were present in all 18 samples. These included three miRNAs previously reported in literature: hsa-miR-199a-5p and hsa-miR-671-3p in early OA by Ali et al. (2020) and hsa-miR-361-5p for early RA by Romo-Garcia et al. (2019). PCA with 285 miRNAs showed distinct clustering between early OA and early RA [Fig. 1A], while clustering was not observed when samples were coded by sex, age, and BMI [Fig. 2B]. DE analysis identified 100 miRNAs that were significantly dysregulated between early OA and early RA at p-value <0.05, including hsa-miR-671-3p (p=0.02). More stringent analysis using FDR <0.05 identified 24 upregulated and 19 downregulated miRNAs in early OA compared to early RA. Conclusions: Utilizing miRNA-seq as the current gold-standard approach for profiling circulating miRNAs, we found a distinct profile differentiating early OA and early RA samples. Our findings also support previously reported miRNAs identified in early OA and early RA. Ongoing experiments seek to first validate the top DE miRNAs filtered based on FDR in independent samples, and second construct a predictive model to determine their accuracy in distinguishing early OA from early RA. We expect findings from this study to pave the way for developing diagnostic blood tests to reliably distinguish early OA and early RA patients in primary car settings, thereby expediting delivery of interventions at stages of disease when opportunities for mitigation still exist. [Formula presented]

Orthopedics/Bone and Joint Center

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Purpose (the aim of the study): To reduce the immense burden of disease associated with knee osteoarthritis (OA), there is an urgent need for molecular biomarkers for earlier diagnosis and therapeutic targets for effective intervention. MicroRNAs (miRNAs) are small non-coding RNAs with the potential to meet both these needs given their specificity and stability in liquid biopsies as well as their ability to regulate key biological processes through direct inhibition of gene targets. Found across tissues, miRNAs are expressed as primary transcripts (pri-miRNAs) that are processed into precursor transcripts (pre-miRNAs) then mature miRNAs. To identify important miRNAs in knee OA, we performed secondary analysis of two miRNA-sequencing datasets and discovered circulating miR-126-3p to be elevated compared to non-OA controls, a finding we validated in our Henry Ford Health OA cohort. Existing literature indicates miR-126-3p is primarily expressed by endothelial cells and regulates angiogenesis through inhibition of its gene target SPRED1. In a rat model of OA, exosomes carrying miR-126-3p were shown to attenuate the severity of disease. Based on these findings, the objectives of this study are to assess miR-126-3p as a diagnostic biomarker, mechanistic driver, and therapeutic target for knee OA. Methods: To investigate the biomarker potential of miR-126-3p, we assessed its predictive ability with area under the receiver operating characteristic curve (AUC) analysis and explored correlations with common confounding variables. To investigate the mechanistic potential of miR-126-3p, we collected subchondral bone, infrapatellar fat pad, synovium, anterior cruciate ligament, meniscus and articular cartilage from N=20 OA patients undergoing knee replacement. We measured pri-mir-126, pre-mir-126, and miR-126-3p in each tissue by real-time PCR and quantified miR-126-3p secretion from tissue explants into culture medium over time. We transfected bone, fat pad and synovium explants and cells with 100nM miR-126-3p mimic, inhibitor, or controls and measured candidate gene expression changes. To investigate the therapeutic potential of miR-126-3p, we performed medial meniscectomy or sham surgery in right knees of 12-week-old mice and delivered 4 weekly injections of miR-126-3p mimic, inhibitor, or controls. At 20 weeks, harvested knee joints were assessed by OARSI grading in a blinded manner. Results: Exploring its potential as a biomarker for radiographic knee OA, we found that circulating miR-126-3p showed greater accuracy for predicting knee OA (AUC = 0.83) compared to age, sex, and BMI alone (AUC = 0.52), and importantly showed no association with age, sex, or BMI. Exploring miR-126-3p in knee OA tissues, we found the highest levels in bone, fat pad and synovium versus cartilage which showed the lowest levels (Figure 1). Fat pad had high levels of both pri- and pre-mir-126, and exhibited the highest rate of miR-126-3p secretion over time, suggesting it may be a source of circulating miR-126-3p. Prioritizing bone, fat pad and synovium, we treated explants with miR-126-3p mimic and found reduced expression of OSX and OCN in bone, ADIPOQ and LEP in fat pad, and IL1b, IL6 and TNF in fat pad and synovium; we also found reduced NGF in all three tissues. For canonical functions of miR-126-3p, we found reduced SPRED1 and increased angiogenesis in endothelial cells isolated from bone, fat pad and synovium. Exploring the therapeutic potential of miR-126-3p in a mouse model, treatment with miR-126-3p mimic reduced the severity of knee OA, while inhibitor increased the severity. Conclusions: Our data-driven strategy identified circulating miR-126-3p in radiographic knee OA and further characterization revealed its potential as a candidate diagnostic biomarker. Systematic profiling of primary human knee OA tissues suggests miR-126-3p impacts specific mechanisms in bone, fat pad and synovium, reducing markers of osteogenesis, adipogenesis, inflammation and pain, with a concomitant increase in angiogenesis potentially indicating anabolism. Ta en together, our findings suggest that miR-126-3p may become elevated during OA as a mechanism to mitigate disease processes and therefore should be further evaluated as a therapeutic target for OA, where delivery at earlier stages may prevent progression to later stages. [Formula presented]

Palliative Medicine

Fagan T, **Miller ME**, and **Henkin D**. Use of Buprenorphine for Cancer Related Pain in Pregnancy. *J Pain Symptom Manage* 2024; 67(5):e755. Full Text

Outcomes: 1. Participants will be able to recognize buprenorphine as a safe and effective analgesic for cancer pain in pregnancy 2. Participants will be able to integrate buprenorphine into more facets of clinical practice in treatment of cancer-related pain. Key Message: There is paucity of literature describing the treatment of cancer associated pain in pregnancy. Buprenorphine is an increasingly recognized analgesic used to treat cancer pain with an established safety profile studied in maternal opioid use disorder (OUD). We present a case demonstrating the safe and efficacious use of buprenorphine for cancer-related pain in a pregnant woman with a pancreatic neoplasm. Opioids often are utilized for the optimization of cancer related pain; however, managing cancer-related pain in pregnancy can present challenges, particularly due to opioid-related risks to the fetus in utero. In addition, there is a paucity of literature with regard to treating cancer related pain in pregnancy. Here we present a case where buprenorphine was successfully used to manage cancer related pain for a pregnant female. We present a case of a 36-year-old G3P2 female diagnosed with metastatic solid pseudopapillary epithelial neoplasm (SPEN) of the pancreas at 27 weeks gestation. She began experiencing severe nociceptive visceral abdominal pain, which impaired her ability to perform activities of daily living and even sleep throughout the night. She was started on very low doses of buprenorphine (partial Suboxone SL films), three times a day with improved pain control, physical functioning and sleep with minimal to no side effects. Labor was induced at 34 weeks secondary to intrauterine growth restriction and oligohydramnios, with APGAR scores 8/8 at birth. Buprenorphine was continued for pain control postpartum at varying doses, compatible with patient's wish to continue to breastfeed with appropriate analgesia. Buprenorphine is becoming increasingly more recognized for its efficacy in treating cancer-related pain. The literature describing buprenorphine for pain management in pregnancy is limited; however, its use in treating opioid use disorder in pregnancy and fetal safety profile is well understood. In presenting this case, we demonstrate the safe and efficacious utility of buprenorphine for cancer-related pain during pregnancy Keywords: Disease specific management / Pharmacotherapeutics / Pharmacopalliation

Palliative Medicine

Samaha H, **Grech A**, and **Shaban H**. Use of Subcutaneous Ketamine for Refractory Pain in Home Hospice Patients: A Case Report. *J Pain Symptom Manage* 2024; 67(5):e628. Full Text

Outcomes: 1. Participants will learn different dosing intervals used in two cases where subcutaneous ketamine was used to treat opioid refractory pain. 2. Participants will be exposed to outcomes related to pain relief when using subcutaneous ketamine in the home hospice setting. Key Message: Sub-anesthetic ketamine has been used to treat opioid refractory pain in palliative care patients. It is typically administered intravenously in a monitored setting which is a barrier for home hospice patients. These cases suggest subcutaneous ketamine administration is safe and feasible in the home hospice setting. Background: Sub-anesthetic ketamine is effective for opioid refractory pain. It is typically administered intravenously in a monitored ambulatory or inpatient setting which is a barrier for home hospice patients as transportation to an infusion center and obtaining IV access are oftentimes not feasible at the end of life. Case Description: Ms. G is a 58-year-old female with vulvar melanoma with osseous and hepatic metastases. She had severe cancer pain refractory to a multimodal treatment regimen including high-dose opioids of up to 255 OME daily. She received an initial 0.5 mg/kg sub-anesthetic ketamine infusion given as three equally divided subcutaneous injections every 15-minutes (time 0, 15-minutes, and 30-minutes). The infusion was tolerated well with rapid improvement in pain and without side effect or hemodynamic changes. She received three additional infusions on a weekly basis and was then rotated to an oral regimen. Case 2: Ms. M is a 72-year-old female with inclusion body myositis causing severe bilateral leg pain refractory to high dose opioids including methadone and a hydromorphone PCA totaling 947.5 daily OME. A 0.5 mg/kg sub-anesthetic ketamine infusion was administered subcutaneously in the patient's home in the same fashion as case #1. The infusion was well tolerated with rapid improvement in pain, and without side effects or significant hemodynamic changes. Her pain worsened 48 hours later along with terminal agitation requiring a general inpatient level of care. Her symptoms were ultimately managed with an intravenous 0.3 mg/kg ketamine bolus followed by 0.1 mg/hg/hr continuous infusion, hydromorphone PCA, and intravenous chlorpromazine until her death 48-hours later. Conclusion: These cases suggest subcutaneous ketamine administration is safe and feasible in the home hospice setting. Treatment response was rapid but short and highlights future area of research in dosing intervals for subcutaneous ketamine. Keywords: Managing Suffering and Distress; Emergencies / Refractory Symptom Management

Palliative Medicine

Tennant T, **Grech A**, and **Shaban H**. Ease and Efficacy of Subcutaneous Ketamine for Depression in Home Hospice Patients: 2 Case Reports. *J Pain Symptom Manage* 2024; 67(5):e623-e624. Full Text

Outcomes: 1. Identify hospice patients that would benefit from the use of ketamine in the home setting. 2. List the acceptable routes of administration and starting dose of Ketamine. Key Message: Patients suffering from depression at the end of life often do not have weeks to wait for antidepressants to take effect. Ketamine is a promising treatment as it offers rapid and durable response; however, often requires infusion in a clinic or inpatient setting. These two cases demonstrate the safety and feasibility of administering subcutaneous ketamine in the home hospice setting. Background: Ketamine is known to relieve treatment-resistant depression and opioid refractory pain. While antidepressants take several weeks, ketamine has a rapid onset, making it a promising therapy for depression in patients at end of life (EOL). Literature demonstrates that cancer patients may experience rapid and sustained improvement in depression and anxiety. These studies largely use compounded oral or intravenous (IV) formulations of ketamine which are barriers to widespread implementation. Hospices may not have access to compounding pharmacies and the IV route may not be feasible for patients at EOL, especially in the home setting. Case Description: Mrs. C was an 80-year-old female with metastatic cervical cancer, severe pulmonary hypertension, and depression. She experienced severe major depression after home hospice enrollment. She was administered intravenous ketamine 0.5 mg/kg over 40 minutes in her home under physician and nurse supervision. She experienced rapid improvement in mood within an hour and no significant side effects or changes in vital signs. Her son stated, “I got my mom back.” Due to difficulty obtaining IV access two subsequent infusions were administered subcutaneously (SQ) over 45 minutes on weeks 2 and 3 following the initial. Effects on mood were sustained for the following 20 weeks until death. In case #2, Mrs. B was a 74-year-old female with congestive heart failure and depression. Her depression was poorly controlled on five agents. Subcutaneous ketamine was administered at the same dose and supervision as the first case while rotating her oral antidepressant regimen. She did not experience improvement in mood, but tolerated the injection without significant side effect or change in vital signs. Conclusion: These cases suggest SQ ketamine administration is safe and feasible in the home hospice setting. Treatment response was mixed and highlights need for further research in dosing intervals and titration for apparent ketamine non-responders. Keywords: Managing Suffering and Distress; Models of Palliative Care Delivery

Pharmacy

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Public Health Sciences

Arora S, **Wang Y**, **Wilder S**, **Fisher E**, **Stephens A**, **Peabody JO**, and **Jeong W**. Impact of a novel anterior suspension stitch on return of urinary continence after Robotic Radical Prostatectomy (RRP), with description of surgical technique. *Eur Urol* 2024; 85:S593-S594. Full Text

Introduction & Objectives: During radical prostatectomy, the pubourethral angle is increased due to the loss of periprostatic supportive tissue, and the symphysis to bladder neck distance is increased due to the loss of prostatic urethral length. We hypothesize that recreating the pubourethral angle and decreasing the symphysis to bladder neck distance during RRP improves continence outcomes. We achieved this by performing an anterior suspension stitch (“Jeong suspension”). Materials & Methods: 41 patients underwent ‘Jeong suspension’ (suspension group) by two surgeons at a single institution between 2017-2021. In this suspension procedure, the anterior bladder wall attached to the symphysis of pubis is identified during the bladder takedown. This point is then suspended to the symphysis pubis after anastomosis, pulling the urethrovesical anastomosis anterior and superior, restoring the periurethral anatomy. Outcomes were compared to contemporary 2:1 propensity-score matched patients who did not

undergo ‘Jeong suspension’ (control). The patients were administered validated questionnaires at 1, 3, 6, and 12 months after the procedure and social Continence defined as the use of no pads or one security pad. Outcomes were assessed independently by a state-wide quality collaborative. Kaplan Meier analysis was used to calculate median time to continence in weeks. Cox regression tested the effect of ‘Jeong stitch’ accounting for known confounders. Results: After propensity score matching, groups were similar in all baseline variables, except PSA which was statistically, but not clinically higher in suspension group (mean 12 ng/dl vs 9 in control;p<0.01). 36 patients in the suspension group achieved continence(88%), compared to 58 (71%) in control group. Median time to social continence was 20 weeks for suspension group, compared to 36 for control;p=0.003. Cox regression confirmed independent association of suspension to continence [HR 1.90 (CI 1.24-2.92)]. Conclusions: The Jeong suspension stitch during RRP is technically easy-to-perform and safe. This stitch significantly improves time to social continence when compared to matched patients not undergoing the technique. [Figure presented]

Public Health Sciences
Chiarelli G, **Cirulli GO**, **Finati M**, **Stephens A**, **Tinsley S**, **Butaney M**, **Arora S**, Sood A, Carrieri G, Briganti A, Montorsi F, Lughezzani G, Buffi N, **Rogers C**, and **Abdollah F**. Active surveillance follow-up for prostate cancer: From guidelines to real-world clinical practice. *Eur Urol* 2024; 85:S1869. Full Text

Introduction & Objectives: In the management of patients on active surveillance (AS) for prostate cancer (PCa), the major guidelines including the European Association of Urology (EAU), American Urological Association (AUA), and National Comprehensive Cancer Network (NCCN), slightly vary for monitoring recommendations, but all emphasize the importance of regular follow-up. EAU advises at least two PSA tests and one DRE annually, with a re-biopsy at least once every three years for a decade. Conversely, AUA and NCCN both recommend up to two PSA tests and one DRE yearly. AUA advises re-biopsies ranging from every one to four years, while NCCN proposes at least biennially, not surpassing once a year. Our study aimed to assess AS adherence in a “real-world” clinical practice. Materials & Methods: We utilized our institutional database which was built by interrogating our electronic medical records for all men who got diagnosed with PCa within Henry Ford Health. Our cohort included all patients aged < 76 years, who had a diagnosis of PCa Gleason Grade (GG) 1 or 2, with clinical tumor stage ≤cT2b, with PSA≤20 ng/ml, enrolled on AS following a diagnosis before 2022. This allows one year's time worth of eventual treatment information in our database. Median and Interquartile Range (IQR) were used to represent continuous variables, while frequencies and percentages were used for categorical variables. Cumulative incidence was used to depict PCSM. Results: A total of 1214 men met the inclusion criteria, of whom 722 (59%) were low-risk PCa and 492 (41%) intermediate-risk, according to the D'amico risk score, with a median age at diagnosis of 65 (IQR 60-70). Median PSA at diagnosis was 5.3 (4.3-7.1) ng/ml. The most represented Gleason Grade and clinical tumor stage were GG 1 (65%) and cT1 (88%). Follow-up time was 5.9 years (2.4-9.6). Prostate cancer-specific mortality was 2.7% within the follow-up period. Median PSA tests count after diagnosis was 8 (2-14) with a PSAs testing/years of 1.4 (0.4-2.7). Median biopsies count performed after diagnosis was 0 (0-1). Patients who underwent at least one re-biopsy were 544 (45%), ≥2 re-biopsies were 219 (18%), ≥3 re-biopsies were 75 (6%), with a median biopsies/year of 0.0 (0.0-0.2). At 10 years, the cumulative incidence of PCSM was 3.2%. Conclusions: Our data reported discrepancies with guidelines regarding follow-up intensity for AS patients, particularly concerning biopsies, which occurred less frequently than recommended. While our cohort showed a trend towards PSA testing in alignment with AUA and NCCN, re-biopsies were underutilized according to all three guidelines. These findings emphasize the importance of patient education and counseling regarding AS follow-up, as an integral part of this management strategy. Our report is one of the few on the intensity of AS monitoring in a “real-world” practice.

Public Health Sciences
Chiarelli G, **Davis M**, **Stephens A**, **Finati M**, **Cirulli G**, **Morrison C**, Sood A, Carrieri G, Briganti A, Montorsi F, Lughezzani G, Buffi N, **Rogers C**, and **Abdollah F**. Midlife baseline PSA as a predictor of lethal prostate cancer: Racial differences between black and white men. *Eur Urol* 2024; 85:S54. Full Text

Introduction & Objectives: Most previous reports have examined prostate cancer (PCa) mortality in homogenous populations based on midlife baseline PSA (MB PSA), defined as the first PSA test performed between 40 and 59 years old. Our study aims to investigate racial disparities in the predictive

value of MB PSA for lethal PCa, defined as death from PCa or the development of metastatic disease either at diagnosis or during follow-up, in a diverse, contemporary, North American population. Materials & Methods: Our cohort included White and Black men aged 40-59 years, who underwent MB PSA through our health system between 1995 and 2019. Patients were divided into 4 categories based on age: 40 to 44, 45 to 49, 50 to 54, and 55 to 59 years. MB PSA testing during the study period represented the main predictor of interest, and it was categorized based on PSA above/below the median in the entire cohort and for each age group. Multivariable Fine-Gray regression (MVA) was used to examine the impact of the MB PSA in predicting lethal PCa by race, after accounting for all confounders including the Charlson comorbidity index among others. Results: A total of 112,967 men met the inclusion criteria, of whom 82,084 (73%) were White and 30,883 (27%) were Black. White patients had their first PSA most frequently in the 50–54 age group (33.9%) while Black patients at 40-44 (27.6%). The rate of PCa diagnosis was 7.0% in Black patients vs. 3.9% in White patients, and lethal PCa was 1.2% vs 0.6%, respectively (both p<0.0001). White patients harbored more frequent Gleason score 3+3 disease (23.7% vs 16.0%), and less frequent cM+ (12.7% vs. 15.2%) than Black patients (both p<0.05). Median follow-up was 6.7 (IQR 2.9 - 14.4) years for White patients and 9.9 (4.4 - 16.4) years for Black patients. At MVA, using White patients with PSA≤median as the reference group, the HR of lethal PCa for White men with PSA>median aged 40-44, 45-49, 50-54, and 55-59 was respectively 2.98 (1.59-5.57), 3.01 (1.89-4.81), 5.10 (3.38-7.70) and 3.38 (2.32-4.92). While the HR of lethal PCa for Black men with PSA>median aged 40-44, 45-49, 50-54 and 55-59 was respectively 5.50 (2.94-10.27), 4.19 (2.59-6.78), 9.79 (6.37-15.04) and 7.53 (5.03- 11.26) (all p < 0.001). Conclusions: Our findings indicate that for the same MB PSA and within the same age category, Black men have almost double the risk of developing lethal PCa than White men. This implies that separate and different cut-offs should be created for MB PSA, if this is to be used to guide PSA screening in clinical practice.

Public Health Sciences

Chiarelli G, **Finati M**, **Cirulli GO**, **Butaney M**, **Stephens A**, **Arora S**, **Morrison C**, **Tinsley S**, **Sood A**, Carrieri G, Briganti A, Montorsi F, Lughezzani G, Buffi N, **Rogers C**, and **Abdollah F**. Active surveillance for prostate cancer in real-world setting: Exploring racial disparities in surveillance intensity and cancer control outcomes. *Eur Urol* 2024; 85:S1817. Full Text

Introduction & Objectives: Black men have worse outcomes from prostate cancer (PCa) compared to White men. This is, at least partially, due to the racial disparity and health care delivery. Our aim was to evaluate the impact of race on surveillance intensity and Prostate Cancer Specific Mortality (PCSM) in patients on AS for PCa in a contemporary, real-world North American cohort. Materials & Methods: We utilized our institutional database which was built by interrogating our electronic medical records for all men who got diagnosed with PCa. Our cohort included White and Black men aged < 76 years, who had a diagnosis of Pca Gleason Grade (GG) 1 or 2, with clinical stage ≤cT2b, with PSA≤20 ng/ml, enrolled on AS following a diagnosis before 2022. This allows one year's worth of eventual treatment information in our database. Cumulative incidence was used to depict PCSM by race. Multivariable Fine-Gray regression analysis (MVA) was used to examine the impact of race in predicting PCSM in AS patients, after accounting for all confounders including the Charlson comorbidity index (CCI), among others. Results: A total of 1068 men met the inclusion criteria, of whom 443 (42%) were Black and 625 (58%) were White, with a median age at diagnosis of 65 (IQR 58-69) and 66 (60-70), respectively. CCI>2 was reported in 44.1% of Black patients and 31.2% of White patients (p<0001). Median PSA at diagnosis was 5.7 (4.6-8.0) ng/ml in Black patients and 5.0 (4.0-6.6) ng/ml in White patients (p<0.0001). The rate of GG 2 was higher in Black than in White patients (43,6% vs 30.1%, p<0.0001). Follow-up time was 6 years (2.5-9.6). Median PSAs testing/years after diagnosis was 1.4 (0.6-2.5) for Black patients and 1.6 (0.6-3.2) for Black patients (p<0.05). The rate of patients who underwent more than one biopsy after diagnosis was 14.6% of Black and 22.6% of White patients (p<0.001). In the overall period, PCSM was 4.1% in Black and 1.6% in White patients (p<0.01). The cumulative incidence of PCSM at 10 years was double for Black patients compared to White patients (5.2% vs 2.6% CI 95%, p=0.0502). At MVA Black patients had 2.1 folds higher PCSM than White patients (p=0.08). Conclusions: Black patients on AS tend to have more aggressive disease at diagnosis and seem to undergo less PSA testing and postdiagnosis biopsies. This might, at least partially, be explained by higher PCSM in Black patients on AS that we observed in our cohort. Our report is one of few examining the intensity and outcomes of AS in real-world practice with a focus on racial disparities.

Public Health Sciences

Cirulli GO, **Davis M**, **Finati M**, **Chiarelli G**, **Stephens A**, **Corsi N**, **Williams E**, **Affas R**, **Arora S**, Sood A, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Differential impact of prostate-specific antigen screening pattern on prostate cancermortality among non-Hispanic black and non-Hispanic white men: A large, urban health system cohort analysis. *Eur Urol* 2024; 85:S404-S405. Full Text

Introduction & Objectives: Randomized studies assessing the effect of prostate-specific antigen (PSA) screening on mortality in Non- Hispanic Black men (NHB) are lacking. The aim of our study was to assess the association between PSA screening and survival among NHB men in comparison to Non-Hispanic White (NHW) men in a racially diverse real-world North American population. Materials & Methods: The study cohort included 6,378 men who self-identified as NHB or NHW and were diagnosed with prostate cancer (PCa). They received PSA screening and subsequent PCa treatment and follow-up at our institution between the years 2000 and 2019. Patients were sorted based on PSA testing intensity for the 5 years prior to diagnosis, as follows: never, some (<1 test/year), and annual testing (1 test/year). The primary outcome was risk of prostate cancer-specific mortality (PCSM) among NHB and NHW. Competing-risk cumulative incidence curves estimated PCSM rates. Fine-Gray regression analyses examined the impact of PSA testing on PCSM. Results: Median (IQR) age and PSA at diagnosis were 67 (60 - 73) years and 5.8 (4.4 - 9.6) ng/ml, respectively and 2,929 (45.9%) men were NHB. Annual PSA testing was more frequent in NHW (5.2%) than in NHB (3.2%) men (p<0.001). On cumulative incidence analysis, in the never, some, and annual PSA testing groups, the 10-year PCSM was respectively 12.3%, 5.8%, and 4.6% in NHW and 18.5%, 7.0%, 1.2% in NHB patients (both p<0.001). On multivariable analysis, a more intensive PSA testing strategy was associated with more favorable PCSM rates for NHB (HR: 0.38; 95% CI 0.22-0.64; p < 0.001) as well as NHW men (HR: 0.56; 95% CI 0.34-0.93; p=0.025). Conclusions: In this retrospective cohort study, annual PSA testing was associated with a reduced risk of PCSM in both NHB and NHW men who were diagnosed with PCa. NHB men seemed to benefit from frequent PSA testing compared to their NHW counterparts. [Figure presented]

Public Health Sciences

Cirulli GO, **Davis M**, **Finati M**, **Chiarelli G**, **Stephens A**, **Morrison C**, **Tinsley S**, **Arora S**, Sood A, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Superiority of midlife baseline prostate-specific antigen value over PSA doubling time and velocity in the prediction of lethal prostate cancer development, and mortality: A system wide analysis of a racially diverse North American cohort. *Eur Urol* 2024; 85:S1615. Full Text

Introduction & Objectives: Midlife baseline PSA (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. We aimed to examine the ability of MB PSA vs PSA doubling time (PSADT) and PSA velocity (PSAV) in predicting development of lethal prostate cancer (PCa) in a diverse and contemporary North American population. Materials & Methods: Men aged 40–59 years, 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 78,625 patients with at least 2 PSA test results and 13,062 patients with at least 3 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 ROC/AUC curves 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 CCI 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 636 (0.8%) patients. The median (IQR) follow-up time was 11 (5.1 – 17.4) years. In the main cohort, MB PSA and PSADT were significant predictors for lethal PCa, with a HR 5.47 (95% CI: 4.40-6.78) and HR 2.81(95% CI: 1.45-5.45) for patients in the top 10th percentile MB PSA group and in the PSADT between 0-<6 months group, respectively. In patients with 3 PSA results available, MB PSA and PSAV were significant predictors for lethal PCa, with a HR 5.05 (95% CI: 3.16-8.06) and 3.26 (95% CI: 2.09-5.07) 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 have higher AUCs than MB PSA in predicting lethal PCa. Specifically, they were 0.712 and 0.639 at 10- and 15-year, respectively, for the PSADT; 0.749 and 0.708 at 10- and 15- year, respectively, for the PSAV and 0.840 and 0.750 at 10- and 15-year, respectively, for the MB PSA (all p> 0.05). Conclusions: PSAV or PSADT were not superior to midlife baseline PSA in predicting the development of lethal PCa. This suggests that these variables may not have practical utility in enhancing PSA screening strategies in a clinical setting.

Public Health Sciences

Cirulli GO, **Finati M**, **Chiarelli G**, **Stephens A**, **Davis M**, **Morrison C**, **Tinsley S**, **Etta P**, **Butaney M**, Sood A, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Testing free PSA percentage as a tool in predicting future risk of developing prostate cancer: A system wide analysis of a contemporary North American cohort. *Eur Urol* 2024; 85:S435. Full Text

Introduction & Objectives: Free PSA percentage (%fPSA) has been proposed by International Guidelines as a useful serum marker in guiding biopsy decisions when further risk stratification is needed, especially in patients with mildly elevated PSA. On the other hand, it is not explicitly recommended to consider %fPSA as a tool to guide future PSA screening. We aimed to examine the potential role of %fPSA in predicting future development of PCa in a contemporary North American population. Materials & Methods: Men aged 40–59 years, who received their %fPSA between the years 1995 and 2019 were included. These selection criteria resulted in a total of 1,308 patients. Based on previously published methodology, Free PSA % was categorized in 3 different groups (< 10%, 10% to 25% and >25%). Main outcome was PCa incidence. Cumulative incidence curves were used to depict the risk of deveoloping PCa over time, based on %fPSA categories. Multivariable Fine-Gray regression was used to examine the role of %fPSA as a predictor of future development of PCa after adjusting for available confounders. Results: In our cohort, patients were most frequently in the 55–59 age category (33.4%), had a CCI of 0 (51.3%), and were white (75.6%). Most patients (68.8%) had a %fPSA between 10% and 25%. The median (IQR) follow-up time was 2.9 (0.9-5.1) years. Within this period, 228 (17.4%) patients, developed PCa. At 5-year the risk of developing PCa in patients with a %fPSA <10% vs10%-25% vs >25%, was 22.8% vs 8.9% vs 3.1%, respectively (p<0.001). On multivariable analysis, patients with a %fPSA <10%, had a 6.21-fold (95% CI: 3.62-10.64) higher risk of developing PCa when compared to those with a %fPSA >25% (p: <0.001). Conclusions: Our report is the first to examine the rule of %fPSA in the PSA screening context. Our findings showed that %fPSA measured in men without PCa is an important predictor of the future risk of developing PCa. This suggests that %fPSA has practical utility in enhancing PSA screening strategies in clinical practice, where patients with highest risk of developing PCa can receive more intense screening, and vice versa.

Public Health Sciences

Cirulli GO, **Finati M**, **Chiarelli G**, **Stephens A**, **Davis M**, **Tinsley S**, **Morrison C**, **Arora S**, **Butaney M**, Sood A, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Comparing PSA screening patterns and their role as predictor of prostate cancer incidence and mortality: A system wide analysis of a contemporary North American cohort. *Eur Urol* 2024; 85:S434. Full Text

Introduction & Objectives: Prostate-specific antigen (PSA) screening, despite the risks of over-diagnosis and over-treatment, remains a pivotal tool for early prostate cancer (PCa) detection. International guidelines rely on evidence from three major randomized clinical trials: the European Randomized Study of Screening for Prostate Cancer (ERSPC), the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO), and the Cluster Randomized Trial of PSA Testing for Prostate Cancer (CAP). Our study aims to examine the percentage of patients in real-world practice who get PSA screening, as defined by each of the aforementioned trials. Moreover, we seek to evaluate if the different PSA screening patterns have a different impact on PCa incidence and mortality (PCSM). Materials & Methods: Our institutional database was queried to identify men aged 55 to 69 who received at least one PSA test and did not develop PCa or died within 6 years of the initial test. A total of 54,131 patients met our selection criteria. We categorized patients into three distinct PSA screening patterns based on testing frequency (PLCO: 1 PSA test per year for 6 years; ERSPC: 2 or 3 PSA tests over 6 years; CAP: 1 PSA test over 6 years). Our primary outcome measure was PCa incidence, with PCSM as the secondary outcome. Cumulative incidence curves were used to depict PCa diagnosis and PCSM rates. Multivariable

Fine-Gray regression assessed the impact of the different Screening patterns on PCa incidence and PCSM, after adjusting for confounding factors. Results: Within our cohort, the median (IQR) age at the first PSA test was 61 (58-65), and the median (IQR) initial PSA level was 1 (0.5-2) ng/ml. The most prevalent PSA screening pattern was ERSPC, including 26,103 patients (48.2%), followed by the CAP with 22,991 patients (42.5%), and the PLCO with only 5,037 patients (9.3%). The median (IQR) follow-up time was 6.4 (2.9-11.3) years. At 10-year, PCa incidence rates was 16.5% vs 5.3% vs 1.6% for patients with PLCO vs ERSPC vs CAP screening pattern, respectively (p<0.001). The 10-year PCSM rates for the same groups were 1.5% vs 0.7% vs 0.7%, respectively (p=0.016). On multivariable analysis, PLCO Screening and ERSPC Screening patterns were associated with, respectively, 8.18-fold (95% CI: 7.23-9.27) and 2.79-fold (95% CI: 2.49-3.13) higher risks of PCa diagnosis, compared to those with a CAP Screening pattern (both p<0.001). Conversley, screening pattern was not an independent predictor of PCSM on multivariable analysis (all p>0.05). Conclusions: Our study is the first to examine screening patterns in a real world setting and to assess the predictive potential of distinct screening patterns on cancer control outcomes. Notably, more intense screening patterns (PLCO and ERSPC) seemed to result in 3-8 fold higher risk of being diagnosed with PCa without resulting in more favorable PCSM.

Public Health Sciences

Cirulli GO, **Finati M**, **Chiarelli G**, **Stephens A**, **Tinsley S**, **Butaney M**, **Etta P**, **Arora S**, **Morrison C**, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Association of area deprivation index and race with prostate cancer-specific mortality among Non-Hispanic black and Non-Hispanic white men in a contemporary North American population. *Eur Urol* 2024; 85:S357. Full Text

Introduction & Objectives: Increasing evidence indicates poor socioeconomic status and geographic residency in underprivileged areas as potential contributors to disparities in cancer outcomes. For this reason, the measurement of area-level social and economic deprivation index (ADI) can be useful as a predictor of a more comprehensive cancer treatment outcomes assessment. We aimed to examine the impact of ADI and race on Prostate Cancer-Specific Mortality (PCSM) among Non-Hispanic Black (NHB) and Non-Hispanic White (NHW) men in a contemporary North American population. Materials & Methods: We utilized our institutional database which was built by interrogating our electronic medical records for all men who got diagnosed whit PCa within Henry Ford Health (HFH), between 1995 and 2019. ADI is a percentile rank of socio-economic disadvantage, calculated using indicators of income level, income disparity, educational level, employment rate, home values and quality of life. All these indicators were weighted to create a deprivation score and patients were categorized by race and for ADI quartiles (based on the available National ADI decile values).The highest quartile (Q4: 75-100) represented individuals with the most disadvantageous socioeconomic status. The main outcome for our study was PCSM. Competing-risk cumulative incidence curves were used to depict PCSM, after stratifying patients into sub-cohorts based on race and ADI quartiles. MVA was used to examine the impact of ADI quartiles on PCSM after adjusting for all available confounders. Results: A total of 13,039 patients were included. Of these, 4,402 (33.8%) were NHB men. Median (IQR) PSA at diagnosis was 6.0 (4.5, 9.5) ng/ml. In the 4th ADI quartile, there were more NHB patients (60.1%) than White patients (39.9%) (p<0.001). The median (IQR) follow-up time was 5.7 (2.3-10.3) years. At 10-year, PCSM in NHW vs NHB patients was statistically different in the 1st ADI quartile (5.2% vs 10.4%, p<0.001), but not in the 2nd, 3rd, and 4th ADI quartile groups (all p > 0.05). On MVA, NHW and NHB patients in the 4th ADI quartile (most disadvantaged area) had a 1.27-fold (95% CI: 1.02-1.58; p=0.030) higher cancer-specific mortality compared to NHW and NHB patients in the 1st ADI quartile, but race was not an independent predictor of cancer-specific mortality (HR:1.05; 95% CI:0.89-1.23; p=0.564). Conclusions: Our study was the first to assess the differential impact of ADI as a predictor of PCSM based on race in a large contemporary North American cohort. Within the first quartile, NHB patients showed higher cancer-specific mortality compared to NHW patients. Interestingly, race itself was not identified as an independent predictor of cancer-specific mortality, underscoring the significant influence of socio-economic factors, particularly in areas with higher deprivation, on prostate cancer outcomes.

Public Health Sciences

Finati M, **Cirulli GO**, **Chiarelli G**, **Stephens A**, **Davis M**, **Tinsley S**, **Butaney M**, **Arora S**, **Morrison C**, Sood A, Buffi N, Lughezzani G, Salonia A, Briganti A, Montorsi F, Bettocchi C, Carrieri G, **Rogers C**, and **Abdollah F**. Association of area of deprivation index with prostate cancer incidence and lethality over a contemporary North American cohort. *Eur Urol* 2024; 85:S53. Full Text

Introduction & Objectives: Increasing evidence indicate that poor socioeconomic status and residence in underprivileged areas contribute to disparities in prostate cancer (PCa) outcomes. While comprehensively assessing the impact of these factors might be might be intricate, the Area of Deprivation Index (ADI) could offer a distinctive and valuable metric for these considerations. Our study examined the impact of ADI on Prostate Cancer (PCa) incidence and lethality over a contemporary North American population. Materials & Methods: Our institutional database included electronic medical records for all men who received at least one PSA test within Henry Ford Health (HFH), between 1995 and 2019. An ADI score were assigned to each patients based on their residential census block group, ranked as a percentile of deprivation relative to the national level. All patients were further categorized into ADI quartile, where the highest quartile (Q4: 75-100) represented individuals with the most disadvantageous socio-economic status. The main outcomes were PCa incidence and lethal PCa, defined as any metastatic PCa or death due to PCa occurred within our cohort. Cumulative incidence curves were used to depict PCa incidence and lethality, after stratifying patients into sub-cohorts based on ADI quartile. Multivariable Fine-Gray regression examined the impact of ADI quartiles on PCa incidence and lethality, after adjusting for all available confounders. Results: A total of 148,892 patients were included, with a median follow-up f of 8.8 (5-17) years. When patients were categorized based on their ADI quartile, the 20-years PCa incidence rates were 9.1%, 8.4%, 7.7% and 8.5%% for the first, second, third and fourth quartile respectively. For the same quartile categories, the 20-years lethal PCa rates were 1.3%, 0.90%, 1.0% and 1.7%. At multivariable analysis, both the third (HR: 0.01, 95% IC: 0'85-0.97, p=0.007) and the fourth quartile (HR: 0.83, 95% IC: 0.77-0.88, p=0.007) had a lower risk of being diagnosed with PCa, when compared with patients in the lowest ADI quartile. On the other side, ADI did not result an independent predictor for lethal PCa. Of note, Non-Hispanic black patients had almost 2-fold the risk both for PCa incidence and lethality, when compared with Non- Hispanic White patients (all p<0.001). Conclusions: Our study is the first to evaluate the role of ADI in predicting PCa incidence and lethality in a contemporary North American cohort. Patients from less disadvantaged areas were more likely diagnosed with PCa, while those from the most deprived areas showed increased lethal PCa rates, though not reaching the conventional significance at multivariable analysis. Notably, race emerged as an independent predictor for both lethal PCa and its incidence, regardless of any socioeconomic and deprivation influences.

Public Health Sciences

Finati M, **Cirulli GO**, **Chiarelli G**, **Stephens A**, **Tinsley S**, **Butaney M**, **Arora S**, Sood A, Buffi N, Lughezzani G, Briganti A, Montorsi F, Busetto GM, Carrieri G, **Rogers C**, and **Abdollah F**. Radical cystectomy versus trimodal therapy for non-metastatic muscle-invasive bladder cancer: Analysis of an other-cause mortality matched cohort. *Eur Urol* 2024; 85:S1963. Full Text

Introduction & Objectives: Although Trimodal therapy (TMT) is now accepted for well-selected patients with muscle-invasive bladder cancer (MIBC), in clinical practice it is often reserved for sicker patients for whom radical cystectomy (RC) is not a feasible option. Thus, comparative effectiveness studies (TMT vs RC) based on retrospective studes are usually hindered by selection bias. To circumvent this limitation, we designed a novel approach matching patients based on their calculated other-cause mortality (OCM) risk. Using this homogeneous cohort, we tested the impact of TMT vs RC on cancer-specific mortality (CSM). Materials & Methods: The Surveillance, Epidemiology and End Results (SEER) database was queried to identify patients diagnosed with histologically confirmed T2-4 MIBC between 2004 and 2018. A Cox regression model calculating 5-years OCM was used to create a 1:1 propensity-score matched cohort of patients treated with RC vs TMT. Cumulative incidence curves depicted CSM and OCM, while Fine-Gray regression tested the impact of treatment type on CSM in the matched cohort. Patients were further stratified according to Chemotherapy receipt and clinical stage based on transurethral resection of bladder tumor (cT2 vs T3-4) and the aforementioned methodology was repeated. Results: We identified 6,587 (76%) treated with RC and 2,057 (24%) TMT. Median follow-up was 3.0 years (IQR 1.1-6.7). In the unmatched cohort, 5-year OCM and CSM rates were 14% and 40% in RC group respectively, versus

23% and 47% in TMT (all p<0.001). Our matched cohort included 6,506 patients equally distributed for treatment type (RT vs RP), with no difference in 5-years OCM. In the matched cohort, the 5-year CSM rate was 42% in RC patients versus 48% in TMT (p=0.001). This trend was confirmed at multivariable analysis, where TMT patients had a 1.54-fold higher CSM risk than their RC counterparts. After stratifying the matched cohort for Chemotherapy receipt, the 5-year CSM rate was significantly higher for TMT versus RC who did not receive Chemotherapy (48% vs 41%, p<0.001). On the other hand, no difference in CSM was recorded when compare patients treated with TMT vs RC plus Chemotherapy (46% vs 45%, p=0.2). When stratified patients based on their clinical stage, TMT shower higher CSM rates than RC both in cT2 (44% vs 26%, p<0.001) and cT3-T4 (59% vs 53%, p < 0.02), albeit not being an independent predictor of CSM in cT3-T4 patients. Conclusions: In comparison with previous literature, our study is the first to mitigate the impact of selection bias by matching based on OCM. Our findings showed invariably CSM advantage of RC over TMT in pT2 patients. Conversely, TMT prooved to be a valid option for patients who showed advanced clinical disease, as RC did not showed any oncological survival advantage in cT3-cT4 patients or for those who required chemotherapy in combination with surgery.

Public Health Sciences

Finati M, **Cirulli GO**, **Chiarelli G**, **Tinsley S**, **Morrison C**, **Davis M**, **Arora S**, **Etta P**, **Butaney M**, Akshay S, Buffi N, Lughezzani G, Salonia A, Briganti A, Montorsi F, Bettocchi C, Carrieri G, **Rogers C**, and **Abdollah F**. The role of cytoreductive nephrectomy in metastatic clear cell carcinoma: Analisys of an other-cause mortality matched population from the contemporary immunotherapy era. *Eur Urol* 2024; 85:S1866. Full Text

Introduction & Objectives: In the recent randomized CARMENA trial, performing cytoreductive nephrectomy (CN) did not improve overall survival in metastatic renal cell carcinoma (RCC) patients treated with Sunitinib. However, this trial raised concerns about possible selection bias of patients with higher metastatic burden and consequent poor prognosis. Conversely, population-based studies showed how patients referred to CN usually have better health status, which reflects in lower risk for any cause of death. We aimed to evaluate the role of CN on cancer-specific mortality (CSM) within an immunotherapy-era cohort of metastatic RCC patients matched for their other-cause mortality (OCM) risk. Materials & Methods: The Surveillance, Epidemiology and End Results Registry was queried to identify > 18 years patients diagnosed with metastatic RCC, between 2010 and 2017. We included only patients treated with immunotherapy. A Cox regression model including treatment type (CN versus no surgery of the primary site) was used to calculate the other-cause mortality (OCM) risk. Therefore, a 1:1 propensity score match was used to create a cohort of metastatic RCC patients, treated or not with CN, having the same OCM risk. Cumulative incidence curves were depicted to assess CSM and OCM, while Fine-Gray regression tested the impact of CN on CSM. Patients were further stratified according to number of metastasis (1, 2 or more than 2 sites) and the same aforementioned analyses were repeated for these sub-cohorts. Results: We identified 3138 patients with metastatic RCC treated with immunotherapy, of whom 1597 (51%) were treated with CN. In the unmatched cohort, 3-years CSM and OCM rates were 80.8% and 15.5% for non-surgery arm respectively, versus 54.3% and 8.4% for CN patients (all p<0.001). Our Cox Regression model matching yielded to 1662 patients equally distributed, with no difference in OCM rate (11.7% vs 10.8%, p=0.8). In the matched cohort, the 3-years CSM was 54.1% for CN patients vs 80.3% in non-surgery arm (p<0.001). At multivariable analysis, patients who did not receive surgery had 1.79-fold higher CSM risk, when compared with those who underwent CN (95% CI: 1.56-2.06, p<0.001). When stratifying patients for metastases sites, patients who did not undergo CN had higher CSM rates when they harboured metastasis in 1 (84.5% vs 70.0%) or 2 sites (87.8% vs 73.4%, all p<0.001). Conversely, no difference in CSM rate where observed for patients with 3 or more metastases sites, regardless of nephrectomy receipt (89.1% vs 86.8%, p=0.06). Conclusions: We evaluate the role of CN in a immunotherapy-era cohort of metastatic RCC, using OCM risk matching as a proxy of similar health status. In this setting, performing CN yielded a survival advantage in patients with low-to intermediate metastatic burden. Conversely, CN did not CSM for patients with widespread metastases.

Public Health Sciences

Finati M, Corsi NJ, **Chiarelli G**, **Cirulli GO**, **Stephens A**, **Tinsley S**, **Davis M**, **Butaney M**, **Arora S**, Sood A, Buffi N, Lughezzani G, Briganti A, Salonia A, Montorsi F, Bettocchi C, Carrieri G, **Rogers C**, and **Abdollah F**. The impact of radical prostatectomy versus radiation therapy on cancer-specific-mortality for

non-metastatic prostate cancer: Analysis of an other-cause-mortality matched cohort. *Eur Urol* 2024; 85:S1273-S1274. Full Text

Introduction & Objectives: Studies comparing radical prostatectomy (RP) to radiation therapy (RT) have consistently shown that patients undergoing RT have a higher risk of other-cause mortality (OCM) compared to RP, signifying poor health status of the former patients. We aimed to evaluate the impact of RP vs RT on cancer-specific mortality (CSM) over a cohort with equivalent OCM risk. Materials & Methods: The Surveillance, Epidemiology and End Results (SEER) database was queried to identify patients diagnosed with non-metastatic PCa between 2004-2009, treated with RP or RT. A Cox-regression model was used to calculate the 10-year OCM risk. Propensity-scores based on the calculated OCM risk were used to match RP and RT patients. Cumulative incidence curves and multivariable Fine-Gray regression analyses were used to examine the impact of type on CSM in the matched cohort. Results: We identified 55,106 PCa patients treated with RP and 36,674 treated with RT. After match, 6,506 patients were equally distributed for RT vs RP, with no difference in OCM rates (p=0.2). After stratifying the matched cohort for D'Amico risk and Gleason Score, 10-year CSM rates were 8.8% vs 0.6% (p=0.01) for RT vs RP in patients with unfavorable-intermediate-risk (Gleason Score 4+3) and 7.9% vs 3.9% (p=0.003) for high-risk disease. There was no difference in CSM rates among RT and RP patients for favorable-intermediate-risk (Gleason Score 3+4) and low-risk disease. Conclusions: In a matched cohort of PCa patients with comparable OCM between the two arms, RP yielded a more favorable CSM rate compared to RT only for unfavorable-intermediate- and high-risk groups. [Figure presented]

Public Health Sciences
Tinsley SA, **Stephens A**, **Marco F**, **Chiarelli G**, **Cirulli GO**, Davis M, Corsi N, Sood A, Buffi N, Lughezzani G, Bettocchi C, Salonia A, Briganti A, Montorsi F, Carrieri G, **Rogers C**, and **Abdollah F**. The impact of radical prostatectomy versus radiation therapy on cancer-specific mortality for patients with localized prostate cancer and positive nodal disease: An analysis of other cause mortality weighted cohort. *Eur Urol* 2024; 85:S1261-S1262. Full Text

Introduction & Objectives: There is controversy regarding the survival benefit of radical prostatectomy (RP) versus radiation therapy (RT) for the primary management for prostate cancer (PCa) in men with clinically positive nodes (cN1). Virtually, all previous retrospective reports on this subject are limited by selection bias, where “unhealthy” patients are more frequently treated with RT. To circumvent this limitation, we sought to compare prostate cancer specific mortality (PCSM) in cN1 PCa patients who underwent RP versus RT, in an othercause mortality (OCM) weighted cohort. Materials & Methods: The Surveillance, Epidemiology, and End Results (SEER) database was queried to identify men with cN1 PCa at diagnosis between 2004 to 2017, and were treated with RP or RT. A Cox regression model was used to calculate the 10-year OCM risk using all available covariates, including treatment type. Then, a competing risk multivariate model, which was weighted on the calculated OCM risk, was used to examine the impact of treatment type (RP vs. RT) on PCSM, after accounting for available covariates. Results: There were a total of 5778 patients included in our final cohort, with 4739 (82.02%) patients underwent RP, versus 1039 (17.98%) who underwent RT. The median with the interquartile range had a follow-up of 4.7 years (2.6-8.2). OCM has statistically significant differences between RP and RT patients in the unweighted (p-value = 0.005), but that difference disappeared in the weighted cohort (p-value = 0.2). Based on cumulative incidence function (CIF), the 10-year PCSM rate was 32.2% (95% CI: 27.6% - 35.6%) for patients treated with RT versus 17.1% (95% CI: 15.9% - 19.0%) for those that treated with RP (p-value <0.001). Conclusions: Our results show that cN1 PCa patients treated initially with RT fare worst in terms of PCSM than their counterparts that underwent RP. Our report is the first comparative effectiveness study that compares those treatments cohorts, after alleviating the known selection bias in “real-world” practice by weighting our models using calculated OCM. [Figure presented]

Public Health Sciences
Wilson TG, **Baghel M**, **Kaur N**, **Loveless I**, **Datta I**, Potla P, **Mendez D**, **Hansen L**, **Baker K**, **Lynch TS**, **Moutzouros V**, **Davis J**, and **Ali SA**. IDENTIFICATION AND CHARACTERIZATION OF MIR-126-3P AS A DIAGNOSTIC BIOMARKER, MECHANISTIC DRIVER, AND THERAPEUTIC TARGET FOR KNEE OSTEOARTHRITIS. *Osteoarthritis Cartilage* 2024; 32:S52-S53. Full Text

Purpose (the aim of the study): To reduce the immense burden of disease associated with knee osteoarthritis (OA), there is an urgent need for molecular biomarkers for earlier diagnosis and therapeutic targets for effective intervention. MicroRNAs (miRNAs) are small non-coding RNAs with the potential to meet both these needs given their specificity and stability in liquid biopsies as well as their ability to regulate key biological processes through direct inhibition of gene targets. Found across tissues, miRNAs are expressed as primary transcripts (pri-miRNAs) that are processed into precursor transcripts (pre-miRNAs) then mature miRNAs. To identify important miRNAs in knee OA, we performed secondary analysis of two miRNA-sequencing datasets and discovered circulating miR-126-3p to be elevated compared to non-OA controls, a finding we validated in our Henry Ford Health OA cohort. Existing literature indicates miR-126-3p is primarily expressed by endothelial cells and regulates angiogenesis through inhibition of its gene target SPRED1. In a rat model of OA, exosomes carrying miR-126-3p were shown to attenuate the severity of disease. Based on these findings, the objectives of this study are to assess miR-126-3p as a diagnostic biomarker, mechanistic driver, and therapeutic target for knee OA. Methods: To investigate the biomarker potential of miR-126-3p, we assessed its predictive ability with area under the receiver operating characteristic curve (AUC) analysis and explored correlations with common confounding variables. To investigate the mechanistic potential of miR-126-3p, we collected subchondral bone, infrapatellar fat pad, synovium, anterior cruciate ligament, meniscus and articular cartilage from N=20 OA patients undergoing knee replacement. We measured pri-mir-126, pre-mir-126, and miR-126-3p in each tissue by real-time PCR and quantified miR-126-3p secretion from tissue explants into culture medium over time. We transfected bone, fat pad and synovium explants and cells with 100nM miR-126-3p mimic, inhibitor, or controls and measured candidate gene expression changes. To investigate the therapeutic potential of miR-126-3p, we performed medial meniscectomy or sham surgery in right knees of 12-week-old mice and delivered 4 weekly injections of miR-126-3p mimic, inhibitor, or controls. At 20 weeks, harvested knee joints were assessed by OARSI grading in a blinded manner. Results: Exploring its potential as a biomarker for radiographic knee OA, we found that circulating miR-126-3p showed greater accuracy for predicting knee OA (AUC = 0.83) compared to age, sex, and BMI alone (AUC = 0.52), and importantly showed no association with age, sex, or BMI. Exploring miR-126-3p in knee OA tissues, we found the highest levels in bone, fat pad and synovium versus cartilage which showed the lowest levels (Figure 1). Fat pad had high levels of both pri- and pre-mir-126, and exhibited the highest rate of miR-126-3p secretion over time, suggesting it may be a source of circulating miR-126-3p. Prioritizing bone, fat pad and synovium, we treated explants with miR-126-3p mimic and found reduced expression of OSX and OCN in bone, ADIPOQ and LEP in fat pad, and IL1b, IL6 and TNF in fat pad and synovium; we also found reduced NGF in all three tissues. For canonical functions of miR-126-3p, we found reduced SPRED1 and increased angiogenesis in endothelial cells isolated from bone, fat pad and synovium. Exploring the therapeutic potential of miR-126-3p in a mouse model, treatment with miR-126-3p mimic reduced the severity of knee OA, while inhibitor increased the severity. Conclusions: Our data-driven strategy identified circulating miR-126-3p in radiographic knee OA and further characterization revealed its potential as a candidate diagnostic biomarker. Systematic profiling of primary human knee OA tissues suggests miR-126-3p impacts specific mechanisms in bone, fat pad and synovium, reducing markers of osteogenesis, adipogenesis, inflammation and pain, with a concomitant increase in angiogenesis potentially indicating anabolism. Ta en together, our findings suggest that miR-126-3p may become elevated during OA as a mechanism to mitigate disease processes and therefore should be further evaluated as a therapeutic target for OA, where delivery at earlier stages may prevent progression to later stages. [Formula presented]

Rheumatology

Baghel M, **Wilson TG**, **Davis J**, **Moutzouros V**, Ormseth M, **Yousif P**, **Alkhatib A**, **Meysami A**, and **Ali SA**. PROFILING CIRCULATING MICRORNAS IN EARLY OSTEOARTHRITIS AND EARLY RHEUMATOID ARTHRITIS. *Osteoarthritis Cartilage* 2024; 32:S140. Full Text

Purpose (the aim of the study): In clinical settings, osteoarthritis (OA) and rheumatoid arthritis (RA) can present similarly and therefore can be difficult to distinguish, especially at early stages of single-joint disease when symptoms overlap. OA is most often assessed through radiography [e.g., Kellgren-Lawrence (KL) grading] by changes in bone (e.g., osteophytes) and joint space narrowing, features that are less obvious in early stages. Meanwhile, RA is diagnosed through symptom duration and serological

factors which can overlap with other inflammatory conditions, especially in early stages. These limitations in current diagnostic methods for early stages of OA and RA can lead to delays in timely diagnosis and management, which is particularly problematic for RA since treatments are available. Accordingly, there is a need to identify biomarkers that can reliably differentiate early OA from early RA. A promising group of candidate biomarkers are circulating microRNAs (miRNAs) given their specificity, stability, and ease of detection in liquid biopsies. Here we aim to use microRNA-sequencing (miRNA-seq) to profile circulating miRNAs that can distinguish early OA patients from early RA patients. Methods: We collected plasma samples that were carefully matched for sex, age, and BMI, utilizing our Henry Ford Health Arthritis Biobank and the Nashville VA Medical Center Biobank. Early OA was defined as individuals with knee pain and radiographic KL 0 or 1, and early RA was defined as treatment-naïve individuals with <6 months of symptoms and anti-citrullinated protein antibodies within 24-2613.5 U/mL. We subjected these samples to miRNA-seq according to our previously published protocols. Briefly, RNA isolated from plasma was sequenced on an Illumina NextSeq2000 system using a 75-bp single-end read protocol at a depth of approximately 12 million reads/sample. Analysis through our previously optimized pipeline involved alignment to reference databases (miRBase v22.1 and human genome vGRCh38), filtering out low count miRNAs, and principal component analysis (PCA) to assess potential confounding variables. Following normalization by total counts, differentially expressed (DE) miRNAs were identified using a quasi-likelihood F-test with trended dispersion. The list of DE miRNAs was filtered by FDR <0.05 to identify statistically significant miRNAs in early OA versus early RA. Results: We performed miRNA-seq on plasma samples obtained from N=12 early OA individuals [6 female, 49 years (SD 11), BMI 28 kg/m2(SD 5)] and N=6 early RA individuals [2 female, 56 years (SD 8), BMI 27 kg/m2 (SD 5)]. Following initial filtering for abundance (miRNAs with >10 counts/million in more than 2 samples), we identified 285 miRNAs that were present in all 18 samples. These included three miRNAs previously reported in literature: hsa-miR-199a-5p and hsa-miR-671-3p in early OA by Ali et al. (2020) and hsa-miR-361-5p for early RA by Romo-Garcia et al. (2019). PCA with 285 miRNAs showed distinct clustering between early OA and early RA [Fig. 1A], while clustering was not observed when samples were coded by sex, age, and BMI [Fig. 2B]. DE analysis identified 100 miRNAs that were significantly dysregulated between early OA and early RA at p-value <0.05, including hsa-miR-671-3p (p=0.02). More stringent analysis using FDR <0.05 identified 24 upregulated and 19 downregulated miRNAs in early OA compared to early RA. Conclusions: Utilizing miRNA-seq as the current gold-standard approach for profiling circulating miRNAs, we found a distinct profile differentiating early OA and early RA samples. Our findings also support previously reported miRNAs identified in early OA and early RA. Ongoing experiments seek to first validate the top DE miRNAs filtered based on FDR in independent samples, and second construct a predictive model to determine their accuracy in distinguishing early OA from early RA. We expect findings from this study to pave the way for developing diagnostic blood tests to reliably distinguish early OA and early RA patients in primary car settings, thereby expediting delivery of interventions at stages of disease when opportunities for mitigation still exist. [Formula presented]

Sleep Medicine

Van Dongen HPA, Leary EB, **Drake C**, Bogan R, Jaeger J, Rosenberg R, Streicher C, Kwak H, Bates J, and Tabuteau H. Effects of solriamfetol on cognition in participants with cognitive impairment associated with excessive daytime sleepiness in obstructive sleep apnea: SHARP study results. *Sleep Med* 2024; 115:75. Full Text

Introduction: The SHARP study evaluated whether solriamfetol improves cognitive function in patients with obstructive sleep apnea (OSA) experiencing excessive daytime sleepiness (EDS) and extant impaired cognition. OSA is characterized by repeated intermittent airway collapse resulting in disrupted sleep and excessive daytime sleepiness (EDS). EDS often persists even with Positive Airway Pressure (PAP) therapy. Cognitive impairment is a burdensome symptom in many patients with OSA and EDS, leading to occupational and social dysfunction and degraded quality of life. Solriamfetol (Sunosi®) is approved in the U.S., Canada, and Europe to improve wakefulness in adults with OSA and EDS; its effect on cognitive impairment was not previously assessed. Methods: SHARP (NCT04789174) was a randomized, double-blind, placebo-controlled, crossover trial in 59 patients with OSA and EDS and concurrent cognitive impairment. All patients received solriamfetol (75 mg for 3 days followed by 150 mg/day) for 2 weeks, and placebo for 2 weeks, with treatment periods separated by a 1-week washout. The primary endpoint was the score on the Coding Subtest (a variation of the Digit Symbol Substitution

Test) of the Repeatable Battery for the Assessment of Neuropsychological Status (DSST RBANS) at the end of each treatment period, averaged across 2, 4, 6, and 8 hour time points post-dose. Secondary endpoints included DSST RBANS scores at each of the individual time points, as well as scores on the British Columbia Cognitive Complaints Inventory (BC-CCI), the Epworth Sleepiness Scale (ESS), and a Patient Global Impression of Severity (PGI-S) scale measuring perceived symptom severity. All endpoints were expressed relative to baseline. Results: The study completion rate was 96.7%. Solriamfetol treatment improved performance on the DSST RBANS compared to placebo (6.49 vs. 4.75, p=0.009), with an effect size (Cohen's d) of 0.36. Across individual time points, solriamfetol yielded DSST-RBANS score improvements (solriamfetol–placebo difference) at 2 hours (1.91, p=0.033), 4 hours (1.38, p=0.089; not significant), 6 hours (2.33, p=0.004), and 8 hours (1.58, p=0.022) post-dose. There were improvements in self-reported cognitive complaints and daytime sleepiness in the solriamfetol group compared to the placebo group, as measured by the BC-CCI (-4.70 vs -3.11, d=0.43, p=0.002) and the ESS (-4.41 vs -2.31, d=0.50, p=0.004), respectively. Scores on the PGI-S improved with solriamfetol compared to placebo (-0.90 vs -0.61, p=0.034). The most common adverse events with solriamfetol were nausea (6.9%) and anxiety (3.4%). Conclusions: Solriamfetol (150 mg/day) improved objective and subjective measures of cognitive function in patients with impaired cognition associated with OSA and EDS and exhibited sustained effects over an 8-hour period while reducing perceived symptom severity. The adverse events profile and high study completion rate suggest solriamfetol was well tolerated. These findings support the use of solriamfetol to improve cognitive performance and daytime sleepiness through the day in patients with cognitive impairment associated with OSA and EDS. Support, Axsome Therapeutics and Jazz Pharmaceuticals

Surgery

Huddleston S, Loor G, Garcha P, Smith M, Walia R, Hashimi S, Schaheen L, Song T, Siddique A, Langer N, Lee A, Kukreja J, Hartwig M, **Nemeh H**, Toyoda Y, Daneshmand M, Neujahr D, Durham L, Ardehali A, Bush E, Suarez E, Hertz M, Schwartz G, Grazia T, Katlaps G, Qureshi M, Belli E, and Patel K. Thoracic Organ Perfusion (TOP) Registry Annual Report - More Than 350 OCS Lung Transplants in the US. *J Heart Lung Transplant* 2024; 43(4):S415-S416. Full Text

Purpose: TOP registry is an all-inclusive registry established to collect donor/recipient and post-transplant clinical outcomes on all OCS Lung transplants in the real world in the US. Methods: The TOP OCS cohort includes three donor sub-groups: 1) standard criteria donor lungs (SCDL) 2) donor lungs initially deemed unacceptable (DLIDU) and 3) others not meeting SCDL/DLIDU criteria. To benchmark clinical outcomes, data from the Organ Procurement and Transplantation Network (OPTN) database for consecutive lung transplants from same centers, transplanted using other preservation methods during the same time, constituted the Control cohort. TOP registry provided additional primary graft dysfunction (PGD) data for the OCS arm (not available for Control cohort). Cohorts were propensity matched to account for differences in recipient/donor characteristics. Results: A total of 372 OCS and 3959 Control patients were analyzed. 364/372 donor lungs placed on OCS were transplanted (utilization rate 97.8%). There were 77 SCDL, 202 DLIDU and 73 other lung transplants in the OCS cohort. Donors in the OCS cohort were older (39 vs 36 yrs; p<0.001), more likely to be donation after circulatory death (DCD) (25% vs 7%; p<0.001), expected cross clamp time>6 hrs (70% vs 37%; p<0.001) and more likely to have significant smoking history (9% vs 6%; p=0.022). Recipients in the OCS group were younger (58 vs 60 yrs; p=0.004) and more likely to be on ECMO at transplant (11% vs 7%; p=0.010) compared to Control cohort. When propensity matched on DCD, P/F ratio, donor age, recipient LAS and transplant year, OCS group had similar 1-year survival compared to the Control cohort (84.3 vs. 86.5%) (p=0.533). Despite the propensity match, OCS group had significantly longer cross clamp time (mean 664 vs 396 mins; p<0.001) compared to Control, so this was unable to be matched on due to lack of samples with similarly longer times in the Control cohort. Conclusion: OCS Lung enabled the use of extended criteria donor lungs from DBD and DCD donors and resulted in post-transplant outcomes that are similar to a matched cohort of standard criteria lung transplants. These results were achieved despite the OCS cohort having nearly double the cross-clamp time (>50% of OCS cohort had 10+ hours of cross-clamp time). These results support the broader use of OCS Lung technology to expand donor lung utilization for transplants from DBD and DCD donors.

Surgery

Nassif G, **Oulabi K**, **Boules T**, **Savage K**, **Kavousi Y**, Mansour M, **Osinbowale O**, **Jackson M**, **Daley B**, and **Kabbani L**. The Utility of Chat GPT in Venous Education. *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 2024; 12(3). Full Text

Objectives: Chat GPT is an artificial intelligence-powered language model that is being increasingly used in the medical setting. Although quick access to large amounts of information is promising for vascular surgical education, the quality and depth of information provided by the current Chat GPT model is not well-understood. We aimed to study the utility of Chat GPT in teaching medical students and vascular surgery residents about varicose veins. We hypothesized that Chat GPT can provide a basic overview to medical students' and possibly residents' education. Methods: We generated two learning documents using Chat GPT, one for medical students and one for residents. We asked Chat GPT 3.5 to produce a document for "varicose veins explained to a medical student" and another for "varicose veins explained to a vascular surgery resident." We asked it to "include background, anatomy, pathophysiology, risk factors, clinical presentation, complications, diagnostic evaluation, and management." Texts generated for students and residents were compared and reviewed by seven academic vascular surgeons practicing in a teaching hospital. Five-point Likert scales were used to rate the accuracy, completeness, complexity, and applicability of each text (Table I). Average values of each survey question were compared using Mann-Whitney U tests. Results: Aside from increased use of more advanced medical terminology in residents' texts, content was similar in the two texts. Overall, the scores were slightly higher for the text generated for the residents (average, 3.91) vs the students (average, 3.71) (Table II). All surgeons believed that information was accurate (average, 4.5), although more accurate for residents (average, 4.71) vs students (average, 4.29). Most surgeons believed that information was not advanced enough (average, 3.21), albeit slightly more advanced for residents (average, 3.29 vs 3.14 for students). Most surgeons were on the fence on whether they would use the text to teach medical students (average, 3.43) or residents (average, 3.57). Conclusions: Although Chat GPT offers promising prospects in venous education, the current Chat GPT is not up to standards when used for medical education. Although the information was accurate and concise, it was not advanced enough for medical education, and most surgeons were not very enthusiastic about using it to teach students or residents. Optimizing Chat GPT-generated searches and expanding its applicability to specialized education is subject to future development and research. [Formula presented] [Formula presented]

Urology

Arora S, **Wang Y**, **Wilder S**, **Fisher E**, **Stephens A**, **Peabody JO**, and **Jeong W**. Impact of a novel anterior suspension stitch on return of urinary continence after Robotic Radical Prostatectomy (RRP), with description of surgical technique. *Eur Urol* 2024; 85:S593-S594. Full Text

Introduction & Objectives: During radical prostatectomy, the pubourethral angle is increased due to the loss of periprostatic supportive tissue, and the symphysis to bladder neck distance is increased due to the loss of prostatic urethral length. We hypothesize that recreating the pubourethral angle and decreasing the symphysis to bladder neck distance during RRP improves continence outcomes. We achieved this by performing an anterior suspension stitch ("Jeong suspension"). Materials & Methods: 41 patients underwent 'Jeong suspension' (suspension group) by two surgeons at a single institution between 2017-2021. In this suspension procedure, the anterior bladder wall attached to the symphysis of pubis is identified during the bladder takedown. This point is then suspended to the symphysis pubis after anastomosis, pulling the urethrovesical anastomosis anterior and superior, restoring the periurethral anatomy. Outcomes were compared to contemporary 2:1 propensity-score matched patients who did not undergo 'Jeong suspension' (control). The patients were administered validated questionnaires at 1, 3, 6, and 12 months after the procedure and social Continence defined as the use of no pads or one security pad. Outcomes were assessed independently by a state-wide quality collaborative. Kaplan Meier analysis was used to calculate median time to continence in weeks. Cox regression tested the effect of 'Jeong stitch' accounting for known confounders. Results: After propensity score matching, groups were similar in all baseline variables, except PSA which was statistically, but not clinically higher in suspension group (mean 12 ng/dl vs 9 in control;$p<0.01$). 36 patients in the suspension group achieved continence(88%), compared to 58 (71%) in control group. Median time to social continence was 20 weeks for suspension group, compared to 36 for control;$p=0.003$. Cox regression confirmed independent association of

suspension to continence [HR 1.90 (CI 1.24-2.92)]. Conclusions: The Jeong suspension stitch during RRP is technically easy-to-perform and safe. This stitch significantly improves time to social continence when compared to matched patients not undergoing the technique. [Figure presented]

Urology
Chiarelli G, **Cirulli GO**, **Finati M**, **Stephens A**, **Tinsley S**, **Butaney M**, **Arora S**, Sood A, Carrieri G, Briganti A, Montorsi F, Lughezzani G, Buffi N, **Rogers C**, and **Abdollah F**. Active surveillance follow-up for prostate cancer: From guidelines to real-world clinical practice. *Eur Urol* 2024; 85:S1869. Full Text

Introduction & Objectives: In the management of patients on active surveillance (AS) for prostate cancer (PCa), the major guidelines including the European Association of Urology (EAU), American Urological Association (AUA), and National Comprehensive Cancer Network (NCCN), slightly vary for monitoring recommendations, but all emphasize the importance of regular follow-up. EAU advises at least two PSA tests and one DRE annually, with a re-biopsy at least once every three years for a decade. Conversely, AUA and NCCN both recommend up to two PSA tests and one DRE yearly. AUA advises re-biopsies ranging from every one to four years, while NCCN proposes at least biennially, not surpassing once a year. Our study aimed to assess AS adherence in a “real-world” clinical practice. Materials & Methods: We utilized our institutional database which was built by interrogating our electronic medical records for all men who got diagnosed with PCa within Henry Ford Health. Our cohort included all patients aged < 76 years, who had a diagnosis of PCa Gleason Grade (GG) 1 or 2, with clinical tumor stage ≤cT2b, with PSA≤20 ng/ml, enrolled on AS following a diagnosis before 2022. This allows one year's time worth of eventual treatment information in our database. Median and Interquartile Range (IQR) were used to represent continuous variables, while frequencies and percentages were used for categorical variables. Cumulative incidence was used to depict PCSM. Results: A total of 1214 men met the inclusion criteria, of whom 722 (59%) were low-risk PCa and 492 (41%) intermediate-risk, according to the D'amico risk score, with a median age at diagnosis of 65 (IQR 60-70). Median PSA at diagnosis was 5.3 (4.3-7.1) ng/ml. The most represented Gleason Grade and clinical tumor stage were GG 1 (65%) and cT1 (88%). Follow-up time was 5.9 years (2.4-9.6). Prostate cancer-specific mortality was 2.7% within the follow-up period. Median PSA tests count after diagnosis was 8 (2-14) with a PSAs testing/years of 1.4 (0.4-2.7). Median biopsies count performed after diagnosis was 0 (0-1). Patients who underwent at least one re-biopsy were 544 (45%), ≥2 re-biopsies were 219 (18%), ≥3 re-biopsies were 75 (6%), with a median biopsies/year of 0.0 (0.0-0.2). At 10 years, the cumulative incidence of PCSM was 3.2%. Conclusions: Our data reported discrepancies with guidelines regarding follow-up intensity for AS patients, particularly concerning biopsies, which occurred less frequently than recommended. While our cohort showed a trend towards PSA testing in alignment with AUA and NCCN, re-biopsies were underutilized according to all three guidelines. These findings emphasize the importance of patient education and counseling regarding AS follow-up, as an integral part of this management strategy. Our report is one of the few on the intensity of AS monitoring in a “real-world” practice.

Urology
Chiarelli G, **Davis M**, **Stephens A**, **Finati M**, **Cirulli G**, **Morrison C**, Sood A, Carrieri G, Briganti A, Montorsi F, Lughezzani G, Buffi N, **Rogers C**, and **Abdollah F**. Midlife baseline PSA as a predictor of lethal prostate cancer: Racial differences between black and white men. *Eur Urol* 2024; 85:S54. Full Text

Introduction & Objectives: Most previous reports have examined prostate cancer (PCa) mortality in homogenous populations based on midlife baseline PSA (MB PSA), defined as the first PSA test performed between 40 and 59 years old. Our study aims to investigate racial disparities in the predictive value of MB PSA for lethal PCa, defined as death from PCa or the development of metastatic disease either at diagnosis or during follow-up, in a diverse, contemporary, North American population. Materials & Methods: Our cohort included White and Black men aged 40-59 years, who underwent MB PSA through our health system between 1995 and 2019. Patients were divided into 4 categories based on age: 40 to 44, 45 to 49, 50 to 54, and 55 to 59 years. MB PSA testing during the study period represented the main predictor of interest, and it was categorized based on PSA above/below the median in the entire cohort and for each age group. Multivariable Fine-Gray regression (MVA) was used to examine the impact of the MB PSA in predicting lethal PCa by race, after accounting for all confounders including the Charlson comorbidity index among others. Results: A total of 112,967 men met the inclusion criteria, of

whom 82,084 (73%) were White and 30,883 (27%) were Black. White patients had their first PSA most frequently in the 50–54 age group (33.9%) while Black patients at 40-44 (27.6%). The rate of PCa diagnosis was 7.0% in Black patients vs. 3.9% in White patients, and lethal PCa was 1.2% vs 0.6%, respectively (both p<0.0001). White patients harbored more frequent Gleason score 3+3 disease (23.7% vs 16.0%), and less frequent cM+ (12.7% vs. 15.2%) than Black patients (both p<0.05). Median follow-up was 6.7 (IQR 2.9 - 14.4) years for White patients and 9.9 (4.4 - 16.4) years for Black patients. At MVA, using White patients with PSA≤median as the reference group, the HR of lethal PCa for White men with PSA>median aged 40-44, 45-49, 50-54, and 55-59 was respectively 2.98 (1.59-5.57), 3.01 (1.89-4.81), 5.10 (3.38-7.70) and 3.38 (2.32-4.92). While the HR of lethal PCa for Black men with PSA>median aged 40-44, 45-49, 50-54 and 55-59 was respectively 5.50 (2.94-10.27), 4.19 (2.59-6.78), 9.79 (6.37-15.04) and 7.53 (5.03- 11.26) (all p < 0.001). Conclusions: Our findings indicate that for the same MB PSA and within the same age category, Black men have almost double the risk of developing lethal PCa than White men. This implies that separate and different cut-offs should be created for MB PSA, if this is to be used to guide PSA screening in clinical practice.

Urology
Chiarelli G, **Finati M**, **Cirulli GO**, **Butaney M**, **Stephens A**, **Arora S**, **Morrison C**, **Tinsley S**, **Sood A**, Carrieri G, Briganti A, Montorsi F, Lughezzani G, Buffi N, **Rogers C**, and **Abdollah F**. Active surveillance for prostate cancer in real-world setting: Exploring racial disparities in surveillance intensity and cancer control outcomes. *Eur Urol* 2024; 85:S1817. Full Text

Introduction & Objectives: Black men have worse outcomes from prostate cancer (PCa) compared to White men. This is, at least partially, due to the racial disparity and health care delivery. Our aim was to evaluate the impact of race on surveillance intensity and Prostate Cancer Specific Mortality (PCSM) in patients on AS for PCa in a contemporary, real-world North American cohort. Materials & Methods: We utilized our institutional database which was built by interrogating our electronic medical records for all men who got diagnosed with PCa. Our cohort included White and Black men aged < 76 years, who had a diagnosis of Pca Gleason Grade (GG) 1 or 2, with clinical stage ≤cT2b, with PSA≤20 ng/ml, enrolled on AS following a diagnosis before 2022. This allows one year's worth of eventual treatment information in our database. Cumulative incidence was used to depict PCSM by race. Multivariable Fine-Gray regression analysis (MVA) was used to examine the impact of race in predicting PCSM in AS patients, after accounting for all confounders including the Charlson comorbidity index (CCI), among others. Results: A total of 1068 men met the inclusion criteria, of whom 443 (42%) were Black and 625 (58%) were White, with a median age at diagnosis of 65 (IQR 58-69) and 66 (60-70), respectively. CCI>2 was reported in 44.1% of Black patients and 31.2% of White patients (p<0001). Median PSA at diagnosis was 5.7 (4.6-8.0) ng/ml in Black patients and 5.0 (4.0-6.6) ng/ml in White patients (p<0.0001). The rate of GG 2 was higher in Black than in White patients (43,6% vs 30.1%, p<0.0001). Follow-up time was 6 years (2.5-9.6). Median PSAs testing/years after diagnosis was 1.4 (0.6-2.5) for Black patients and 1.6 (0.6-3.2) for Black patients (p<0.05). The rate of patients who underwent more than one biopsy after diagnosis was 14.6% of Black and 22.6% of White patients (p<0.001). In the overall period, PCSM was 4.1% in Black and 1.6% in White patients (p<0.01). The cumulative incidence of PCSM at 10 years was double for Black patients compared to White patients (5.2% vs 2.6% CI 95%, p=0.0502). At MVA Black patients had 2.1 folds higher PCSM than White patients (p=0.08). Conclusions: Black patients on AS tend to have more aggressive disease at diagnosis and seem to undergo less PSA testing and postdiagnosis biopsies. This might, at least partially, be explained by higher PCSM in Black patients on AS that we observed in our cohort. Our report is one of few examining the intensity and outcomes of AS in real-world practice with a focus on racial disparities.

Urology
Cirulli GO, **Davis M**, **Finati M**, **Chiarelli G**, **Stephens A**, **Corsi N**, **Williams E**, **Affas R**, **Arora S**, Sood A, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Differential impact of prostate-specific antigen screening pattern on prostate cancermortality among non-Hispanic black and non-Hispanic white men: A large, urban health system cohort analysis. *Eur Urol* 2024; 85:S404-S405. Full Text

Introduction & Objectives: Randomized studies assessing the effect of prostate-specific antigen (PSA) screening on mortality in Non- Hispanic Black men (NHB) are lacking. The aim of our study was to assess the association between PSA screening and survival among NHB men in comparison to Non-Hispanic White (NHW) men in a racially diverse real-world North American population. Materials & Methods: The study cohort included 6,378 men who self-identified as NHB or NHW and were diagnosed with prostate cancer (PCa). They received PSA screening and subsequent PCa treatment and follow-up at our institution between the years 2000 and 2019. Patients were sorted based on PSA testing intensity for the 5 years prior to diagnosis, as follows: never, some (<1 test/year), and annual testing (1 test/year). The primary outcome was risk of prostate cancer-specific mortality (PCSM) among NHB and NHW. Competing-risk cumulative incidence curves estimated PCSM rates. Fine-Gray regression analyses examined the impact of PSA testing on PCSM. Results: Median (IQR) age and PSA at diagnosis were 67 (60 - 73) years and 5.8 (4.4 - 9.6) ng/ml, respectively and 2,929 (45.9%) men were NHB. Annual PSA testing was more frequent in NHW (5.2%) than in NHB (3.2%) men (p<0.001). On cumulative incidence analysis, in the never, some, and annual PSA testing groups, the 10-year PCSM was respectively 12.3%, 5.8%, and 4.6% in NHW and 18.5%, 7.0%, 1.2% in NHB patients (both p<0.001). On multivariable analysis, a more intensive PSA testing strategy was associated with more favorable PCSM rates for NHB (HR: 0.38; 95% CI 0.22-0.64; p < 0.001) as well as NHW men (HR: 0.56; 95% CI 0.34-0.93; p=0.025). Conclusions: In this retrospective cohort study, annual PSA testing was associated with a reduced risk of PCSM in both NHB and NHW men who were diagnosed with PCa. NHB men seemed to benefit from frequent PSA testing compared to their NHW counterparts. [Figure presented]

Urology

Cirulli GO, **Davis M**, **Finati M**, **Chiarelli G**, **Stephens A**, **Morrison C**, **Tinsley S**, **Arora S**, Sood A, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Superiority of midlife baseline prostate-specific antigen value over PSA doubling time and velocity in the prediction of lethal prostate cancer development, and mortality: A system wide analysis of a racially diverse North American cohort. *Eur Urol* 2024; 85:S1615. Full Text

Introduction & Objectives: Midlife baseline PSA (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. We aimed to examine the ability of MB PSA vs PSA doubling time (PSADT) and PSA velocity (PSAV) in predicting development of lethal prostate cancer (PCa) in a diverse and contemporary North American population. Materials & Methods: Men aged 40–59 years, 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 78,625 patients with at least 2 PSA test results and 13,062 patients with at least 3 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 ROC/AUC curves 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 CCI 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 636 (0.8%) patients. The median (IQR) follow-up time was 11 (5.1 – 17.4) years. In the main cohort, MB PSA and PSADT were significant predictors for lethal PCa, with a HR 5.47 (95% CI: 4.40-6.78) and HR 2.81(95% CI: 1.45-5.45) for patients in the top 10th percentile MB PSA group and in the PSADT between 0-<6 months group, respectively. In patients with 3 PSA results available, MB PSA and PSAV were significant predictors for lethal PCa, with a HR 5.05 (95% CI: 3.16-8.06) and 3.26 (95% CI: 2.09-5.07) 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 have higher AUCs than MB PSA in predicting lethal PCa. Specifically, they were 0.712 and 0.639 at 10- and 15-year, respectively, for the PSADT; 0.749 and 0.708 at 10- and 15- year, respectively, for the PSAV and 0.840 and 0.750 at 10- and 15-year, respectively, for the MB PSA (all p> 0.05). Conclusions: PSAV or PSADT were not superior to midlife baseline PSA in predicting the development of lethal PCa. This suggests that these variables may not have practical utility in enhancing PSA screening strategies in a clinical setting.

Urology

Cirulli GO, **Finati M**, **Chiarelli G**, **Stephens A**, **Davis M**, **Morrison C**, **Tinsley S**, **Etta P**, **Butaney M**, Sood A, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Testing free PSA percentage as a tool in predicting future risk of developing prostate cancer: A system wide analysis of a contemporary North American cohort. *Eur Urol* 2024; 85:S435. Full Text

Introduction & Objectives: Free PSA percentage (%fPSA) has been proposed by International Guidelines as a useful serum marker in guiding biopsy decisions when further risk stratification is needed, especially in patients with mildly elevated PSA. On the other hand, it is not explicitly recommended to consider %fPSA as a tool to guide future PSA screening. We aimed to examine the potential role of %fPSA in predicting future development of PCa in a contemporary North American population. Materials & Methods: Men aged 40–59 years, who received their %fPSA between the years 1995 and 2019 were included. These selection criteria resulted in a total of 1,308 patients. Based on previously published methodology, Free PSA % was categorized in 3 different groups (< 10%, 10% to 25% and >25%). Main outcome was PCa incidence. Cumulative incidence curves were used to depict the risk of deveoloping PCa over time, based on %fPSA categories. Multivariable Fine-Gray regression was used to examine the role of %fPSA as a predictor of future development of PCa after adjusting for available confounders. Results: In our cohort, patients were most frequently in the 55–59 age category (33.4%), had a CCI of 0 (51.3%), and were white (75.6%). Most patients (68.8%) had a %fPSA between 10% and 25%. The median (IQR) follow-up time was 2.9 (0.9-5.1) years. Within this period, 228 (17.4%) patients, developed PCa. At 5-year the risk of developing PCa in patients with a %fPSA <10% vs10%-25% vs >25%, was 22.8% vs 8.9% vs 3.1%, respectively (p<0.001). On multivariable analysis, patients with a %fPSA <10%, had a 6.21-fold (95% CI: 3.62-10.64) higher risk of developing PCa when compared to those with a %fPSA >25% (p: <0.001). Conclusions: Our report is the first to examine the rule of %fPSA in the PSA screening context. Our findings showed that %fPSA measured in men without PCa is an important predictor of the future risk of developing PCa. This suggests that %fPSA has practical utility in enhancing PSA screening strategies in clinical practice, where patients with highest risk of developing PCa can receive more intense screening, and vice versa.

Urology

Cirulli GO, **Finati M**, **Chiarelli G**, **Stephens A**, **Davis M**, **Tinsley S**, **Morrison C**, **Arora S**, **Butaney M**, Sood A, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Comparing PSA screening patterns and their role as predictor of prostate cancer incidence and mortality: A system wide analysis of a contemporary North American cohort. *Eur Urol* 2024; 85:S434. Full Text

Introduction & Objectives: Prostate-specific antigen (PSA) screening, despite the risks of over-diagnosis and over-treatment, remains a pivotal tool for early prostate cancer (PCa) detection. International guidelines rely on evidence from three major randomized clinical trials: the European Randomized Study of Screening for Prostate Cancer (ERSPC), the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO), and the Cluster Randomized Trial of PSA Testing for Prostate Cancer (CAP). Our study aims to examine the percentage of patients in real-world practice who get PSA screening, as defined by each of the aforementioned trials. Moreover, we seek to evaluate if the different PSA screening patterns have a different impact on PCa incidence and mortality (PCSM). Materials & Methods: Our institutional database was queried to identify men aged 55 to 69 who received at least one PSA test and did not develop PCa or died within 6 years of the initial test. A total of 54,131 patients met our selection criteria. We categorized patients into three distinct PSA screening patterns based on testing frequency (PLCO: 1 PSA test per year for 6 years; ERSPC: 2 or 3 PSA tests over 6 years; CAP: 1 PSA test over 6 years). Our primary outcome measure was PCa incidence, with PCSM as the secondary outcome. Cumulative incidence curves were used to depict PCa diagnosis and PCSM rates. Multivariable Fine-Gray regression assessed the impact of the different Screening patterns on PCa incidence and PCSM, after adjusting for confounding factors. Results: Within our cohort, the median (IQR) age at the first PSA test was 61 (58-65), and the median (IQR) initial PSA level was 1 (0.5-2) ng/ml. The most prevalent PSA screening pattern was ERSPC, including 26,103 patients (48.2%), followed by the CAP with 22,991 patients (42.5%), and the PLCO with only 5,037 patients (9.3%). The median (IQR) follow-up time was 6.4 (2.9-11.3) years. At 10-year, PCa incidence rates was 16.5% vs 5.3% vs 1.6% for patients with PLCO vs ERSPC vs CAP screening pattern, respectively (p<0.001). The 10-year PCSM rates for the

same groups were 1.5% vs 0.7% vs 0.7%, respectively (p=0.016). On multivariable analysis, PLCO Screening and ERSPC Screening patterns were associated with, respectively, 8.18-fold (95% CI: 7.23-9.27) and 2.79-fold (95% CI: 2.49-3.13) higher risks of PCa diagnosis, compared to those with a CAP Screening pattern (both p<0.001). Conversley, screening pattern was not an independent predictor of PCSM on multivariable analysis (all p>0.05). Conclusions: Our study is the first to examine screening patterns in a real world setting and to assess the predictive potential of distinct screening patterns on cancer control outcomes. Notably, more intense screening patterns (PLCO and ERSPC) seemed to result in 3-8 fold higher risk of being diagnosed with PCa without resulting in more favorable PCSM.

Urology

Cirulli GO, **Finati M**, **Chiarelli G**, **Stephens A**, **Tinsley S**, **Butaney M**, **Etta P**, **Arora S**, **Morrison C**, Lughezzani G, Buffi N, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Association of area deprivation index and race with prostate cancer-specific mortality among Non-Hispanic black and Non-Hispanic white men in a contemporary North American population. *Eur Urol* 2024; 85:S357. Full Text

Introduction & Objectives: Increasing evidence indicates poor socioeconomic status and geographic residency in underprivileged areas as potential contributors to disparities in cancer outcomes. For this reason, the measurement of area-level social and economic deprivation index (ADI) can be useful as a predictor of a more comprehensive cancer treatment outcomes assessment. We aimed to examine the impact of ADI and race on Prostate Cancer-Specific Mortality (PCSM) among Non-Hispanic Black (NHB) and Non-Hispanic White (NHW) men in a contemporary North American population. Materials & Methods: We utilized our institutional database which was built by interrogating our electronic medical records for all men who got diagnosed whit PCa within Henry Ford Health (HFH), between 1995 and 2019. ADI is a percentile rank of socio-economic disadvantage, calculated using indicators of income level, income disparity, educational level, employment rate, home values and quality of life. All these indicators were weighted to create a deprivation score and patients were categorized by race and for ADI quartiles (based on the available National ADI decile values).The highest quartile (Q4: 75-100) represented individuals with the most disadvantageous socioeconomic status. The main outcome for our study was PCSM. Competing-risk cumulative incidence curves were used to depict PCSM, after stratifying patients into sub-cohorts based on race and ADI quartiles. MVA was used to examine the impact of ADI quartiles on PCSM after adjusting for all available confounders. Results: A total of 13,039 patients were included. Of these, 4,402 (33.8%) were NHB men. Median (IQR) PSA at diagnosis was 6.0 (4.5, 9.5) ng/ml. In the 4th ADI quartile, there were more NHB patients (60.1%) than White patients (39.9%) (p<0.001). The median (IQR) follow-up time was 5.7 (2.3-10.3) years. At 10-year, PCSM in NHW vs NHB patients was statistically different in the 1st ADI quartile (5.2% vs 10.4%, p<0.001), but not in the 2nd, 3rd, and 4th ADI quartile groups (all p > 0.05). On MVA, NHW and NHB patients in the 4th ADI quartile (most disadvantaged area) had a 1.27-fold (95% CI: 1.02-1.58; p=0.030) higher cancer-specific mortality compared to NHW and NHB patients in the 1st ADI quartile, but race was not an independent predictor of cancer-specific mortality (HR:1.05; 95% CI:0.89-1.23; p=0.564). Conclusions: Our study was the first to assess the differential impact of ADI as a predictor of PCSM based on race in a large contemporary North American cohort. Within the first quartile, NHB patients showed higher cancer-specific mortality compared to NHW patients. Interestingly, race itself was not identified as an independent predictor of cancer-specific mortality, underscoring the significant influence of socio-economic factors, particularly in areas with higher deprivation, on prostate cancer outcomes.

Urology

Ditonno F, Franco A, Wu Z, Wang L, Correa A, Margulis V, Djaladat H, Veccia A, Simone G, Tuderti G, Derweesh IH, **Abdollah F**, Singla N, Ferro M, Porpiglia F, Checcucci E, Amparore D, Gonzalgo ML, Perdonà S, Tufano A, Mehrazin R, Sundaram CP, Antonelli A, and Autorino R. Robotic distal ureterectomy for high-risk distal ureteral urothelial carcinoma: A retrospective multicenter comparative analysis (ROBUUST collaborative analysis). *Eur Urol* 2024; 85:S817-S818. Full Text

Introduction & Objectives: The role of kidney-sparing surgery (KSS) in patients with high-risk upper urinary tract urothelial carcinoma (UTUC) is controversial. The aim of this study was to assess the outcomes of distal ureterectomy in patients with high-risk distal ureteral tumors. Materials & Methods: The

ROBUUST (ROBotic surgery for Upper Tract Urothelial Cancer Study) multicenter international (2015-2022) dataset was used for this retrospective cohort analysis. After identifying high-risk patients with tumors of the distal ureter, the study population was divided into two subgroups according to surgical procedure, robot-assisted distal ureterectomy (RADU) or robot-assisted nephroureterectomy (RANU). A survival analysis of the primary endpoint recurrence-free survival (RFS), defined as the time elapsed between diagnosis and disease recurrence, was performed. Secondary endpoints were metastasis-free survival (MFS), as the time between diagnosis and metastasis onset, and overall survival (OS), as the time between diagnosis and death by any cause. After adjusting for clinical features of the high-risk prognostic group, Cox proportional hazard model was plotted to evaluate significant predictors of time-to-event outcomes. Results: Overall, 477 patients with distal ureteral high-risk UTUC were retrieved, of which 58 received RADU and 419 RANU, respectively, with a mean (±SD) follow-up of 29.6 months (±2.6). No significant difference in terms of baseline features was observed between the two treatment groups, including preoperative serum creatinine (SCr) (p=0.6) and estimated glomerular filtration rate (eGFR) (p=0.1). Mean (±SD) tumor size was significantly higher in the RANU group (2.9 ±2 vs 2.3 ±1.6, p=0.03), even though no difference was observed in the proportion of lesions of ≥2 cm (66.1% vs 58.5%, p=0.3). Likewise, a comparable number of patients had cT≥2 (12.4% vs 8.6%, p=0.4) tumors. At survival analysis a RFS of 8.2 months (±2.6) and 9.3 months (±4) was observed for RADU and RANU, respectively, with no significant difference between the treatment modalities (p=0.6). The two cohorts were comparable also in terms of MFS (p=0.5) and OS (p=0.7). At Cox regression analysis, in each model for the different time-to-event outcomes, the type of surgery was never a significant predictor of worse oncological outcomes. At last follow-up patients undergoing RADU had significantly better post-operative renal function in terms of mean (±SD) eGFR (60.7 ±2.4 vs 52.3 ±4.9, p=0.01). Conclusions: Within the limitations related to the retrospective study design, our findings suggest comparable outcomes in terms of RFS, MFS and OS between RADU and RANU patients, and an advantage of in terms of post-operative renal function preservation. KSS might be considered as a potential option for selected high-risk patients.

Urology

Ditonno F, Veccia A, Montanaro F, Pettenuzzo G, Costantino S, Franco A, Wu Z, Correa A, Margulis V, Djaladat H, Simone G, Derweesh IH, **Abdollah F**, Nirmish S, Ferro M, Porpiglia F, Checcucci E, Gonzalgo ML, Perdonà S, Mehrazin R, Sundaram CP, Autorino R, and Antonelli A. Decisional and prognostic impact of diagnostic ureteroscopy in high-risk upper tract urothelial carcinoma: A multi-institutional collaborative analysis (ROBUUST collaborative group). *Eur Urol* 2024; 85:S713-S714. Full Text

Introduction & Objectives: Current guidelines strongly recommend against the use of diagnostic ureteroscopy (URS) in the diagnostic pathway for upper tract urothelial carcinoma (UTUC). We aimed at analysing the decision-making and prognostic role of diagnostic URS in high-risk patients undergoing radical nephroureterectomy (RNU). Materials & Methods: Data were retrieved from the ROBUUST (ROBotic surgery for Upper Tract Urothelial Cancer Study) multicenter international (2015-2022) dataset. A retrospective comparative analysis was conducted to evaluate the characteristics of high-risk patients who either underwent pre-operative URS and biopsy before RNU or did not, and its impact on surgical and oncological outcomes. Survival analysis included recurrence-free survival (RFS), as the time between diagnosis and disease recurrence; metastasis-free survival (MFS), as the time between diagnosis and metastasis onset; cancer-specific survival (CSS) and overall survival (OS), as the time between diagnosis and death by UTUC or from any cause, respectively. After adjusting for clinical features of the high-risk prognostic group, Cox proportional hazard model was used to evaluate significant predictors of time-to-event outcomes. Logistic regression analysis was performed to evaluate differences between patients receiving URS and, based on their URS status, to determine their likelihood of receiving kidney-sparing surgery and a specific surgical approach. Results: Overall, 1912 patients were included, 1035 undergoing URS and biopsy and 877 not receiving endoscopic diagnosis. A mean follow-up of 28.9 months was obtained. Patients undergoing pre-operative URS were more likely female (OR 0.67, 95% CI 0.51-0.87), with smaller (OR 0.31, 95% CI 0.22-0.43), and organ-confined tumors (OR 0.47, 95% CI 0.34-0.64), compared to patients not receiving URS. Robot-assisted RNU was the most common procedure (55.1%), in both subgroups. At survival analysis, CSS was significantly higher for patients undergoing URS (37 months vs 20 months, p<.001). However, the two cohorts were comparable in terms of RFS (p=.6), MFS

(p=.3) and OS (p=.07). In Cox regression analysis, URS was not a significant predictor of worse oncological outcomes for each time-to-event outcome. Likewise, in logistic regression analysis, pre-operative ureteroscopy was not a significant predictor of a certain surgical approach or technique. Conclusions: Within the limitations related to the retrospective study design, our findings suggest that diagnostic ureteroscopy is performed mostly in patients with smaller localized tumors. Patients undergoing ureteroscopy had a longer CSS, even though statistical significance was lost at Cox analysis. Surgical strategy is likely determined more by tumour features than by ureteroscopy findings.

Urology

Finati M, **Cirulli GO**, **Chiarelli G**, **Stephens A**, **Davis M**, **Tinsley S**, **Butaney M**, **Arora S**, **Morrison C**, Sood A, Buffi N, Lughezzani G, Salonia A, Briganti A, Montorsi F, Bettocchi C, Carrieri G, **Rogers C**, and **Abdollah F**. Association of area of deprivation index with prostate cancer incidence and lethality over a contemporary North American cohort. *Eur Urol* 2024; 85:S53. Full Text

Introduction & Objectives: Increasing evidence indicate that poor socioeconomic status and residence in underprivileged areas contribute to disparities in prostate cancer (PCa) outcomes. While comprehensively assessing the impact of these factors might be might be intricate, the Area of Deprivation Index (ADI) could offer a distinctive and valuable metric for these considerations. Our study examined the impact of ADI on Prostate Cancer (PCa) incidence and lethality over a contemporary North American population. Materials & Methods: Our institutional database included electronic medical records for all men who received at least one PSA test within Henry Ford Health (HFH), between 1995 and 2019. An ADI score were assigned to each patients based on their residential census block group, ranked as a percentile of deprivation relative to the national level. All patients were further categorized into ADI quartile, where the highest quartile (Q4: 75-100) represented individuals with the most disadvantageous socio-economic status. The main outcomes were PCa incidence and lethal PCa, defined as any metastatic PCa or death due to PCa occurred within our cohort. Cumulative incidence curves were used to depict PCa incidence and lethality, after stratifying patients into sub-cohorts based on ADI quartile. Multivariable Fine-Gray regression examined the impact of ADI quartiles on PCa incidence and lethality, after adjusting for all available confounders. Results: A total of 148,892 patients were included, with a median follow-up f of 8.8 (5-17) years. When patients were categorized based on their ADI quartile, the 20-years PCa incidence rates were 9.1%, 8.4%, 7.7% and 8.5%% for the first, second, third and fourth quartile respectively. For the same quartile categories, the 20-years lethal PCa rates were 1.3%, 0.90%, 1.0% and 1.7%. At multivariable analysis, both the third (HR: 0.01, 95% IC: 0'85-0.97, p=0.007) and the fourth quartile (HR: 0.83, 95% IC: 0.77-0.88, p=0.007) had a lower risk of being diagnosed with PCa, when compared with patients in the lowest ADI quartile. On the other side, ADI did not result an independent predictor for lethal PCa. Of note, Non-Hispanic black patients had almost 2-fold the risk both for PCa incidence and lethality, when compared with Non- Hispanic White patients (all p<0.001). Conclusions: Our study is the first to evaluate the role of ADI in predicting PCa incidence and lethality in a contemporary North American cohort. Patients from less disadvantaged areas were more likely diagnosed with PCa, while those from the most deprived areas showed increased lethal PCa rates, though not reaching the conventional significance at multivariable analysis. Notably, race emerged as an independent predictor for both lethal PCa and its incidence, regardless of any socioeconomic and deprivation influences.

Urology

Finati M, **Cirulli GO**, **Chiarelli G**, **Stephens A**, **Tinsley S**, **Butaney M**, **Arora S**, Sood A, Buffi N, Lughezzani G, Briganti A, Montorsi F, Busetto GM, Carrieri G, **Rogers C**, and **Abdollah F**. Radical cystectomy versus trimodal therapy for non-metastatic muscle-invasive bladder cancer: Analysis of an other-cause mortality matched cohort. *Eur Urol* 2024; 85:S1963. Full Text

Introduction & Objectives: Although Trimodal therapy (TMT) is now accepted for well-selected patients with muscle-invasive bladder cancer (MIBC), in clinical practice it is often reserved for sicker patients for whom radical cystectomy (RC) is not a feasible option. Thus, comparative effectiveness studies (TMT vs RC) based on retrospective studes are usually hindered by selection bias. To circumvent this limitation, we designed a novel approach matching patients based on their calculated other-cause mortality (OCM) risk. Using this homogeneous cohort, we tested the impact of TMT vs RC on cancer-specific mortality (CSM). Materials & Methods: The Surveillance, Epidemiology and End Results (SEER) database was

queried to identify patients diagnosed with histologically confirmed T2-4 MIBC between 2004 and 2018. A Cox regression model calculating 5-years OCM was used to create a 1:1 propensity-score matched cohort of patients treated with RC vs TMT. Cumulative incidence curves depicted CSM and OCM, while Fine-Gray regression tested the impact of treatment type on CSM in the matched cohort. Patients were further stratified according to Chemotherapy receipt and clinical stage based on transurethral resection of bladder tumor (cT2 vs T3-4) and the aforementioned methodology was repeated. Results: We identified 6,587 (76%) treated with RC and 2,057 (24%) TMT. Median follow-up was 3.0 years (IQR 1.1-6.7). In the unmatched cohort, 5-year OCM and CSM rates were 14% and 40% in RC group respectively, versus 23% and 47% in TMT (all p<0.001). Our matched cohort included 6,506 patients equally distributed for treatment type (RT vs RP), with no difference in 5-years OCM. In the matched cohort, the 5-year CSM rate was 42% in RC patients versus 48% in TMT (p=0.001). This trend was confirmed at multivariable analysis, where TMT patients had a 1.54-fold higher CSM risk than their RC counterparts. After stratifying the matched cohort for Chemotherapy receipt, the 5-year CSM rate was significantly higher for TMT versus RC who did not receive Chemotherapy (48% vs 41%, p<0.001). On the other hand, no difference in CSM was recorded when compare patients treated with TMT vs RC plus Chemotherapy (46% vs 45%, p=0.2). When stratified patients based on their clinical stage, TMT shower higher CSM rates than RC both in cT2 (44% vs 26%, p<0.001) and cT3-T4 (59% vs 53%, p < 0.02), albeit not being an independent predictor of CSM in cT3-T4 patients. Conclusions: In comparison with previous literature, our study is the first to mitigate the impact of selection bias by matching based on OCM. Our findings showed invariably CSM advantage of RC over TMT in pT2 patients. Conversely, TMT prooved to be a valid option for patients who showed advanced clinical disease, as RC did not showed any oncological survival advantage in cT3-cT4 patients or for those who required chemotherapy in combination with surgery.

Urology

Finati M, **Cirulli GO**, **Chiarelli G**, **Tinsley S**, **Morrison C**, **Davis M**, **Arora S**, **Etta P**, **Butaney M**, Akshay S, Buffi N, Lughezzani G, Salonia A, Briganti A, Montorsi F, Bettocchi C, Carrieri G, **Rogers C**, and **Abdollah F**. The role of cytoreductive nephrectomy in metastatic clear cell carcinoma: Analisys of an other-cause mortality matched population from the contemporary immunotherapy era. *Eur Urol* 2024; 85:S1866. Full Text

Introduction & Objectives: In the recent randomized CARMENA trial, performing cytoreductive nephrectomy (CN) did not improve overall survival in metastatic renal cell carcinoma (RCC) patients treated with Sunitinib. However, this trial raised concerns about possible selection bias of patients with higher metastatic burden and consequent poor prognosis. Conversely, population-based studies showed how patients referred to CN usually have better health status, which reflects in lower risk for any cause of death. We aimed to evaluate the role of CN on cancer-specific mortality (CSM) within an immunotherapy-era cohort of metastatic RCC patients matched for their other-cause mortality (OCM) risk. Materials & Methods: The Surveillance, Epidemiology and End Results Registry was queried to identify > 18 years patients diagnosed with metastatic RCC, between 2010 and 2017. We included only patients treated with immunotherapy. A Cox regression model including treatment type (CN versus no surgery of the primary site) was used to calculate the other-cause mortality (OCM) risk. Therefore, a 1:1 propensity score match was used to create a cohort of metastatic RCC patients, treated or not with CN, having the same OCM risk. Cumulative incidence curves were depicted to assess CSM and OCM, while Fine-Gray regression tested the impact of CN on CSM. Patients were further stratified according to number of metastasis (1, 2 or more than 2 sites) and the same aforementioned analyses were repeated for these sub-cohorts. Results: We identified 3138 patients with metastatic RCC treated with immunotherapy, of whom 1597 (51%) were treated with CN. In the unmatched cohort, 3-years CSM and OCM rates were 80.8% and 15.5% for non-surgery arm respectively, versus 54.3% and 8.4% for CN patients (all p<0.001). Our Cox Regression model matching yielded to 1662 patients equally distributed, with no difference in OCM rate (11.7% vs 10.8%, p=0.8). In the matched cohort, the 3-years CSM was 54.1% for CN patients vs 80.3% in non-surgery arm (p<0.001). At multivariable analysis, patients who did not receive surgery had 1.79-fold higher CSM risk, when compared with those who underwent CN (95% CI: 1.56-2.06, p<0.001). When stratifying patients for metastases sites, patients who did not undergo CN had higher CSM rates when they harboured metastasis in 1 (84.5% vs 70.0%) or 2 sites (87.8% vs 73.4%, all p<0.001). Conversely, no difference in CSM rate where observed for patients with 3 or more metastases sites, regardless of nephrectomy receipt (89.1% vs 86.8%, p=0.06). Conclusions: We evaluate the role of CN in a

immunotherapy-era cohort of metastatic RCC, using OCM risk matching as a proxy of similar health status. In this setting, performing CN yielded a survival advantage in patients with low-to intermediate metastatic burden. Conversely, CN did not CSM for patients with widespread metastases.

Urology
Finati M, Corsi NJ, **Chiarelli G**, **Cirulli GO**, **Stephens A**, **Tinsley S**, **Davis M**, **Butaney M**, **Arora S**, Sood A, Buffi N, Lughezzani G, Briganti A, Salonia A, Montorsi F, Bettocchi C, Carrieri G, **Rogers C**, and **Abdollah F**. The impact of radical prostatectomy versus radiation therapy on cancer-specific-mortality for non-metastatic prostate cancer: Analysis of an other-cause-mortality matched cohort. *Eur Urol* 2024; 85:S1273-S1274. Full Text

Introduction & Objectives: Studies comparing radical prostatectomy (RP) to radiation therapy (RT) have consistently shown that patients undergoing RT have a higher risk of other-cause mortality (OCM) compared to RP, signifying poor health status of the former patients. We aimed to evaluate the impact of RP vs RT on cancer-specific mortality (CSM) over a cohort with equivalent OCM risk. Materials & Methods: The Surveillance, Epidemiology and End Results (SEER) database was queried to identify patients diagnosed with non-metastatic PCa between 2004-2009, treated with RP or RT. A Cox-regression model was used to calculate the 10-year OCM risk. Propensity-scores based on the calculated OCM risk were used to match RP and RT patients. Cumulative incidence curves and multivariable Fine-Gray regression analyses were used to examine the impact of type on CSM in the matched cohort. Results: We identified 55,106 PCa patients treated with RP and 36,674 treated with RT. After match, 6,506 patients were equally distributed for RT vs RP, with no difference in OCM rates (p=0.2). After stratifying the matched cohort for D'Amico risk and Gleason Score, 10-year CSM rates were 8.8% vs 0.6% (p=0.01) for RT vs RP in patients with unfavorable-intermediate-risk (Gleason Score 4+3) and 7.9% vs 3.9% (p=0.003) for high-risk disease. There was no difference in CSM rates among RT and RP patients for favorable-intermediate-risk (Gleason Score 3+4) and low-risk disease. Conclusions: In a matched cohort of PCa patients with comparable OCM between the two arms, RP yielded a more favorable CSM rate compared to RT only for unfavorable-intermediate- and high-risk groups. [Figure presented]

Urology
Pallauf M, Fletcher SA, Rezaee M, Roupret M, Boorjian SA, Potretzke AM, Djaladat H, Ghoreifi A, Soria F, Mari A, Campi R, Khene ZE, Kikuchi E, Rink M, Fujita K, D'Andrea D, Boormans JL, Ploussard G, Breda A, **Abdollah F**, Raman JD, Shariat SF, Pradere B, and Singla N. Oncologic outcomes in patients with variant histologies of upper tract urothelial cancer: Results from an international multicenter cohort. *Eur Urol* 2024; 85:S369-S370. Full Text

Introduction & Objectives: Histologic variants (VH) of urothelial carcinoma (UC) of the lower urinary tract are associated with worse oncologic outcomes than pure UC. However, outcomes for patients with VH in the upper urinary tract are poorly described, given their rarity. We sought to elucidate the oncologic outcomes for patients with upper tract urothelial carcinoma (UTUC) with VH. Materials & Methods: We queried an international, multicenter cohort of non-metastatic UTUC patients treated with radical nephrouterectomy (RNU). We categorized patients into pure UC (no-VH) and VH. VH was sub-categorized based on the distribution of subtypes into ‘squamous/glandular/trophoblastic’ (VH-S) and ‘other’ (VH-O), comprising all other VH. We compared clinicopathologic characteristics and oncologic outcomes, including recurrence-free (RFS), cancer-specific (CSS), and overall survival (OS), among groups. We performed subanalyses matched by pathologic stage: organ-confined (OC: ≤pT2 and pN0-x) and non-organ-confined (NOC: ≥pT3 or pN1-2). Kaplan Meier methods and multivariable proportional hazards Cox regression with multivariate imputation by chained equations (MICE) for missing predictor covariates were performed to evaluate outcomes. Results: We included 3,435 patients treated from 1985-2022 across 23 centers worldwide and identified 201 (6%) with VH. The median follow-up was 30 months (IQR 12-61). The most common VH subtype was VH-S (133/201, 66%). Neoadjuvant (12% vs. 5%, p<0.001) and adjuvant (27% vs. 13%, p<0.001) systemic therapy were more often administered in VH than in no-VH patients. Lymph node dissection was also more often performed in VH patients (54% vs. 39%, p<0.001). Patients with VH presented with more advanced pT (p<0.001) and pN (p<0.001) stage. In patients with OC disease, VH had worse RFS than no-VH (5-year RFS 58% vs. 80%, p=0.004), though

CSS and OS were not significantly different. Stratified by VH subtype, VH-S exhibited similar oncologic outcomes as no-VH, but VH-O demonstrated worse stage-matched RFS (4-year RFS 39% vs. 83%, p<0.001 [OC] and 28% vs. 46%, p=0.01 [NOC]) and OS (5-year OS 45% vs. 75%, p=0.004 [OC]) compared to no-VH. VH-O independently predicted worse survival outcomes on multivariable Cox regression analyses. Conclusions: UTUC patients with VH exhibit more aggressive disease at presentation compared to pure UC. Despite the increased use of systemic therapy, certain VH subtypes demonstrate worse oncologic outcomes compared to pure UC. Further study is warranted to elucidate the biology of different UTUC VH subtypes to optimize treatment approaches.

Urology
Saitta C, Meagher MF, Autorino R, Porpiglia F, Bell S, **Abdollah F**, Simone G, Yong C, Lughezzani G, Afari J, Tozzi M, Jacob T, Ghoreifi A, Wang L, Margulis V, Sundaram C, Djaladat H, Mehrazin R, Gonzalgo M, Buffi N, Wu Z, Ferro M, and Derweesh I. Development and validation of a novel nomogram to predict lymph node invasion in upper tract urothelial carcinoma. *Eur Urol* 2024; 85:S716-S717. Full Text

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

Urology
Tinsley SA, **Stephens A**, **Marco F**, **Chiarelli G**, **Cirulli GO**, Davis M, Corsi N, Sood A, Buffi N, Lughezzani G, Bettocchi C, Salonia A, Briganti A, Montorsi F, Carrieri G, **Rogers C**, and **Abdollah F**. The impact of radical prostatectomy versus radiation therapy on cancer-specific mortality for patients with localized prostate cancer and positive nodal disease: An analysis of other cause mortality weighted cohort. *Eur Urol* 2024; 85:S1261-S1262. Full Text

Introduction & Objectives: There is controversy regarding the survival benefit of radical prostatectomy (RP) versus radiation therapy (RT) for the primary management for prostate cancer (PCa) in men with clinically positive nodes (cN1). Virtually, all previous retrospective reports on this subject are limited by selection bias, where “unhealthy” patients are more frequently treated with RT. To circumvent this limitation, we sought to compare prostate cancer specific mortality (PCSM) in cN1 PCa patients who underwent RP versus RT, in an othercause mortality (OCM) weighted cohort. Materials & Methods: The Surveillance, Epidemiology, and End Results (SEER) database was queried to identify men with cN1 PCa at diagnosis between 2004 to 2017, and were treated with RP or RT. A Cox regression model was used to calculate the 10-year OCM risk using all available covariates, including treatment type. Then, a competing risk multivariate model, which was weighted on the calculated OCM risk, was used to examine

the impact of treatment type (RP vs. RT) on PCSM, after accounting for available covariates. Results: There were a total of 5778 patients included in our final cohort, with 4739 (82.02%) patients underwent RP, versus 1039 (17.98%) who underwent RT. The median with the interquartile range had a follow-up of 4.7 years (2.6-8.2). OCM has statistically significant differences between RP and RT patients in the unweighted (p-value = 0.005), but that difference disappeared in the weighted cohort (p-value = 0.2). Based on cumulative incidence function (CIF), the 10-year PCSM rate was 32.2% (95% CI: 27.6% - 35.6%) for patients treated with RT versus 17.1% (95% CI: 15.9% - 19.0%) for those that treated with RP (p-value <0.001). Conclusions: Our results show that cN1 PCa patients treated initially with RT fare worst in terms of PCSM than their counterparts that underwent RP. Our report is the first comparative effectiveness study that compares those treatments cohorts, after alleviating the known selection bias in “real-world” practice by weighting our models using calculated OCM. [Figure presented]

Urology
Tuderti G, Proietti F, Wu Z, Franco A, **Abdollah F**, **Finati M**, Ferro M, Tozzi M, Porpiglia F, Checcucci E, Margulis V, Singla N, Derweesh IH, Correa A, Gonzalgo ML, Mehrazin R, Sundaram CP, Tufano A, Perdonà S, Djaladat H, Ditonno F, Antonelli A, Autorino R, and Simone G. Real-world management of high-risk upper tract urothelial carcinoma: Level of adherence to EAU guidelines - analysis of the ROBUUST registry. *Eur Urol* 2024; 85:S798-S799. Full Text

Introduction & Objectives: The European Association of Urology (EAU) guidelines (GL) for Upper Tract Urothelial Carcinoma (UTUC) are mainly based on retrospective studies. We aimed to assess the adherence to EAU GL in a large multicenter cohort of patients with UTUC, treated with nephroureterectomy (NU). Materials & Methods: A multicenter retrospective analysis utilizing the ROBUUST (ROBotic surgery for Upper tract Urothelial cancer Study) registry was performed. We assessed the region-specific GL adherence rates for bladder cuff management, post-operative bladder instillation, adoption of adjuvant chemotherapy (AdCHT), and performance of lymphadenectomy (LND). We subsequently assessed the impact of these variables on oncologic outcomes with the Kaplan-Meier (KM) method. Results: Overall, data of 2,307 patients were evaluated. With regard to bladder cuff management, excision was the most adopted approach world-wide (US 88.6%, Europe (EU) 90.5%, Asia (A) 89.8%). Regarding post-operative bladder instillation, although strongly recommended, its adoption rate was only 28.4%; notably, at KM analysis patients receiving instillation did not display improved bladder recurrence-free survival (BRFS) (p=0.45). Concerning LND, harbouring a weak recommendation for muscle-invasive disease, it appears underused in both locally advanced (cT3-4: US 35.8%, EU 46.8%, A 25%) and cN positive stages (US 41.9%, EU 47.9%, A 43%); however, at KM analysis, patients receiving LND had not any benefit in terms of cancer-specific survival (CSS); this data was homogenous across all stages (all p≥0.53). Concerning the use of AdCHT, strongly recommended for pT2–T4 and/or pN+ disease, overall administration rate was only 27.7% for pT2-T4, with a significantly higher adoption in Asia (p=0.03); moreover, in pN+ disease, overall its use was 30.2%, homogeneously low across all regions. At KM analysis, patients receiving AdCHT hadn't significant CSS benefit. Conclusions: Real word data highlights poor adherence to the UTUC EAU GL for all main topics, namely post-operative bladder instillation, performance of LND and AdCHT administration for advanced stages of disease. Despite the retrospective nature of data, real word data seem to support the need for further research supporting clinical benefits of these intra and postoperative procedure. [Figure presented]

Urology
Tuderti G, Proietti F, Wu Z, Franco A, **Abdollah F**, **Finati M**, Ferro M, Tozzi M, Porpiglia F, Checcucci E, Margulis V, Singla N, Derweesh IH, Correa A, Gonzalgo ML, Mehrazin R, Sundaram CP, Tufano A, Perdonà S, Djaladat H, Ditonno F, Antonelli A, Autorino R, and Simone G. Real-world data: Call for paradigm shift towards neoadjuvant chemotherapy in patients with upper tract urothelial carcinoma treated with nephroureterectomy - analysis of the ROBUUST registry. *Eur Urol* 2024; 85:S796-S797. Full Text

Introduction & Objectives: Preliminary results of phase II trials support the effectiveness of neoadjuvant (Nad) chemotherapy (CHT) for high-grade upper tract urothelial carcinoma (UTUC), although available data are still immature. In this study we assessed the role of perioperative CHT in a large multicenter cohort of patients with UTUC, treated with nephroureterectomy (NUT). Materials & Methods: A multicenter

retrospective analysis utilizing the ROBUUST (Robotic surgery for Upper Tract Urothelial Cancer Study) registry was performed. Baseline, preoperative, perioperative, and pathologic variables of three groups of patients receiving NUT only, Nad-CHT or Adjuvant (Ad) CHT were compared. Categorical and continuous variables among the three subgroups were compared with Chi square and ANOVA tests, respectively. Stage-specific (cT 0-2, cT≥3 and cN +) Kaplan-Meier analysis were performed to compare Cancerspecific survival (CSS) probabilities. Results: Overall, 1994 patients were included. Nad-CHT patients displayed a significantly higher rate of cT stage ≥ 3 ($p<0.001$) and cN positive stage ($p<0.001$). Overall complications and Clavien grade ≥ 3 complications rates were comparable among the three subgroups ($p=0.65$ and $p=0.92$, respectively). At Kaplan-Meier analysis specific for cT0-2 patients, no significant differences were detected among the three groups of patients (24-mo: Nad-CHT 89.2%, NUT 91.5%, Ad-CHT 88.8%; $p=0.34$). On the other hand, at Kaplan-Meier curve specific for cT≥ 3 stage, Nad-CHT showed a significantly higher rate of CSS than the other two cohorts (24-mo: Nad-CHT 81.1%, NUT 66.9%, Ad-CHT 69.9%; $p=0.03$). Accordingly, at Kaplan-Meier analysis specific for cN positive patients, Nad-CHT showed a significantly higher rate of CSS than the other two cohorts (24-mo: Nad-CHT 75.6%, NUT 63.6%, Ad-CHT 59.4%, $p=0.03$). Conclusions: Our retrospective analysis of a large multicenter dataset suggests that neither Nad-CHT nor Ad-CHT provide an CSS advantage over surgical treatment alone. However, in specific scenarios, such as locally advanced and clinically positive nodes disease, NadCHT seems to offer a significant benefit in terms of CSS, with a negligible impact on surgical morbidity. Further data from randomised controlled trials are expected. [Figure presented]

Urology
Wang Y, **Arora S**, **Bazzi M**, **Zhuo J**, **Leavitt D**, and **Rogers CG**. Combined HoLEP and transvesical single port robotic simple prostatectomy. *Eur Urol* 2024; 85:S582. Full Text

Introduction & Objectives: Obstructive benign prostatic hyperplasia (BPH) for very large glands can be managed with Holmium laser enucleation (HoLEP) or robotic assisted simple prostatectomy (RASP). HoLEP may allow for easier access to the apex of the prostate than the base, whereas RASP may have easier exposure of the base than the apex. Additionally, HoLEP may have a higher risk of transient urinary incontinence, particularly in patients with larger prostates. In this video, we report the first case of combined HoLEP and RASP using a single port (SP) transvesical approach. Materials & Methods: Our patient presented with urinary retention and an enlarged prostate of 332g on pre-operative MRI and elected for a combined HoLEP and RASP approach. HoLEP was first used to release the apex of the adenoma and the enucleation plane was carried past the midpoint of the prostate. We then transitioned to the RASP portion. A cystotomy was made for the placement of the DaVinci access port. The SP robot was docked. The enucleation plane was developed at the base of the prostate and dissected distally to connect to the enucleated portion from HoLEP. The adenoma was excised in a piece-wise manner and retrieved through the access port. Results: Both procedures were performed uneventfully with successful removal of the prostate gland through the access trocar with a combined operative time was 457 minutes and an estimated blood loss of 200 mL. The patient remained inpatient for one day and experienced an uneventful post-operative course with no peri-operative complications. The patient had a successful trial of void after one week and continues to report excellent continence. Conclusions: We demonstrate a novel procedure combining HoLEP and SP transvesical RASP for a very large gland that may be more challenging by either procedure alone. This combination can be done safely and effectively while leveraging the potential advantages of both approaches.

Urology
Wang Y, **Wilder S**, Hijazi M, Mirza M, Van Til M, Maatman T, Ghani KR, Lane BR, and **Rogers CG**. Surgeon skill is associated with positive surgical margins in robot-assisted partial nephrectomy: Results of a video-based evaluation. *Eur Urol* 2024; 85:S2061-S2062. Full Text

Introduction & Objectives: There is growing interest in understanding the clinical implications of surgeon proficiency levels for complex procedures such as robot-assisted partial nephrectomy (RAPN). We conducted a peer surgeon video review exercise to determine if surgeon scores representing technical skills in RAPN are associated with patient outcomes. Materials & Methods: From July 2021 to September 2022, 11 experienced surgeons participating in a statewide quality improvement collaborative (MUSIC-KIDNEY) submitted one to seven videos of themselves performing RAPN. Videos were segmented into

six key steps of the procedure, yielding 127 video clips. Video clips were deidentified and distributed to 24 blinded peer reviewer surgeons who also perform RAPN. Reviewers provided written feedback and rated technical skill using a published evaluation tool: Scoring for Partial Nephrectomy (SPaN), 1=lowest and 5=highest. Outcomes from the MUSIC registry for all submitting surgeons were assessed for length of stay (LOS), estimated blood loss (EBL)>500, warm ischemia time (WIT) >30 min, positive surgical margin (PSM), and readmission. Risk adjusted outcomes were correlated with scores representing surgeon skills, with significance at p-value<0.05. Score cards and written comments were provided to all participants. Participant survey results were collected 2 months after video review. Results: 11 surgeons submitted a total of 127 video clips; 383 total reviews were performed by 24 reviewers over the span of 6 months. The average score for reviewed clips was 4.2, ranging between 3.5 and 4.7. Greater technical skill, represented by overall score, correlated with lower rates of PSM (p=0.038) (Figure). Specifically, higher scores in the clamping and tumor resection step were correlated with lower rates of PSM (p=0.041). Surveys indicated submitters and reviewers found the process and score card valuable for identifying areas of improvement, learning different RPN techniques, and educating trainees. Conclusions: Video review demonstrated that higher technical skill with RAPN was associated with lower frequency of PSM. These findings suggest that video-based peer evaluation plays a role in assessing surgical skill and could be used in quality improvement initiatives to improve patient care and oncologic outcomes. [Figure presented]

Urology

Wang Y, **Wilder S**, **Rogers CG**, and **Patel AK**. A single center evaluation of single use, disposable transperineal prostate biopsy guide with pivot feature. *Eur Urol* 2024; 85:S651. Full Text

Introduction & Objectives: Transrectal biopsy is associated with a 1-2% risk of serious infection leading to hospitalization. Transperineal (TP) prostate biopsy has been gaining popularity due to a lower rate of post-procedural sepsis. There are several TP biopsy guides, which are categorized into single-use disposable and reusable. In this video, we demonstrate the safety and efficacy of our technique performing TP biopsy in both clinic and OR settings using a disposable needle guide with a pivot feature. Materials & Methods: An adjustable disposable needle guide with a pivot capability (TP Pivot Pro™ transperineal needle guide, Civco Medical Solutions) attached to a biplanar ultrasound probe was evaluated for TP biopsy. Biopsies were performed in the clinic setting with local anesthesia, and in the OR with sedation and local anesthesia. Prostate samples were obtained using an 18-gauge x 25 cm biopsy gun. After each biopsy, physicians were asked to fill out an evaluation form regarding procedural set up, post-procedural outcomes, and physician perception of device usability scored from 1 to 5 on a Likert scale (1=completely disagree, 5 = completely agree). Forms were collected to determine overall complication rates and efficacy of the biopsy guides. Results: From January to June 2023, five urologists performed a total of 61 TP biopsies using the disposable needle guide. The needle guide was used with the Mindray, ExactVu, BK Medical, and Koelis Trinity ultrasound systems. 33% of TP biopsies utilized MRI fusion technique. 53% of biopsies were only performed systematically, while the remaining also included targeted biopsies. 44% of procedures occurred in the clinic setting. Overall, physicians reported a positive user experience with the disposable needle guide. The mean survey response for each question ranged from 4.2 and 4.9 (between agree and completely agree). Physicians specifically appreciated the guide's ability to pivot the biopsy needle angle, which allowed better access to the anterior and posterior prostate. Only 2 (3.3%) patients experienced post-procedural complications. One patient experienced urinary retention due to large prostate and another patient experienced hematuria. 75% of patients did not receive prophylactic antibiotics, and there were no reported post-procedural infections. Conclusions: We demonstrated that TP prostate biopsy using a disposable needle guide can be safely used in the clinic and OR setting with minimal complications. There is a potential reduction in infections with the use of a disposable needle guide. Additionally, the pivoting function of the needle guide is a unique feature not present in other guides.