

## Henry Ford Health System Publication List – July 2021

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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 System personnel. Searches were conducted in PubMed, Embase, and Web of Science during the month, and then imported into EndNote for formatting. There are **133 unique citations** listed this month, with **12 articles** and **1 conference abstract** on **COVID-19**. [Articles](#) are listed first, followed by [conference abstracts](#), [books and book chapters](#), and a [bibliography of publications on COVID-19](#). Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health System authors.

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## **Articles**

[Administration](#)  
[Anesthesiology](#)  
[Behavioral Health](#)  
[Services/Psychiatry](#)  
[Cardiology/Cardiovascular](#)  
[Research](#)  
[Center for Health Policy and](#)  
[Health Services Research](#)  
[Clinical Quality and Safety](#)  
[Dermatology](#)  
[Diagnostic Radiology](#)  
[Emergency Medicine](#)  
[Endocrinology and](#)  
[Metabolism](#)  
[Family Medicine](#)  
[Gastroenterology](#)  
[Global Health Initiative](#)  
[Graduate Medical Education](#)  
[Hematology-Oncology](#)  
[Hospital Medicine](#)  
[Infectious Diseases](#)  
[Internal Medicine](#)

### **Conference Abstracts**

[Administration](#)  
[Anesthesiology](#)  
[Gastroenterology](#)  
[Hematology-Oncology](#)  
[Neurology](#)  
[Neurosurgery](#)  
[Orthopedics/Bone and Joint Center](#)  
[Research Administration](#)  
[Surgery](#)

[Neurology](#)  
[Neurosurgery](#)  
[Nursing](#)  
[Obstetrics, Gynecology and](#)  
[Women's Health Services](#)  
[Orthopedics/Bone and Joint Center](#)  
[Otolaryngology – Head and Neck](#)  
[Surgery](#)  
[Pathology and Laboratory Medicine](#)  
[Podiatry](#)  
[Public Health Sciences](#)  
[Pulmonary and Critical Care](#)  
[Medicine](#)  
[Radiation Oncology](#)  
[Rehabilitation Services/Physical](#)  
[Therapy/Occupational Health](#)  
[Research Administration](#)  
[Rheumatology](#)  
[Sleep Medicine](#)  
[Surgery](#)  
[Urology](#)

### **Books and Book Chapters**

[Otolaryngology](#)  
[Surgery](#)

## Articles

### Administration

**Jamil ML, Wurst H, Robinson P, Rubinfeld I, Suleyman G, Pollak E, and Dabaja AA.** URINARY CATHETER ALLEVIATION NAVIGATOR PROTOCOL (UCANP): OVERVIEW OF PROTOCOL AND REVIEW OF INITIAL EXPERIENCE. *Am J Infect Control* 2021; Epub ahead of print. PMID: 34273463. [Full Text](#)

**BACKGROUND:** Given the associated morbidity, mortality, and financial consequences of catheter associated urinary tract infections (CAUTIs), efforts should be made to mitigate the risk. We sought to describe, and report results for a post-catheter removal bladder management protocol focused on decreasing catheter reinsertion, catheter days, and overall CAUTI risk. **METHODS:** This was a quality improvement initiative implemented over a 3-month period at a single urban, tertiary health care center. Patients with an indwelling urinary catheter deemed eligible for removal were followed and cared for according to the study protocol. Rates of catheter reinsertion, catheter days and assessment of CAUTI risk were compared between cohorts. **RESULTS:** A total of 173 patients were eligible for protocol enrollment. Catheter reinsertion rate was 16% during the pilot, compared to 21% and 27% for the historical cohorts, ( $p = 0.02$ ). The mean number of catheter days during the study was 1.4 days, compared to 9.5 and 5.6 days in the historical cohorts ( $p=0.004$ ). Catheter hours (OR 1.010 95% CI 1.005 - 1.015  $p < 0.0001$ .) was a predictor of catheter reinsertion during the pilot. **CONCLUSIONS:** Our protocol resulted in a reduction of catheter reinsertion rates and number of catheter days. Expansion of this protocol to a larger patient cohort is required.

### Anesthesiology

Morita Y, Kariya T, **Ei-Bashir J, Galusca D, Guruswamy J,** and Tanaka K. TEE image quality improvement with our devised probe cover. *Echocardiography* 2021; Epub ahead of print. PMID: 34296438. [Full Text](#)

**OBJECTIVE(S):** Our hypothesis was that our devised transesophageal echocardiography probe cover with the capacity for pinpoint suction would improve image quality. **DESIGN:** Prospective cohort study. **SETTING:** Single tertiary medical center. **PARTICIPANTS:** Patients undergoing surgery requiring intraoperative transesophageal echocardiography. **INTERVENTIONS:** Suctioning with inserted orogastric tube. **MEASUREMENTS AND MAIN RESULTS:** Changes in image quality with suctioning were assessed by 2 methods. In method #1, investigators categorized the quality of all acquired images on a numeric scale based on each investigator's impression (1: very poor, 2: poor, 3: acceptable, 4: good, and 5: very good). In method #2, the reproducibility of the left ventricular fraction area change (LV FAC) was assessed, assuming that improved transgastric midpapillary short-axis view image quality would yield better LV FAC reproducibility. With method #1, for midesophageal views, 26.5%, 70.5%, and 3.0% of images showed improved, the same, and worsened image quality, respectively. For transgastric views, 55.3%, 43.3%, and 1.4% showed improved, the same, and worsened image quality, respectively. For deep transgastric views, 60.0%, 38.0%, and 2.0% showed improved, the same, and worsened image quality, respectively. With method #2, the presuction group had an ICC of 0.942 (95% CI: 0.91, 0.965). The postsuction group had an ICC of 0.988 (95% CI: 0.981, 0.993). **CONCLUSIONS:** Our investigation validates the potential image quality improvement with our devised TEE probe cover. However, its clinical validity needs to be confirmed by further studies.

### Anesthesiology

Sagir A, **Ahuja S**, Soliman LM, and Farag E. Co-presentation of Posterior Reversible Encephalopathy Syndrome in a patient with Post Dural Puncture Headache. *Pain Med* 2021; Epub ahead of print. PMID: 34260726. [Full Text](#)

**INTRODUCTION:** Post Dural Puncture Headache (PDPH) is a well-known complication of neuraxial anesthesia, however the occurrence of seizures and vision loss within few days after dural puncture could be alarming. Posterior Reversible Encephalopathy Syndrome (PRES) is associated with reversible edema and leukoencephalopathy in the posterior parieto-occipital cortex. We report the co-presentation of PRES and PDPH after labor epidural analgesia. **CASE PRESENTATION:** 25-year-old multiparous African-American woman was admitted for evaluation of new onset seizures and headache in the postpartum period. She had a recent history of multiple needle insertion attempts and inadvertent dural puncture during epidural analgesia for delivery. Soon after delivery, she was diagnosed with PDPH and was treated with epidural blood patch, with no relief of symptoms. Six days later, she developed sudden onset transient blindness, seizures and altered sensorium and magnetic resonance imaging (MRI) of the brain revealed white matter changes suggestive of PRES. **CONCLUSION:** PRES is an uncommon complication of cerebrospinal fluid (CSF) leak and intracranial hypotension. We report the occurrence of PRES in a patient with no known risk factors, except a traumatic dural tap. Is it important to expand the differentials for headache after dural puncture to encompass PRES as a possibility, especially in patients with a delayed presentation of seizures and cortical blindness.

### Behavioral Health Services/Psychiatry

**Beebani G, Fabian N, Bhatia N, and Sivananthan M.** Case Report: Clozapine-Induced Myocarditis in a Patient with Autism Spectrum Disorder and Schizophrenia. *J Autism Dev Disord* 2021; Epub ahead of print. PMID: 34196891. [Request Article](#)

### Cardiology/Cardiovascular Research

Bansal A, Goldstein D, Schettle S, Pepitone S, Lima B, Pham DT, **Cowger J**, Schubert A, and Pinney SP. Institutional preparedness strategies for heart failure, durable left ventricular assist device, and heart transplant patients during the Coronavirus Disease 2019 (COVID-19) pandemic. *J Thorac Cardiovasc Surg* 2021; 162(1):131-135. PMID: 32994096. [Full Text](#)

### Cardiology/Cardiovascular Research

**Cowger JA**, and **Goldstein DJ.** An opportunity to begin again. *J Heart Lung Transplant* 2021; Epub ahead of print. PMID: 34330607. [Full Text](#)

### Cardiology/Cardiovascular Research

DeVore AD, Granger BB, Fonarow GC, Al-Khalidi HR, Albert NM, Lewis EF, Butler J, Piña IL, Allen LA, Yancy CW, Cooper LB, Felker GM, Kaltenbach LA, McRae AT, **Lanfear DE**, Harrison RW, Disch M, Ariely D, Miller JM, Granger CB, and Hernandez AF. Effect of a Hospital and Postdischarge Quality Improvement Intervention on Clinical Outcomes and Quality of Care for Patients With Heart Failure With Reduced Ejection Fraction: The CONNECT-HF Randomized Clinical Trial. *Jama* 2021; 326(4):314-323. PMID: 34313687. [Full Text](#)

**IMPORTANCE:** Adoption of guideline-directed medical therapy for patients with heart failure is variable. Interventions to improve guideline-directed medical therapy have failed to consistently achieve target metrics, and limited data exist to inform efforts to improve heart failure quality of care. **OBJECTIVE:** To evaluate the effect of a hospital and postdischarge quality improvement intervention compared with usual care on heart failure outcomes and care. **DESIGN, SETTING,**

AND PARTICIPANTS: This cluster randomized clinical trial was conducted at 161 US hospitals and included 5647 patients (2675 intervention vs 2972 usual care) followed up after a hospital discharge for acute heart failure with reduced ejection fraction (HFrEF). The trial was performed from 2017 to 2020, and the date of final follow-up was August 31, 2020. INTERVENTIONS: Hospitals (n = 82) randomized to a hospital and postdischarge quality improvement intervention received regular education of clinicians by a trained group of heart failure and quality improvement experts and audit and feedback on heart failure process measures (eg, use of guideline-directed medical therapy for HFrEF) and outcomes. Hospitals (n = 79) randomized to usual care received access to a generalized heart failure education website. MAIN OUTCOMES AND MEASURES: The coprimary outcomes were a composite of first heart failure rehospitalization or all-cause mortality and change in an opportunity-based composite score for heart failure quality (percentage of recommendations followed). RESULTS: Among 5647 patients (mean age, 63 years; 33% women; 38% Black; 87% chronic heart failure; 49% recent heart failure hospitalization), vital status was known for 5636 (99.8%). Heart failure rehospitalization or all-cause mortality occurred in 38.6% in the intervention group vs 39.2% in usual care (adjusted hazard ratio, 0.92 [95% CI, 0.81 to 1.05]). The baseline quality-of-care score was 42.1% vs 45.5%, respectively, and the change from baseline to follow-up was 2.3% vs -1.0% (difference, 3.3% [95% CI, -0.8% to 7.3%]), with no significant difference between the 2 groups in the odds of achieving a higher composite quality score at last follow-up (adjusted odds ratio, 1.06 [95% CI, 0.93 to 1.21]). CONCLUSIONS AND RELEVANCE: Among patients with HFrEF in hospitals randomized to a hospital and postdischarge quality improvement intervention vs usual care, there was no significant difference in time to first heart failure rehospitalization or death, or in change in a composite heart failure quality-of-care score. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT03035474.

#### Cardiology/Cardiovascular Research

Eng MH. Foreword. *Interv Cardiol Clin* 2021; 10(3):xiii. PMID: 34053627. [Full Text](#)

#### Cardiology/Cardiovascular Research

Gupta K, Dixit P, and **Ananthasubramaniam K**. Cardiac PET in aortic stenosis: Potential role in risk refinement? *J Nucl Cardiol* 2021; Epub ahead of print. PMID: 34228335. [Request Article](#)

#### Cardiology/Cardiovascular Research

Kadavath S, Hawwas D, Strobel A, Mohan J, Bernardo M, Kassier A, Ya'qoub L, Madan N, Ashraf S, Salehi N, **Mawri S**, Rehman KA, Siraj A, Alraies C, Saad M, and Aronow H. How the COVID-19 Pandemic Has Affected Cardiology Fellow Training. *Am J Cardiol* 2021; 151:114-117. PMID: 34052015. [Full Text](#)

With the advent of the COVID-19 pandemic in the United States, resources have been reallocated and elective cases have been deferred to minimize the spread of the disease, altering the workflow of cardiac catheterization laboratories across the country. This has in turn affected the training experience of cardiology fellows, including diminished procedure numbers and a narrow breadth of cases as they approach the end of their training before joining independent practice. It has also taken a toll on the emotional well-being of fellows as they see their colleagues, loved ones, patients or even themselves struggling with COVID-19, with some succumbing to it. The aim of this opinion piece is to focus attention on the impact of the COVID-19 pandemic on fellows and their training, challenges faced as they transition to practicing in the real world in the near future and share the lessons learned thus far. We believe that this is an important contribution and would be of interest not only to cardiology fellows-in-training and cardiologists but also trainees in other procedural specialties.

#### Cardiology/Cardiovascular Research

**Kunkel KJ, Fuller B, and Basir MB.** Management of Cardiogenic Shock in Patients with Acute Myocardial Infarction. *Interv Cardiol Clin* 2021; 10(3):345-357. PMID: 34053621. [Full Text](#)

Acute myocardial infarction and cardiogenic shock (AMI-CS) is associated with significant morbidity and mortality. Early mechanical revascularization improves survival, and development of STEMI systems of care has increased the utilization of revascularization in AMI-CS from 19% in 2001 to 60% in 2014. Mechanical circulatory support devices are increasingly used to support and prevent hemodynamic collapse. These devices provide different levels of univentricular and biventricular support, have different mechanisms of actions, and provide different physiologic effects. Herein, the authors review the definition, incidence, pathophysiology, and treatment of AMI-CS.

#### Cardiology/Cardiovascular Research

Meloche C, Seth M, Madder RD, Kurlander JE, Yaser J, Chattahi J, Collins J, **Lingam N**, Arora D, Gurm HS, and Sukul D. Percutaneous Coronary Intervention in Patients With a History of Gastrointestinal Bleeding (From the Blue Cross Blue Shield of Michigan Cardiovascular Consortium). *Am J Cardiol* 2021; 155:9-15. PMID: 34325106. [Full Text](#)

Potent antithrombotic agents are routinely prescribed after percutaneous coronary intervention (PCI) to reduce ischemic complications. However, in patients who are at an increased bleeding risk, this may pose significant risks. We sought to evaluate the association between a history of gastrointestinal bleeding (GIB) and outcomes after PCI. We linked clinical registry data from PCIs performed at 48 Michigan hospitals between 1/2013 and 3/2018 to Medicare claims. We used 1:5 propensity score matching to adjust for patient characteristics. In-hospital outcomes included bleeding, transfusion, stroke or death. Post-discharge outcomes included 90-day all-cause readmission and long-term mortality. Of 30,206 patients, 1.1% had a history of GIB. Patients with a history of GIB were more likely to be older, female, and have more cardiovascular comorbidities. After matching, those with a history of GIB (n = 312) had increased post-procedural transfusions (15.7% vs 8.4%; p < 0.001), bleeding (11.9% vs 5.2%; p < 0.001), and major bleeding (2.8% vs 0.6%; p = 0.004). Ninety-day readmission rates were similar among those with and without a history of GIB (34.3% vs 31.3%; p = 0.318). There was no significant difference in post-discharge survival (1 year: 78% vs 80%; p = 0.217; 5 years: 54% vs 51%; p = 0.189). In conclusion, after adjusting for baseline characteristics, patients with a history of GIB had increased risk of post-PCI in-hospital bleeding complications. However, a history of GIB was not significantly associated with 90-day readmission or long-term survival.

#### Cardiology/Cardiovascular Research

**Ramireddy S, and Shakir A.** Syncope and Sarcoidosis: A Criss-Cross of Diagnoses. *Cureus* 2021; 13(7):e16367. PMID: 34306898. [Full Text](#)

Syncope has a broad range of differential diagnoses. Sarcoidosis, a multisystem inflammatory disorder characterized by the formation of noncaseating granulomas, is a rare but important diagnosis to consider while evaluating patients presenting with presyncopal or syncopal symptoms. Although sarcoidosis is most commonly known to affect the lungs, it is estimated that at least 25% of patients with sarcoidosis have myocardial involvement, with only 5% of these patients showing clinical symptoms. Here, we present the rare case of a Caucasian male patient diagnosed with cardiac sarcoidosis after presenting to the hospital with presyncope. The patient had an internal cardioverter-defibrillator placed during hospitalization and was initiated on prednisone and methotrexate in the outpatient setting. He exhibited clinical and radiographical improvement in the six-month follow-up period after treatment was initiated.

### Cardiology/Cardiovascular Research

Simard T, Jung RG, Lehenbauer K, Piayda K, Pracoń R, Jackson GG, Flores-Umanzor E, Faroux L, Korsholm K, Chun JKR, Chen S, Maarse M, Montrella K, Chaker Z, Spoon JN, Pastormerlo LE, Meincke F, Sawant AC, Moldovan CM, **Qintar M**, Aktas MK, Branca L, Radinovic A, Ram P, El-Zein RS, Flautt T, Ding WY, Sayegh B, Benito-González T, Lee OH, Badejoko SO, Paitazoglou C, Karim N, Zaghloul AM, Agrawal H, Kaplan RM, Alli O, Ahmed A, Suradi HS, Knight BP, Alla VM, Panaich SS, Wong T, Bergmann MW, Chothia R, Kim JS, Pérez de Prado A, Bazaz R, Gupta D, Valderrabano M, Sanchez CE, El Chami MF, Mazzone P, Adamo M, Ling F, **Wang DD**, **O'Neill W**, Wojakowski W, Pershad A, Berti S, Spoon D, Kawsara A, Jabbour G, Boersma LVA, Schmidt B, Nielsen-Kudsk JE, Rodés-Cabau J, Freixa X, Ellis CR, Fauchier L, Demkow M, Sievert H, Main ML, Hibbert B, Holmes DR, Jr., and Alkhouli M.

Predictors of Device-Related Thrombus Following Percutaneous Left Atrial

Appendage Occlusion. *J Am Coll Cardiol* 2021; 78(4):297-313. PMID: 34294267. [Full Text](#)

**BACKGROUND:** Device-related thrombus (DRT) has been considered an Achilles' heel of left atrial appendage occlusion (LAAO). However, data on DRT prediction remain limited.

**OBJECTIVES:** This study constructed a DRT registry via a multicenter collaboration aimed to assess outcomes and predictors of DRT. **METHODS:** Thirty-seven international centers contributed LAAO cases with and without DRT (device-matched and temporally related to the DRT cases). This study described the management patterns and mid-term outcomes of DRT and assessed patient and procedural predictors of DRT. **RESULTS:** A total of 711 patients (237 with and 474 without DRT) were included. Follow-up duration was similar in the DRT and no-DRT groups, median 1.8 years (interquartile range: 0.9-3.0 years) versus 1.6 years (interquartile range: 1.0-2.9 years), respectively (P = 0.76). DRTs were detected between days 0 to 45, 45 to 180, 180 to 365, and >365 in 24.9%, 38.8%, 16.0%, and 20.3% of patients. DRT presence was associated with a higher risk of the composite endpoint of death, ischemic stroke, or systemic embolization (HR: 2.37; 95% CI, 1.58-3.56; P < 0.001) driven by ischemic stroke (HR: 3.49; 95% CI: 1.35-9.00; P = 0.01). At last known follow-up, 25.3% of patients had DRT. Discharge medications after LAAO did not have an impact on DRT. Multivariable analysis identified 5 DRT risk factors: hypercoagulability disorder (odds ratio [OR]: 17.50; 95% CI: 3.39-90.45), pericardial effusion (OR: 13.45; 95% CI: 1.46-123.52), renal insufficiency (OR: 4.02; 95% CI: 1.22-13.25), implantation depth >10 mm from the pulmonary vein limbus (OR: 2.41; 95% CI: 1.57-3.69), and non-paroxysmal atrial fibrillation (OR: 1.90; 95% CI: 1.22-2.97). Following conversion to risk factor points, patients with ≥2 risk points for DRT had a 2.1-fold increased risk of DRT compared with those without any risk factors. **CONCLUSIONS:** DRT after LAAO is associated with ischemic events. Patient- and procedure-specific factors are associated with the risk of DRT and may aid in risk stratification of patients referred for LAAO.

### Cardiology/Cardiovascular Research

Teerlink JR, Diaz R, Felker GM, McMurray JJV, Metra M, Solomon SD, Biering-Sørensen T, Böhm M, Bonderman D, Fang JC, **Langfear DE**, Lund M, Momomura SI, O'Meara E, Ponikowski P, Spinar J, Flores-Arredondo JH, Claggett BL, Heitner SB, Kupfer S, Abbasi SA, and Malik FI. Effect of Ejection Fraction on Clinical Outcomes in Patients Treated With Omecamtiv Mecarbil in GALACTIC-HF. *J Am Coll Cardiol* 2021; 78(2):97-108. PMID: 34015475. [Full Text](#)

**BACKGROUND:** In GALACTIC-HF (Global Approach to Lowering Adverse Cardiac outcomes Through Improving Contractility in Heart Failure) (n = 8,256), the cardiac myosin activator, omecamtiv mecarbil, significantly reduced the primary composite endpoint (PCE) of time-to-first heart failure event or cardiovascular death in patients with heart failure and reduced ejection fraction (EF) (≤35%). **OBJECTIVES:** The purpose of this study was to evaluate the influence of

baseline EF on the therapeutic effect of omecamtiv mecarbil. METHODS: Outcomes in patients treated with omecamtiv mecarbil were compared with placebo according to EF. RESULTS: The risk of the PCE in the placebo group was nearly 1.8-fold greater in the lowest EF ( $\leq 22\%$ ) compared with the highest EF ( $\geq 33\%$ ) quartile. Amongst the pre-specified subgroups, EF was the strongest modifier of the treatment effect of omecamtiv mecarbil on the PCE (interaction as continuous variable,  $p = 0.004$ ). Patients receiving omecamtiv mecarbil had a progressively greater relative and absolute treatment effect as baseline EF decreased, with a 17% relative risk reduction for the PCE in patients with baseline EF  $\leq 22\%$  ( $n = 2,246$ ; hazard ratio: 0.83; 95% confidence interval: 0.73 to 0.95) compared with patients with EF  $\geq 33\%$  ( $n = 1,750$ ; hazard ratio: 0.99; 95% confidence interval: 0.84 to 1.16; interaction as EF by quartiles,  $p = 0.013$ ). The absolute reduction in the PCE increased with decreasing EF (EF  $\leq 22\%$ ; absolute risk reduction, 7.4 events per 100 patient-years; number needed to treat for 3 years = 11.8), compared with no reduction in the highest EF quartile. CONCLUSIONS: In heart failure patients with reduced EF, omecamtiv mecarbil produced greater therapeutic benefit as baseline EF decreased. These findings are consistent with the drug's mechanism of selectively improving systolic function and presents an important opportunity to improve the outcomes in a group of patients at greatest risk. (Registrational Study With Omecamtiv Mecarbil/AMG 423 to Treat Chronic Heart Failure With Reduced Ejection Fraction [GALACTIC-HF]; NCT02929329).

#### Cardiology/Cardiovascular Research

Vemou E, Nikolakopoulos I, Karacsonyi J, Kostantinis S, Rangan BV, Baechler C, Garcia S, Burke MN, **Alaswad K**, and Brilakis ES. Outcomes of Chronic Total Occlusion (CTO) Percutaneous Coronary Intervention (PCI) According to Race: Insights from the PROGRESS-CTO Registry. *Hellenic J Cardiol* 2021; Epub ahead of print. PMID: 34311103. [Full Text](#)

#### Cardiology/Cardiovascular Research

Zweck E, Thayer KL, Helgestad OKL, Kanwar M, Ayouty M, Garan AR, Hernandez-Montfort J, Mahr C, Wencker D, Sinha SS, Vorovich E, Abraham J, **O'Neill W**, Li S, Hickey GW, Josiassen J, Hassager C, Jensen LO, Holmvang L, Schmidt H, Ravn HB, Møller JE, Burkhoff D, and Kapur NK. Phenotyping Cardiogenic Shock. *J Am Heart Assoc* 2021; 10(14):e020085. PMID: 34227396. [Full Text](#)

Background Cardiogenic shock (CS) is a heterogeneous syndrome with varied presentations and outcomes. We used a machine learning approach to test the hypothesis that patients with CS have distinct phenotypes at presentation, which are associated with unique clinical profiles and in-hospital mortality. Methods and Results We analyzed data from 1959 patients with CS from 2 international cohorts: CSWG (Cardiogenic Shock Working Group Registry) (myocardial infarction [CSWG-MI;  $n=410$ ] and acute-on-chronic heart failure [CSWG-HF;  $n=480$ ]) and the DRR (Danish Retrospective MI Registry) ( $n=1069$ ). Clusters of patients with CS were identified in CSWG-MI using the consensus k means algorithm and subsequently validated in CSWG-HF and DRR. Patients in each phenotype were further categorized by their Society of Cardiovascular Angiography and Interventions staging. The machine learning algorithms revealed 3 distinct clusters in CS: "non-congested (I)", "cardiorenal (II)," and "cardiometabolic (III)" shock. Among the 3 cohorts (CSWG-MI versus DRR versus CSWG-HF), in-hospital mortality was 21% versus 28% versus 10%, 45% versus 40% versus 32%, and 55% versus 56% versus 52% for clusters I, II, and III, respectively. The "cardiometabolic shock" cluster had the highest risk of developing stage D or E shock as well as in-hospital mortality among the phenotypes, regardless of cause. Despite baseline differences, each cluster showed reproducible demographic, metabolic, and hemodynamic profiles across the 3 cohorts. Conclusions Using machine learning, we identified and validated 3 distinct CS phenotypes, with specific and reproducible associations with mortality. These phenotypes may allow for targeted



patient enrollment in clinical trials and foster development of tailored treatment strategies in subsets of patients with CS.

Center for Health Policy and Health Services Research

Bagley SM, Chavez L, **Braciszewski JM**, Akolsile M, Boudreau DM, Lapham G, Campbell CI, Bart G, Yarborough BJH, Samet JH, Saxon AJ, Rossom RC, Binswanger IA, Murphy MT, Glass JE, and Bradley KA. Receipt of medications for opioid use disorder among youth engaged in primary care: data from 6 health systems. *Addict Sci Clin Pract* 2021; 16(1):46. PMID: 34233750. [Full Text](#)

**PURPOSE:** Little is known about prevalence and treatment of OUD among youth engaged in primary care (PC). Medications are the recommended treatment of opioid use disorder (OUD) for adolescents and young adults (youth). This study describes the prevalence of OUD, the prevalence of medication treatment for OUD, and patient characteristics associated with OUD treatment among youth engaged in PC. **METHODS:** This cross-sectional study includes youth aged 16-25 years engaged in PC. Eligible patients had  $\geq 1$  PC visit during fiscal years (FY) 2014-2016 in one of 6 health systems across 6 states. Data from electronic health records and insurance claims were used to identify OUD diagnoses, office-based OUD medication treatment, and patient demographic and clinical characteristics in the FY of the first PC visit during the study period. Descriptive analyses were conducted in all youth, and stratified by age (16-17, 18-21, 22-25 years). **RESULTS:** Among 303,262 eligible youth, 2131 (0.7%) had a documented OUD diagnosis. The prevalence of OUD increased by ascending age groups. About half of youth with OUD had documented depression or anxiety and one third had co-occurring substance use disorders. Receipt of medication for OUD was lowest among youth 16-17 years old (14%) and highest among those aged 22-25 (39%). **CONCLUSIONS:** In this study of youth engaged in 6 health systems across 6 states, there was low receipt of medication treatment, and high prevalence of other substance use disorders and mental health disorders. These findings indicate an urgent need to increase medication treatment for OUD and to integrate treatment for other substance use and mental health disorders.

Center for Health Policy and Health Services Research

Penfold RB, Johnson E, Shortreed SM, Ziebell RA, Lynch FL, Clarke GN, Coleman KJ, Waitzfelder BE, Beck AL, Rossom RC, **Ahmedani BK**, and Simon GE. Predicting suicide attempts and suicide deaths among adolescents following outpatient visits. *J Affect Disord* 2021; 294:39-47. PMID: 34265670. [Full Text](#)

**BACKGROUND:** Few studies report on machine learning models for suicide risk prediction in adolescents and their utility in identifying those in need of further evaluation. This study examined whether a model trained and validated using data from all age groups works as well for adolescents or whether it could be improved. **METHODS:** We used healthcare data for 1.4 million specialty mental health and primary care outpatient visits among 256,823 adolescents across 7 health systems. The prediction target was 90-day risk of suicide attempt following a visit. We used logistic regression with least absolute shrinkage and selection operator (LASSO) and generalized estimating equations (GEE) to predict risk. We compared performance of three models: an existing model, a recalibrated version of that model, and a newly-learned model. Models were compared using area under the receiver operating curve (AUC), sensitivity, specificity, positive predictive value and negative predictive value. **RESULTS:** The AUC produced by the existing model for specialty mental health visits estimated in adolescents alone (0.796; [0.789, 0.802]) was not significantly different than the AUC of the recalibrated existing model (0.794; [0.787, 0.80]) or the newly-learned model (0.795; [0.789, 0.801]). Predicted risk following primary care visits was also similar: existing (0.855; [0.844, 0.866]), recalibrated (0.85

[0.839, 0.862]), newly-learned (0.842, [0.829, 0.854]). LIMITATIONS: The models did not incorporate non-healthcare risk factors. The models relied on ICD9-CM codes for diagnoses and outcome measurement. CONCLUSIONS: Prediction models already in operational use by health systems can be reliably employed for identifying adolescents in need of further evaluation.

#### Clinical Quality and Safety

**Jamil ML, Wurst H, Robinson P, Rubinfeld I, Suleyman G, Pollak E, and Dabaja AA.** URINARY CATHETER ALLEVIATION NAVIGATOR PROTOCOL (UCANP): OVERVIEW OF PROTOCOL AND REVIEW OF INITIAL EXPERIENCE. *Am J Infect Control* 2021; Epub ahead of print. PMID: 34273463. [Full Text](#)

**BACKGROUND:** Given the associated morbidity, mortality, and financial consequences of catheter associated urinary tract infections (CAUTIs), efforts should be made to mitigate the risk. We sought to describe, and report results for a post-catheter removal bladder management protocol focused on decreasing catheter reinsertion, catheter days, and overall CAUTI risk. **METHODS:** This was a quality improvement initiative implemented over a 3-month period at a single urban, tertiary health care center. Patients with an indwelling urinary catheter deemed eligible for removal were followed and cared for according to the study protocol. Rates of catheter reinsertion, catheter days and assessment of CAUTI risk were compared between cohorts. **RESULTS:** A total of 173 patients were eligible for protocol enrollment. Catheter reinsertion rate was 16% during the pilot, compared to 21% and 27% for the historical cohorts, ( $p = 0.02$ ). The mean number of catheter days during the study was 1.4 days, compared to 9.5 and 5.6 days in the historical cohorts ( $p=0.004$ ). Catheter hours (OR 1.010 95% CI 1.005 - 1.015  $p < 0.0001$ .) was a predictor of catheter reinsertion during the pilot. **CONCLUSIONS:** Our protocol resulted in a reduction of catheter reinsertion rates and number of catheter days. Expansion of this protocol to a larger patient cohort is required.

#### Dermatology

**Awosika O, Eleryan MG, and Soleymani T.** Reply to the editor regarding Local recurrence of clinically observed basal cell carcinomas following complete saucerization or punch removal with negative margins: Retrospective case series from 2010 to 2020. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34274411. [Full Text](#)

#### Dermatology

**Bae JM, Zubair R, Ju HJ, Kohli I, Lee HN, Eun SH, Lyons AB, Vellaichamy G, Han TY, Lim HW, and Hamzavi IH.** Development and Validation of the Fingertip Unit for Assessing Facial Vitiligo Area Scoring Index (F-VASI). *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34246695. [Full Text](#)

**BACKGROUND:** Facial involvement of vitiligo is an important factor in patient's life and has often been evaluated separately from body surface area in clinical trials. However, no reliable measurement tools to measure facial vitiligo specifically are available thus far. **OBJECTIVE:** To develop and validate a practical instrument for assessing facial vitiligo **METHODS:** The ratios of a hand to a fingertip unit (FTU) of 98 healthy volunteers (age range: 2-69 years) were calculated to define the FTU. Facial Vitiligo Area Scoring Index (F-VASI) was measured as the sum of all FTUs of each vitiligo lesion on the face (range: 0-112 FTU). In the validation study, 6 raters evaluated 11 patients with facial vitiligo twice at an interval of 2 weeks. **RESULTS:** One hand was measured at  $32.1 \pm 1.3$  FTU, and it was highly consistent among subjects across different age groups, genders, and races. F-VASI showed remarkably high accuracy (concordance correlation coefficient: 0.946, smallest detectable change: 2.2 FTU) as well as high intra-rater

reliability (intraclass correlation coefficient: 0.903) and inter-rater reliability (0.903).  
LIMITATIONS: Lack of dynamic validation of responsiveness CONCLUSION: F-VASI using the FTU is an intuitive, precise, and reliable instrument for assessing the extent of facial involvement in vitiligo patients.

#### Dermatology

Bissonnette R, **Gold LS**, Rubenstein DS, Tallman AM, and Armstrong AW. The preponderance of evidence supports an aryl hydrocarbon receptor-dependent mechanism of action of tapinarof. *J Am Acad Dermatol* 2021; 85(1):e35-e36. PMID: 33677005. [Full Text](#)

#### Dermatology

**Chapman S**, **Kwa M**, **Gold LS**, and **Lim HW**. Janus kinase inhibitors in dermatology: Part I. A comprehensive review. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34246698. [Full Text](#)

The Janus kinase-signal transducer and activator of transcription (JAK-STAT) intracellular signaling pathway is utilized by many proinflammatory molecules to mediate downstream effects and activate gene transcription. Activation of the JAK-STAT pathway contributes to a number of inflammatory dermatoses. Clinical trials and smaller studies have demonstrated the efficacy of JAK inhibitors in the treatment of a variety of dermatologic conditions. Here, we review the use of JAK inhibitors for the treatment of a wide range of dermatologic diseases in a two-part review series.

#### Dermatology

**Chapman S**, **Gold LS**, and **Lim HW**. Janus kinase inhibitors in dermatology: Part II. A comprehensive review. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34228996. [Full Text](#)

The Janus kinase-signal transducer and activator of transcription (JAK-STAT) intracellular signaling pathway is implicated in the pathogenesis of a number of inflammatory dermatoses. Clinical trials and other studies have demonstrated the efficacy of JAK inhibitors in the treatment of a variety of dermatologic conditions. Here we review JAK inhibitors currently under investigation for the treatment of alopecia areata, vitiligo, sarcoidosis, necrobiosis lipoidica, granuloma annulare, and systemic lupus erythematosus with a special emphasis on safety and the implications of JAK inhibitors during the novel coronavirus 2019 pandemic.

#### Dermatology

Davies OMT, Garzon MC, Frieden IJ, Cottrell CE, Gripp KW, Saneto RP, **Shwayder T**, Mirzaa GM, and Drolet BA. Cutaneous vascular anomalies associated with a mosaic variant of AKT3: Genetic analysis continues to refine the diagnosis, nomenclature, and classification of vascular anomalies. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34237354. [Full Text](#)

#### Dermatology

**Ezekwe N**, **Ozog D**, and **Hamzavi IH**. Response to: "Treatment of hidradenitis suppurativa using a long-pulsed hair removal neodymium:yttrium-aluminium-garnet laser: A multicenter, prospective, randomized, intraindividual, comparative trial". *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34293391. [Full Text](#)

#### Dermatology

**Mi QS**, **Wang J**, **Liu Q**, **Wu X**, and **Zhou L**. microRNA dynamic expression regulates invariant NKT cells. *Cell Mol Life Sci* 2021; 78(16):6003-6015. PMID: 34236444. [Request Article](#)

Invariant natural killer T cells (iNKT) are a prevalent population of innate-like T cells in mice, but quite rare in humans that are critical for regulation of the innate and adaptive immune responses during antimicrobial immunity, tumor rejection, and inflammatory diseases. Multiple transcription factors and signaling molecules that contribute to iNKT cell selection and functional differentiation have been identified. However, the full molecular network responsible for regulating and maintaining iNKT populations remains unclear. MicroRNAs (miRNAs) are an abundant class of evolutionarily conserved, small, non-coding RNAs that regulate gene expression post-transcriptionally. Previous reports uncovered the important roles of miRNAs in iNKT cell development and function using Dicer mutant mice. In this review, we discuss the emerging roles of individual miRNAs in iNKT cells reported by our group and other groups, including miR-150, miR-155, miR-181, let-7, miR-17 ~ 92 cluster, and miR-183-96-182 cluster. It is likely that iNKT cell development, differentiation, homeostasis, and functions are orchestrated through a multilayered network comprising interactions among master transcription factors, signaling molecules, and dynamically expressed miRNAs. We provide a comprehensive view of the molecular mechanisms underlying iNKT cell differentiation and function controlled by dynamically expressed miRNAs.

#### Dermatology

**Tisack A, Pourang A, Kohli I, Lim HW, and Hamzavi IH.** Recommendations for Reporting Methods in Phototesting Studies. *Photochem Photobiol* 2021; Epub ahead of print. PMID: 34312877. [Request Article](#)

There are many variations in the way phototesting protocols in clinical research are reported in the photomedicine literature. Specifications regarding the light system, lamp type, irradiance and other components are too often missing or inadequately detailed, making it difficult to fully appreciate the methods used in each study, or compare the findings among different studies. (1-5) This letter discusses important parameters that should be included (Table 1) when describing phototesting methodology used in published clinical research, in order to facilitate overall understanding of such studies. This information will also provide essential details from which other researchers may benefit from when trying to reproduce and build upon discussed research.

#### Diagnostic Radiology

Gleichgerricht E, Munsell BC, Alhusaini S, Alvim MKM, Bargalló N, Bender B, Bernasconi A, Bernasconi N, Bernhardt B, Blackmon K, Caligiuri ME, Cendes F, Concha L, Desmond PM, Devinsky O, Doherty CP, Domin M, Duncan JS, Focke NK, Gambardella A, Gong B, Guerrini R, Hatton SN, Kälviäinen R, Keller SS, Kochunov P, Kotikalapudi R, Kreilkamp BAK, Labate A, Langner S, Larivière S, Lenge M, Lui E, Martin P, Mascalchi M, Meletti S, O'Brien TJ, Pardoe HR, Pariente JC, Xian Rao J, Richardson MP, Rodríguez-Cruces R, Rüber T, Sinclair B, **Soltanian-Zadeh H**, Stein DJ, Striano P, Taylor PN, Thomas RH, Elisabetta Vaudano A, Vivash L, von Podewills F, Vos SB, Weber B, Yao Y, Lin Yasuda C, Zhang J, Thompson PM, Sisodiya SM, McDonald CR, and Bonilha L. Artificial intelligence for classification of temporal lobe epilepsy with ROI-level MRI data: A worldwide ENIGMA-Epilepsy study. *Neuroimage Clin* 2021; 31:102765. PMID: 34339947. [Full Text](#)

Artificial intelligence has recently gained popularity across different medical fields to aid in the detection of diseases based on pathology samples or medical imaging findings. Brain magnetic resonance imaging (MRI) is a key assessment tool for patients with temporal lobe epilepsy (TLE). The role of machine learning and artificial intelligence to increase detection of brain abnormalities in TLE remains inconclusive. We used support vector machine (SV) and deep

learning (DL) models based on region of interest (ROI-based) structural (n = 336) and diffusion (n = 863) brain MRI data from patients with TLE with ("lesional") and without ("non-lesional") radiographic features suggestive of underlying hippocampal sclerosis from the multinational (multi-center) ENIGMA-Epilepsy consortium. Our data showed that models to identify TLE performed better or similar (68-75%) compared to models to lateralize the side of TLE (56-73%, except structural-based) based on diffusion data with the opposite pattern seen for structural data (67-75% to diagnose vs. 83% to lateralize). In other aspects, structural and diffusion-based models showed similar classification accuracies. Our classification models for patients with hippocampal sclerosis were more accurate (68-76%) than models that stratified non-lesional patients (53-62%). Overall, SV and DL models performed similarly with several instances in which SV mildly outperformed DL. We discuss the relative performance of these models with ROI-level data and the implications for future applications of machine learning and artificial intelligence in epilepsy care.

#### Diagnostic Radiology

**Kaur J, Fahmy LM, Davoodi-Bojd E, Zhang L, Ding G, Hu J, Zhang Z, Chopp M, and Jiang Q.** Waste Clearance in the Brain. *Front Neuroanat* 2021; 15:665803. PMID: 34305538. [Full Text](#)

Waste clearance (WC) is an essential process for brain homeostasis, which is required for the proper and healthy functioning of all cerebrovascular and parenchymal brain cells. This review features our current understanding of brain WC, both within and external to the brain parenchyma. We describe the interplay of the blood-brain barrier (BBB), interstitial fluid (ISF), and perivascular spaces within the brain parenchyma for brain WC directly into the blood and/or cerebrospinal fluid (CSF). We also discuss the relevant role of the CSF and its exit routes in mediating WC. Recent discoveries of the glymphatic system and meningeal lymphatic vessels, and their relevance to brain WC are highlighted. Controversies related to brain WC research and potential future directions are presented.

#### Diagnostic Radiology

**Mohammadi-Nejad AR, Hossein-Zadeh GA, Shahsavand Ananloo E, and Soltanian-Zadeh H.** The effect of groupness constraint on the sensitivity and specificity of canonical correlation analysis, a multi-modal anatomical and functional MRI study. *Biomed Signal Process Control* 2021; 68. PMID: Not assigned. [Full Text](#)

While neuroimaging studies reveal that several brain regions may participate in multiple groups (networks), this group overlap is neglected in multi-modal data fusion frameworks. Indeed, it is not clear how much "information" is lost due to this negligence. To study this issue, we present a group-structured sparse canonical correlation analysis (gssCCA) technique by utilizing groupness and sparsity constraints in a unified fusion framework. The approach allows to: 1) compare structures of disjoint and overlapping groups (networks); and 2) consider appropriate levels of overlap among groups. We use simulations to investigate the performance of the proposed approach and compare overlapping gssCCA, disjoint gssCCA, and ssCCA. The gains of considering an overlapping groupness constraint are significant since it can increase detection sensitivity and specificity of associations between multi-modal datasets. They also demonstrate that, even when the ROIs are assumed to be disjoint, the lost structural information is less than the conditions that we do not have any groupness information. We also apply the methods to experimental anatomical magnetic resonance imaging (MRI) and resting-state functional MRI (rs-fMRI) data of schizophrenia (SZ) patients and control subjects (CS). The results show that the first pair of canonical variates (CVs) capture better classification accuracy between SZ and CS with a correlation of 88 % (p-value of less than  $1 \times 10^{-6}$ ). The extracted CVs show the most correlated clusters between anatomical and functional datasets. These

clusters explain differences between the two groups in their own modality that are maximally correlated with the corresponding clusters in the other modality.

#### Emergency Medicine

Bunch CM, Thomas AV, Stillson JE, Gillespie L, Khan RZ, Zackariya N, Shariff F, Al-Fadhl M, Mjaess N, Miller PD, McCurdy MT, Fulkerson DH, **Miller JB**, Kwaan HC, Moore EE, Moore HB, Neal MD, Martin PL, Kricheff ML, and Walsh MM. Preventing Thrombohemorrhagic Complications of Heparinized COVID-19 Patients Using Adjunctive Thromboelastography: A Retrospective Study. *J Clin Med* 2021; 10(14). PMID: 34300263. [Full Text](#)

**BACKGROUND:** The treatment of COVID-19 patients with heparin is not always effective in preventing thrombotic complications, but can also be associated with bleeding complications, suggesting a balanced approach to anticoagulation is needed. A prior pilot study supported that thromboelastography and conventional coagulation tests could predict hemorrhage in COVID-19 in patients treated with unfractionated heparin or enoxaparin, but did not evaluate the risk of thrombosis. **METHODS:** This single-center, retrospective study included 79 severely ill COVID-19 patients anticoagulated with intermediate or therapeutic dose unfractionated heparin. Two stepwise logistic regression models were performed with bleeding or thrombosis as the dependent variable, and thromboelastography parameters and conventional coagulation tests as the independent variables. **RESULTS:** Among all 79 patients, 12 (15.2%) had bleeding events, and 20 (25.3%) had thrombosis. Multivariate logistic regression analysis identified a prediction model for bleeding (adjusted R(2) = 0.787, p < 0.001) comprised of increased reaction time (p = 0.016), decreased fibrinogen (p = 0.006), decreased D-dimer (p = 0.063), and increased activated partial thromboplastin time (p = 0.084). Multivariate analysis of thrombosis identified a weak prediction model (adjusted R(2) = 0.348, p < 0.001) comprised of increased D-dimer (p < 0.001), decreased reaction time (p = 0.002), increased maximum amplitude (p < 0.001), and decreased alpha angle (p = 0.014). Adjunctive thromboelastography decreased the use of packed red cells (p = 0.031) and fresh frozen plasma (p < 0.001). **CONCLUSIONS:** Significantly, this study demonstrates the need for a precision-based titration strategy of anticoagulation for hospitalized COVID-19 patients. Since severely ill COVID-19 patients may switch between thrombotic or hemorrhagic phenotypes or express both simultaneously, institutions may reduce these complications by developing their own titration strategy using daily conventional coagulation tests with adjunctive thromboelastography.

#### Emergency Medicine

Dessie AS, Lewiss RE, Stolz LA, Acuña J, Adhikari S, **Amponsah D**, Del Rios M, Huang RD, Knight RS, Landry A, Liu RB, Gottlieb M, Ng L, Panebianco NL, Rosario J, Weekes AJ, and Jones JD. The state of gender inclusion in the point-of-care ultrasound community. *Am J Emerg Med* 2021; Epub ahead of print. PMID: 34334282. [Full Text](#)

#### Emergency Medicine

Greene SC, **Folt J**, Wyatt K, and Brandehoff NP. Epidemiology of fatal snakebites in the United States 1989-2018. *Am J Emerg Med* 2021; 45:309-316. PMID: 33046301. [Full Text](#)

**BACKGROUND:** There are 5000-10,000 snake envenomations annually in the United States. Fortunately, few are fatal. In this study we review the epidemiology of fatal snakebites. **METHODS:** Native snakebite cases from the American Association of Poison Control Centers (AAPCC) National Poison Data System from 1989 to 2018 were reviewed. Additional cases that were not reported to the AAPCC were identified by reviewing Wikipedia and by searching PubMed and online news outlets using various combinations of relevant keywords. **RESULTS:** We identified 101 fatal bites from native snakes. Rattlesnakes accounted for 74 (90.2%) of the

82 deaths for which the species was known or which occurred where rattlesnakes are the only native crotalids. There were five fatalities attributed to copperheads, two due to cottonmouths, and one caused by an eastern coral snake. Males were disproportionately affected. The median age for victims was 40 years old. In cases for which data were available, many of the snake interactions were intentional, e.g. religious services, animal husbandry, and attempting to kill the snake. CONCLUSIONS: Death following envenomation from a native U.S. snake is unlikely, particularly if medical attention is sought promptly. Rattlesnake envenomations are more likely to be fatal than bites from other species. Intentionally engaging with a venomous snake raises the risk of incurring a fatal bite, as does concurrent alcohol or drug use. Age less than 12 years old does not appear to be a risk factor for a fatal outcome, while elderly patients may have a slightly increased risk of death.

#### Emergency Medicine

**Hamam MS, Klausner HA, France J, Tang A, Swor RA, Paxton JH, O'Neil BJ, Brent C, Neumar RW, Dunne RB, Reddi S, and Miller JB.** Prehospital Tibial Intraosseous Drug Administration is Associated with Reduced Survival Following Out of Hospital Cardiac Arrest: A study for the CARES Surveillance Group. *Resuscitation* 2021; Epub ahead of print. PMID: 34237357. [Full Text](#)

BACKGROUND: Recent reports have questioned the efficacy of intraosseous (IO) drug administration for out-of-hospital cardiac arrest (OHCA) resuscitation. Our aim was to determine whether prehospital administration of resuscitative medications via the IO route was associated with lower rates of return of spontaneous circulation (ROSC) and survival to hospital discharge than peripheral intravenous (IV) infusion in the setting of OHCA. METHODS: We obtained data on all OHCA patients receiving prehospital IV or IO drug administration from the three most populous counties in Michigan over three years. Data was from the Michigan Cardiac Arrest Registry to Enhance Survival (CARES) database. The association between route of drug administration and outcomes was tested using a matched propensity score analysis. RESULTS: From a total of 10,626 OHCA patients, 6869 received parenteral drugs during their prehospital resuscitation (37.8% by IO) and were included in analysis. Unadjusted outcomes were lower in patients with IO vs. IV access: 18.3% vs. 23.8% for ROSC ( $p < 0.001$ ), 3.2% vs. 7.6% for survival to hospital discharge ( $p < 0.001$ ), and 2.0% vs. 5.8% for favorable neurological function ( $p < 0.001$ ). After adjustment, IO route remained associated with lower odds of sustained ROSC (OR 0.72, 95% CI 0.63-0.81,  $p < 0.001$ ), hospital survival (OR 0.48, 95% CI 0.37-0.62,  $p < 0.001$ ), and favorable neurological outcomes (OR 0.42, 95% CI 0.30-0.57,  $p < 0.001$ ). CONCLUSION: In this cohort of OHCA patients, the use of prehospital IO drug administration was associated with unfavorable clinical outcomes.

#### Emergency Medicine

Ma PH, **Joyce KM**, Morton T, **Shih DW, Weiss A**, and **Miller J**. A focused, longitudinal analysis of cannabinoid hyperemesis syndrome symptomatology. *Int J Emerg Med* 2021; 14(1):44. PMID: 34325648. [Full Text](#)

#### Emergency Medicine

Nanishi M, Press VG, **Miller JB**, Eastin C, Aurora T, Crocker E, Fujiogi M, Camargo CA, Jr., and Hasegawa K. Hospital-Initiated Care Bundle, Posthospitalization Care, and Outcomes in Adults with Asthma Exacerbation. *J Allergy Clin Immunol Pract* 2021; Epub ahead of print. PMID: 34265445. [Full Text](#)

BACKGROUND: Hospitalization for asthma exacerbation is an opportune setting for initiating preventive efforts. However, hospital-initiated preventive asthma care remains underdeveloped

and its effectiveness is uncertain. **OBJECTIVE:** To examine the effectiveness of a hospital-initiated asthma care bundle on posthospitalization asthma care and clinical outcomes. **METHODS:** Prospective multicenter study of adults (18-54 years) hospitalized for asthma exacerbation in 2017 to 2019. During the hospitalization, we implemented an asthma-care bundle (inpatient laboratory testing, asthma education, and discharge care), and prospectively measured chronic asthma care (eg, immunoglobulin E testing, specialist care) and asthma exacerbation (ie, systemic corticosteroid use, emergency department [ED] visit, hospitalizations) outcomes. By applying a self-controlled case series method, we examined within-person changes in these outcomes before (2-year period) and after (1-year period) the bundle implementation. **RESULTS:** Of 103 adults hospitalized for asthma exacerbation, the median age was 40 years and 72% were female. Compared with the preimplementation period, the postimplementation period had improved posthospitalized asthma care, including serum specific immunoglobulin E testing (rate ratio [RR] 2.18; 95% confidence interval [95% CI] 0.99-4.84;  $P = .051$ ) and evaluation by asthma specialist (RR 2.66; 95% CI 1.77-4.04;  $P < .001$ ). Likewise, after care bundle implementation, patients had significantly lower annual rates of systemic corticosteroid use (4.2 vs 2.9 per person-year; RR 0.70; 95% CI 0.61-0.80;  $P < .001$ ), ED visits (3.2 vs 2.7 per person-year; RR 0.83; 95% CI 0.72-0.95;  $P = .008$ ), and hospitalizations (2.1 vs 1.8 per person-year; RR 0.82; 95% CI 0.69-0.97;  $P = .02$ ). Stratified analyses by sex, race/ethnicity, and health insurance yielded consistent results. **CONCLUSIONS:** After hospital-initiated care bundle implementation, patients had improved posthospitalization care and reduced rates of asthma exacerbation.

### Emergency Medicine

Steuber ER, Seligowski AV, Roeckner AR, Reda M, Lebois LAM, van Rooij SJH, Murty VP, Ely TD, Bruce SE, House SL, Beaudoin FL, An X, Zeng D, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Rauch SL, **Lewandowski C**, Sheikh S, Jones CW, Panches BE, Swor RA, McGrath ME, Hudak LA, Pascual JL, Chang AM, Pearson C, Peak DA, Domeier RM, O'Neil BJ, Rathlev NK, Sanchez LD, Pietrzak RH, Joormann J, Barch DM, Pizzagalli DA, Elliott JM, Kessler RC, Koenen KC, McLean SA, Ressler KJ, Jovanovic T, Harnett NG, and Stevens JS. Thalamic volume and fear extinction interact to predict acute posttraumatic stress severity. *J Psychiatr Res* 2021; 141:325-332. PMID: 34304036. [Full Text](#)

Posttraumatic stress disorder (PTSD) is associated with lower gray matter volume (GMV) in brain regions critical for extinction of learned threat. However, relationships among volume, extinction learning, and PTSD symptom development remain unclear. We investigated subcortical brain volumes in regions supporting extinction learning and fear-potentiated startle (FPS) to understand brain-behavior interactions that may impact PTSD symptom development in recently traumatized individuals. Participants ( $N = 99$ ) completed magnetic resonance imaging and threat conditioning two weeks following trauma exposure as part of a multisite observational study to understand the neuropsychiatric effects of trauma (AURORA Study). Participants completed self-assessments of PTSD (PTSD Checklist for DSM-5; PCL-5), dissociation, and depression symptoms two- and eight-weeks post-trauma. We completed multiple regressions to investigate relationships between FPS during late extinction, GMV, and PTSD symptom development. The interaction between thalamic GMV and FPS during late extinction at two weeks post-trauma predicted PCL-5 scores eight weeks ( $t(75) = 2.49$ ,  $\beta = 0.28$ ,  $p = 0.015$ ) post-trauma. Higher FPS predicted higher PCL-5 scores in the setting of increased thalamic GMV. Meanwhile, lower FPS also predicted higher PCL-5 scores in the setting of decreased thalamic GMV. Thalamic GMV and FPS interactions also predicted posttraumatic dissociative and depressive symptoms. Amygdala and hippocampus GMV by FPS interactions were not associated with posttraumatic symptom development. Taken together, thalamic GMV and FPS during late extinction interact to contribute to adverse



posttraumatic neuropsychiatric outcomes. Multimodal assessments soon after trauma have the potential to distinguish key phenotypes vulnerable to posttraumatic neuropsychiatric outcomes.

### Emergency Medicine

Wettersten N, Horiuchi Y, van Veldhuisen DJ, Ix JH, Mueller C, Filippatos G, **Nowak R**, Hogan C, Kontos MC, Cannon CM, Müller GA, Birkhahn R, Taub P, Vilke GM, Duff S, McDonald K, Mahon N, Nuñez J, Briguori C, Passino C, Maisel A, and Murray PT. Decongestion discriminates risk for one-year mortality in patients with improving renal function in acute heart failure. *Eur J Heart Fail* 2021; 23(7):1122-1130. PMID: 33788989. [Full Text](#)

AIMS: Improving renal function (IRF) is paradoxically associated with worse outcomes in acute heart failure (AHF), but outcomes may differ based on response to decongestion. We explored if the relationship of IRF with mortality in hospitalized AHF patients differs based on successful decongestion. METHODS AND RESULTS: We evaluated 760 AHF patients from AKINESIS for the relationship between IRF, change in B-type natriuretic peptide (BNP), and 1-year mortality. IRF was defined as a  $\geq 20\%$  increase in estimated glomerular filtration rate (eGFR) relative to admission. Adequate decongestion was defined as a  $\geq 40\%$  decrease in last measured BNP relative to admission. IRF occurred in 22% of patients who had a mean age of 69 years, 58% were men, 72% were white, and median admission eGFR was 49 mL/min/1.73 m<sup>2</sup>. IRF patients had more severe heart failure reflected by lower admission eGFR, higher blood urea nitrogen, lower systolic blood pressure, lower sodium, and higher use of inotropes. IRF patients had higher 1-year mortality (25%) than non-IRF patients (15%) ( $P < 0.01$ ). However, this relationship differed by BNP trajectory ( $P$ -interaction = 0.03). When stratified by BNP change, non-IRF patients and IRF patients with decreasing BNP had lower 1-year mortality than either non-IRF and IRF patients without decreasing BNP. However, in multivariate analysis, IRF was not associated with mortality [adjusted hazard ratio (HR) 1.0, 95% confidence interval (CI) 0.7-1.5] while BNP was (adjusted HR 0.5, 95% CI 0.3-0.7). When IRF was evaluated as transiently occurring or persisting at discharge, again only BNP change was significantly associated with mortality. CONCLUSION: Improving renal function is associated with mortality in AHF but not independent of other variables and congestion status. Achieving adequate decongestion, as reflected by lower BNP, in AHF is more strongly associated with mortality than IRF.

### Endocrinology and Metabolism

Arya AK, Bhadada SK, Kumari P, Agrawal K, Mukhopadhyay S, Sarma D, and **Rao SD**. Differences in Primary Hyperparathyroidism Between Pre- and Postmenopausal Women in India. *Endocr Pract* 2021; 27(7):710-715. PMID: 33685668. [Request Article](#)

OBJECTIVE: Primary hyperparathyroidism (PHPT) is a common endocrine disorder in women which becomes more prevalent after menopause. In this study, we compared the demographic, clinical, and biochemical variables between premenopausal (pre-M) and postmenopausal (post-M) women with PHPT. METHODS: A retrospective analysis (from 2005 to 2019) of enrolled women PHPT patients from an online Indian PHPT registry. RESULTS: Of the women with PHPT, 232 and 122 were pre-M and post-M, respectively. The number of post-M PHPT cases registered had a 3.3-fold increase in 2015-2019 from 2005-2009 compared with only a 2.5-fold increase in pre-M cases in the same duration. The majority were symptomatic (90%), although pre-M had a higher proportion of symptomatic than post-M (92% vs 85%;  $P = .04$ ). Pre-M women showed more prevalence of osteitis fibrosa cystica than post-M women (28% vs 13%;  $P = .03$ ), although hypertension and gallstone disease were seen more frequently in post-M PHPT women. Pre-M women had a significantly higher median PTH (403 vs 246 pg/mL;  $P = .02$ ) and median alkaline phosphatase (202 vs 145 pg/mL;  $P = .02$ ) than post-M women, and vitamin D deficiency was more common in pre-M women (58% vs 45%;  $P = .03$ ). Gland

localization, tumor weight, and disease cure rates did not differ according to menopausal status. CONCLUSION: PHPT was more prevalent in pre-M women, although the number of post-M cases had significantly increased in the last 10 years. Pre-M women had generally more severe clinical and biochemical variables than post-M PHPT women.

#### Endocrinology and Metabolism

Kanwal F, Shubrook JH, Younossi Z, Natarajan Y, Bugianesi E, Rinella ME, Harrison SA, Mantzoros C, Pfothenauer K, Klein S, Eckel RH, **Kruger D**, El-Serag H, and Cusi K. Preparing for the NASH epidemic: A call to action. *Metabolism* 2021; Epub ahead of print.:154822. PMID: 34289945. [Full Text](#)

Nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) are common conditions with a rising burden. Yet there are significant management gaps between clinical guidelines and practice in patients with NAFLD and NASH. Further, there is no single global guiding strategy for the management of NAFLD and NASH. The American Gastroenterological Association, in collaboration with 7 professional associations, convened an international conference comprising 32 experts in gastroenterology, hepatology, endocrinology, and primary care providers from the United States, Europe, Asia, and Australia. Conference content was informed by the results of a national NASH Needs Assessment Survey. The participants reviewed and discussed published literature on global burden, screening, risk stratification, diagnosis, and management of individuals with NAFLD, including those with NASH. Participants identified promising approaches for clinical practice and prepared a comprehensive, unified strategy for primary care providers and relevant specialists encompassing the full spectrum of NAFLD/NASH care. They also identified specific high-yield targets for clinical research and called for a unified, international public health response to NAFLD and NASH.

#### Family Medicine

**Freedman JD**, Novak R, Bratman Morag S, Avitan-Hersh E, and Nikomarov D. Bone Involvement in Hyperphosphatemic Familial Tumoral Calcinosis: A New Phenotypic Presentation. *Rambam Maimonides Med J* 2021; 12(3). PMID: 34270404. [Full Text](#)

Mutations in FGF23, KL, and GALNT3 have been identified as the cause for the development of hyperphosphatemic familial tumoral calcinosis (HFTC). Patients with HFTC typically present in childhood or adolescence with periarticular soft tissue deposits that eventually progress to disrupt normal joint articulation. Mutations in the GALNT3 gene were shown to account for the hyperphosphatemic state in both HFTC and hyperostosis-hyperphosphatemia syndrome (HHS), the latter characterized by bone involvement. We present the case of a patient of a Druze ethnic origin with known HFTC that presented to our department with the first documented case of pathologic fracture occurring secondary to the disease. Our report introduces this new phenotypic presentation, suggests a potential role for prophylactic bone screening, and highlights the need for preconception genetic screening in selected populations.

#### Family Medicine

**Yaphe S**, and **Bahcheli K**. Cutibacterium acnes sternoclavicular joint osteomyelitis in an otherwise healthy 55-year-old man. *BMJ Case Rep* 2021; 14(7). PMID: 34281939. [Full Text](#)

Sternoclavicular joint osteomyelitis is extremely rare, with only 225 reported cases in the last 45 years. We present an unusual case in an otherwise healthy 55-year-old man with a history of well-controlled type 2 diabetes mellitus and hypertension. He presented to the emergency department after a week of left knee pain that worsened to full-body joint pain with left sternoclavicular swelling. He was started on antibiotics with multiple washouts of the left knee

and treated for septic arthritis. By MRI and CT, he was found to have left sternoclavicular joint osteomyelitis and abscess and underwent debridement and resection. We believe that the initial joint injection resulted in haematogenous spread to the left sternoclavicular joint, stressing the importance of a sterile field for joint procedures.

#### Gastroenterology

Ahmed A, Naji A, **Zhang J, Raoufi M, Alhamar M, Salgia R**, and **Mullins K**. Mantle Cell Lymphoma Presenting as Diarrhea in a Liver Transplant Recipient. *ACG Case Rep J* 2021; 8(7):e00635. PMID: 34307713. [Full Text](#)

We present a 63-year-old man with a medical history of hepatocellular carcinoma who underwent orthotopic liver transplant 10 years prior on long-term immunosuppressive therapy. The patient presented to the clinic with diarrhea, and the workup revealed mantle cell lymphoma. Mantle cell lymphoma is an extremely rare finding in transplanted livers. It is essential to include mantle cell lymphoma, along with a broad differential, during the workup of diarrhea in post-transplant patients.

#### Gastroenterology

Elmunzer BJ, Spitzer RL, Foster LD, Merchant AA, Howard EF, Patel VA, West MK, Qayed E, Nustas R, Zakaria A, Piper MS, Taylor JR, Jaza L, Forbes N, Chau M, Lara LF, Papachristou GI, Volk ML, Hilson LG, Zhou S, Kushnir VM, Lenyo AM, McLeod CG, Amin S, Kuftinec GN, Yadav D, Fox C, Kolb JM, Pawa S, Pawa R, Canakis A, Huang C, Jamil LH, Aneese AM, Glamour BK, Smith ZL, Hanley KA, Wood J, Patel HK, Shah JN, Agarunov E, Sethi A, Fogel EL, McNulty G, Haseeb A, Trieu JA, Dixon RE, Yang JY, Mendelsohn RB, Calo D, Aroniadis OC, LaComb JF, Scheiman JM, Sauer BG, **Dang DT, Piraka CR**, Shah ED, Pohl H, Tierney WM, Mitchell S, Condon A, Lenhart A, Dua KS, Kanagala VS, Kamal A, Singh VK, Pinto-Sanchez MI, Hutchinson JM, Kwon RS, Korsnes SJ, Singh H, Solati Z, Willingham FF, Yachimski PS, Conwell DL, Mosier E, Azab M, Patel A, Buxbaum J, Wani S, Chak A, Hosmer AE, Keswani RN, DiMaio CJ, Bronze MS, Muthusamy R, Canto MI, Gjeorgjievski VM, Imam Z, Odish F, Edhi AI, Orosey M, Tiwari A, Patwardhan S, Brown NG, Patel AA, Ordiah CO, Sloan IP, Cruz L, Koza CL, Okafor U, Hollander T, Furey N, Reykhart O, Zbib NH, Damianos JA, Esteban J, Hajidiacos N, Saul M, Mays M, Anderson G, Wood K, Mathews L, Diakova G, Caisse M, Wakefield L, Nitchie H, Waljee AK, Tang W, Zhang Y, Zhu J, Deshpande AR, Rockey DC, Alford TB, and Durkalski V. Digestive Manifestations in Patients Hospitalized With Coronavirus Disease 2019. *Clin Gastroenterol Hepatol* 2021; 19(7):1355-1365.e1354. PMID: 33010411. [Full Text](#)

**BACKGROUND & AIMS:** The prevalence and significance of digestive manifestations in coronavirus disease 2019 (COVID-19) remain uncertain. We aimed to assess the prevalence, spectrum, severity, and significance of digestive manifestations in patients hospitalized with COVID-19. **METHODS:** Consecutive patients hospitalized with COVID-19 were identified across a geographically diverse alliance of medical centers in North America. Data pertaining to baseline characteristics, symptomatology, laboratory assessment, imaging, and endoscopic findings from the time of symptom onset until discharge or death were abstracted manually from electronic health records to characterize the prevalence, spectrum, and severity of digestive manifestations. Regression analyses were performed to evaluate the association between digestive manifestations and severe outcomes related to COVID-19. **RESULTS:** A total of 1992 patients across 36 centers met eligibility criteria and were included. Overall, 53% of patients experienced at least 1 gastrointestinal symptom at any time during their illness, most commonly diarrhea (34%), nausea (27%), vomiting (16%), and abdominal pain (11%). In 74% of cases, gastrointestinal symptoms were judged to be mild. In total, 35% of patients developed an abnormal alanine aminotransferase or total bilirubin level; these were increased to less than 5

times the upper limit of normal in 77% of cases. After adjusting for potential confounders, the presence of gastrointestinal symptoms at any time (odds ratio, 0.93; 95% CI, 0.76-1.15) or liver test abnormalities on admission (odds ratio, 1.31; 95% CI, 0.80-2.12) were not associated independently with mechanical ventilation or death. **CONCLUSIONS:** Among patients hospitalized with COVID-19, gastrointestinal symptoms and liver test abnormalities were common, but the majority were mild and their presence was not associated with a more severe clinical course.

#### Gastroenterology

**Kitajima T, Moonka D, Yeddula S, Collins K, Rizzari M, Yoshida A, Abouljoud MS, and Nagai S.** Reply. *Liver Transpl* 2021; Epub ahead of print. PMID: 33786986. [Full Text](#)

#### Gastroenterology

Rahimi RS, **Brown KA**, Flamm SL, and Brown RS, Jr. Overt Hepatic Encephalopathy: Current Pharmacologic Treatments and Improving Clinical Outcomes. *Am J Med* 2021; Epub ahead of print. PMID: 34242619. [Full Text](#)

Overt hepatic encephalopathy is a generally reversible neurologic complication of cirrhosis. Overt hepatic encephalopathy has been associated with poor hospitalization- and mortality-related outcomes, important given increasing hepatic encephalopathy-related hospitalizations over time. The aim of this narrative review is to provide an overview of hospital- and mortality-related outcomes in patients with overt hepatic encephalopathy and the pharmacologic therapies that may improve these outcomes. Guideline-recommended prophylaxis with lactulose (first-line therapy) or secondary prophylaxis with rifaximin plus lactulose decreases hospital admissions and mortality rates. Rifaximin or lactulose treatment was beneficial for reducing the hospitalization rate in patients with hepatic encephalopathy compared with no treatment. Further, retrospective studies have shown that rifaximin with or without lactulose was effective for decreasing the number of hepatic encephalopathy episodes, hepatic encephalopathy-related hospitalizations, and duration of hospitalization. Ornithine phenylacetate, an ammonia-reducing agent currently in development, is also being investigated in hospitalized patients with hepatic encephalopathy. Overall, data support that prophylaxis for the prevention of hepatic encephalopathy recurrence improves outcomes in patients with cirrhosis and a history of hepatic encephalopathy.

#### Global Health Initiative

Dormanesh A, Wang JH, Mishori R, Cupertino P, Longcoy J, Kassaye S, **Kaljee L**, Smith C, and Loffredo CA. Adherence to clinical follow-up recommendations for liver function tests: A cross-sectional study of patients with HCV and their associated risk behaviors. *Prev Med Rep* 2021; 23:101482. PMID: 34307001. [Full Text](#)

This study examined whether patients with Hepatitis C virus (HCV) infection adhered to their physicians' recommendation and HCV clinical guidelines for obtaining a regular liver function test (LFT), and whether high-risk behaviors are associated with behavioral adherence. A cross-sectional survey was administered to 101 eligible patients with HCV who were recruited from health centers in New Jersey and Washington, DC. Adherence outcomes were defined as the patients' self-report of two consecutive receipts of LFTs in accordance with their physicians' recommended interval or the clinical guidelines for a LFT within 3-6 months. 67.4% of patients (66/98) reported a receipt of their physicians' recommendation for a LFT. The rate of adherence to physician recommendation was about 70% (46/66), however over 50% (52/101) of patients with HCV did not obtain regular LFTs. 15.8% (16/101) of patients continued to use injection drugs. Patients who used injection drugs had 0.87 (adjusted odds ratio (aOR) = 0.13, 95%

confidence interval 0.03-0.59) times lower odds adhering to their physician recommendation, relative to non-users. Patients with HIV co-infection had increased odds of adhering to the clinical guidelines (odds ratio 3.41, 95% confidence interval 1.34-8.70) vs. patients who did not report HIV co-infection. Additionally, patients who had received a physician's recommendation had 7.21 times (95% confidence interval of 2.36-22.2) greater odds adhering to the clinical guidelines than those who had not. Overall, promoting HCV patient-provider communication regarding regular LFTs and reduction of risk behaviors is essential for preventing patients from HCV-related liver disease progression.

#### Graduate Medical Education

**Hoffert M, Passalacqua KD, Haftka-George A, Lanfranco OA**, and Martin RA. A Curriculum for Enhancing Physician Teaching Skills: The Value of Physician-Educator Partnerships. *J Med Educ Curric Dev* 2021; 8. PMID: Not assigned. [Full Text](#)

Developing as a physician requires an enormous amount of complex training, and quality of instruction greatly affects training outcomes. But while physicians are expected to teach trainees within the clinic, they often do not receive formal training in effective instructional practices. Providing faculty development programs is one way that institutions can help physicians develop teaching skills, but these programs often are developed without the input of educational specialists and not based in educational theory. In this methodology paper, we describe a 5-module curriculum that was developed in a cross-disciplinary collaboration between instructional designers and physician faculty. By merging educational and medical expertise and using adult learning theory with the Charlotte-Danielson educational framework, an essentials for clinical teaching educational endorsement program (ECTEEP) was created as a feature of the institutional curriculum within a large, urban teaching hospital. Here we describe how the program was developed through a physician-educator partnership, outline the program's key content, and highlight essential aspects of successful implementation. The ECTEEP incorporates active learning approaches within an abbreviated format, distilling 5 critical aspects of effective teaching that are relevant to the clinical environment: cultural humility and safe learning environments, instruction practices for engaging learners, instruction and assessment strategies, receiving and giving feedback, and mentorship and coaching. A central feature of the program is that facilitators actively model the teaching behaviors they are conveying, which underscores the critical importance of facilitator preparation and skill. Our curriculum is offered here as a basic template for institutions that may want to establish a program for enhancing physician teaching skill.

#### Hematology-Oncology

**Abu Rous F, Li Q**, and **Guo Y**. Renal infarction and papular-purpuric gloves and socks syndrome (PPGSS): rare extra-haematological manifestations of acute parvovirus B-19 infection. *BMJ Case Rep* 2021; 14(7). PMID: 34290030. [Full Text](#)

#### Hematology-Oncology

Argiris A, Miao J, Cristea MC, Chen AM, Sands JM, Decker RH, Gettinger SN, Daly ME, Faller BA, Albain KS, Yanagihara RH, Garland LL, Byers LA, **Wang D**, Koczywas M, Redman MW, Kelly K, and Gandara DR. A Dose-finding Study Followed by a Phase II Randomized, Placebo-controlled Trial of Chemoradiotherapy With or Without Veliparib in Stage III Non-small-cell Lung Cancer: SWOG 1206 (8811). *Clin Lung Cancer* 2021; 22(4):313-323.e311. PMID: 33745865. [Full Text](#)

**BACKGROUND:** We conducted a 2-part study to evaluate the incorporation of veliparib, a PARP inhibitor, into chemoradiotherapy (CRT) for stage III non-small-cell lung cancer.

**PATIENTS AND METHODS:** In the phase I part, patients were treated successively at 3 dose levels of veliparib (40, 80, and 120 mg) twice daily during CRT. In the phase II part, patients were randomized to receive veliparib or placebo during thoracic radiotherapy with concurrent weekly carboplatin and paclitaxel, followed by 2 cycles of consolidation carboplatin and paclitaxel with veliparib or placebo. The study was prematurely discontinued owing to the emergence of adjuvant immunotherapy as standard of care. **RESULTS:** Of 21 patients enrolled in phase I, 2 patients developed dose-limiting toxicities (DLTs): 1 grade 3 esophagitis with dysphagia (at 40 mg) and 1 grade 3 esophagitis with dehydration (at 80 mg). No DLTs were seen at veliparib dose of 120 mg twice daily, which was selected for the phase II part that enrolled 31 eligible patients. Progression-free survival (PFS) was not different between the 2 arms ( $P = .20$ ). For the veliparib and placebo arms, response rates were 56% and 69%, PFS at 1 year 47% and 46%, and overall survival at 1 year 89% and 54%, respectively. **CONCLUSION:** Veliparib with CRT was feasible and well tolerated. Efficacy could not accurately be determined because of early study closure. Nonetheless, there is enthusiasm for the evaluation of PARP inhibitors in lung cancer as predictive biomarkers are being developed and combinations with immunotherapy are attractive.

#### Hematology-Oncology

**Arora K**, Rodgers S, **Alkhatib Y**, Onwubiko IN, Padmanabhan A, and Otrrock ZK. P-selectin expression assay in a repeatedly serotonin-release assay-negative patient with heparin-induced thrombocytopenia. *Blood Coagul Fibrinolysis* 2021; Epub ahead of print. PMID: 34261860. [Full Text](#)

Heparin-induced thrombocytopenia (HIT) is an immune complication of heparin therapy caused by antibodies to complexes of platelet factor 4 (PF4) and heparin. Pathogenic antibodies to PF4/heparin bind and activate platelets to propagate a hypercoagulable state culminating in life-threatening thrombosis. The serotonin-release assay (SRA) is considered the gold-standard test to diagnose HIT. However, the sensitivity of the SRA was questioned with reported cases of clinical diagnosis of HIT and negative SRA. Herein, we present the utility of platelet factor 4-dependent P-selectin expression assay (PEA) in diagnosing HIT in a patient with thrombocytopenia and recurrent thrombosis who repeatedly tested negative with SRA.

#### Hematology-Oncology

Demirkiran O, Almaliti J, Leão T, Navarro G, Byrum T, **Valeriote FA**, Gerwick L, and Gerwick WH. Portobelamides A and B and Cacicqueamide, Cytotoxic Peptidic Natural Products from a *Caldora* sp. Marine Cyanobacterium. *J Nat Prod* 2021; Epub ahead of print. PMID: 34269583. [Request Article](#)

Three new compounds, portobelamides A and B (1 and 2), 3-amino-2-methyl-7-octynoic acid (AMOYA) and hydroxyisovaleric acid (Hiva) containing cyclic depsipeptides, and one long chain lipopeptide caciqueamide (3), were isolated from a field-collection of a *Caldora* sp. marine cyanobacterium obtained from Panama as part of the Panama International Cooperative Biodiversity Group Program. Their planar structures were elucidated through analysis of 2D NMR and MS data, especially high resolution (HR) MS(2)/MS(3) fragmentation methods. The absolute configurations of compounds 1 and 2 were deduced by traditional hydrolysis, derivative formation, and chromatographic analyses compared with standards. Portobelamide A (1) showed good cytotoxicity against H-460 human lung cancer cells (33% survival at 0.9  $\mu\text{M}$ ).

#### Hematology-Oncology

Dziadziuszko R, Mok T, Peters S, Han JY, Alatorre-Alexander J, Leighl N, Sriuranpong V, Pérol M, de Castro Junior G, Nadal E, de Marinis F, Frontera OA, Tan DSW, Lee DH, Kim HR, Yan

M, Riehl T, Schleifman E, Paul SM, Mocci S, Patel R, Assaf ZJ, Shames DS, Mathisen MS, and **Gadgeel SM**. Blood First Assay Screening Trial (BFAST) in Treatment-Naïve Advanced or Metastatic Non-Small Cell Lung Cancer: Initial Results of the Phase 2 ALK-Positive Cohort. *J Thorac Oncol* 2021; Epub ahead of print. PMID: 34311110. [Full Text](#)

**INTRODUCTION:** The Blood First Assay Screening Trial (BFAST) is an ongoing open-label, multi-cohort study, prospectively evaluating the relationship between blood-based next-generation sequencing (NGS) detection of actionable genetic alterations and activity of targeted therapies/immunotherapy in treatment-naïve advanced/metastatic NSCLC. We present data from the ALK-positive cohort. **METHODS:** Patients aged  $\geq 18$  years with stage IIIB/IV NSCLC and ALK rearrangements detected by blood-based NGS using hybrid capture technology (FoundationACT™) received alectinib 600 mg twice-daily. Asymptomatic/treated central nervous system (CNS) metastases were permitted. Primary endpoint: investigator-assessed objective response rate (ORR; RECIST v1.1). Secondary endpoints: independent review facility (IRF)-assessed ORR; duration of response (DoR), progression-free survival (PFS), and overall survival; safety. Exploratory endpoints: investigator-assessed ORR in patients with baseline CNS metastases; relationship between circulating biomarkers and response. **RESULTS:** In total, 2219 patients were screened and blood-based NGS yielded results in 98.6% of cases. Of these, 119 (5.4%) patients had ALK-positive disease; 87 were enrolled and received alectinib. Median follow-up was 12.6 months (range = 2.6-18.7). Confirmed ORR was 87.4% (95% confidence interval [CI]: 78.5-93.5) by investigator and 92.0% (95% CI: 84.1-96.7) by IRF. Investigator-confirmed 12-month DoR was 75.9% (95% CI: 63.6-88.2). In 35 (40%) patients with baseline CNS disease, investigator-assessed ORR was 91.4% (95% CI: 76.9-98.2). Median PFS was not reached; 12-month investigator-assessed PFS was 78.4% (95% CI: 69.1-87.7). Safety data were consistent with the known tolerability profile of alectinib. **CONCLUSIONS:** These results demonstrate the clinical application of blood-based NGS as a method to inform clinical decision-making in ALK-positive NSCLC.

#### Hematology-Oncology

Kemp SB, Pasca di Magliano M, and **Crawford HC**. Myeloid cell mediated immune suppression in pancreatic cancer. *Cell Mol Gastroenterol Hepatol* 2021; Epub ahead of print. PMID: 34303882. [Full Text](#)

Pancreatic ductal adenocarcinoma (PDA), the most common pancreatic cancer, is a nearly-universally lethal malignancy. PDA is characterized by extensive infiltration of immunosuppressive myeloid cells, including tumor-associated macrophages (TAMs) and myeloid-derived suppressor cells (MDSCs). Myeloid cells in the tumor microenvironment (TME) inhibit cytotoxic T cell responses promoting carcinogenesis. Immune checkpoint therapy has not been effective in PDA, most likely due to this robust immune suppression, making it critical to elucidate mechanisms behind this phenomenon. Here, we review myeloid cell infiltration and cellular crosstalk in PDA progression and highlight current therapeutic approaches to target myeloid cell-driven immune suppression.

#### Hematology-Oncology

Lee DH, Hawk F, Seok K, Gliksman M, **Emole J**, Rhea IB, Viganego F, Welter-Frost A, Armanious M, Shah B, Chavez JC, Pinilla-Ibarz J, Schabath MB, and Fradley M. Association between ibrutinib treatment and hypertension. *Heart* 2021; Epub ahead of print. PMID: 34210750. [Full Text](#)

**BACKGROUND:** Ibrutinib is a tyrosine kinase inhibitor most commonly associated with atrial fibrillation. However, additional cardiotoxicities have been identified, including accelerated

hypertension. The incidence and risk factors of new or worsening hypertension following ibrutinib treatment are not as well known. **METHODS:** We conducted a retrospective study of 144 patients diagnosed with B cell malignancies treated with ibrutinib (n=93) versus conventional chemoimmunotherapy (n=51) and evaluated their effects on blood pressure at 1, 2, 3 and 6 months after treatment initiation. Descriptive statistics were used to compare baseline characteristics for each treatment group. Fisher's exact test was used to identify covariates significantly associated with the development of hypertension. Repeated measures analyses were conducted to analyse longitudinal blood pressure changes. **RESULTS:** Both treatments had similar prevalence of baseline hypertension at 63.4% and 66.7%, respectively. There were no differences between treatments by age, sex and baseline cardiac comorbidities. Both systolic and diastolic blood pressure significantly increased over time with ibrutinib compared with baseline, whereas conventional chemoimmunotherapy was not associated with significant changes in blood pressure. Baseline hypertensive status did not affect the degree of blood pressure change over time. A significant increase in systolic blood pressure (defined as more than 10 mm Hg) was noted for ibrutinib (36.6%) compared with conventional chemoimmunotherapy (7.9%) at 1 month after treatment initiation. Despite being hypertensive at follow-up, 61.2% of patients who were treated with ibrutinib did not receive adequate blood pressure management (increase or addition of blood pressure medications). Within the ibrutinib group, of patients who developed more than 20 mm Hg increase in systolic blood pressure, only 52.9% had hypertension management changes. **CONCLUSIONS:** Ibrutinib is associated with the development of hypertension and worsening of blood pressure. Cardiologists and oncologists must be aware of this cardiotoxicity to allow timely management of blood pressure elevations.

#### Hematology-Oncology

Li A, Kuderer NM, Hsu CY, Shyr Y, Warner JL, Shah DP, Kumar V, Shah S, Kulkarni AA, Fu J, Gulati S, Zon RL, Li M, Desai A, Egan PC, Bakouny Z, Kc D, **Hwang C**, Akpan IJ, McKay RR, Girard J, Schmidt AL, Halmos B, Thompson MA, Patel JM, Pennell NA, Peters S, Elshoury A, de Lima Lopes G, Stover DG, Grivas P, Rini BI, Painter CA, Mishra S, Connors JM, Lyman GH, and Rosovsky RP. The CoVID-TE Risk Assessment Model for Venous Thromboembolism in Hospitalized Patients with Cancer and COVID-19. *J Thromb Haemost* 2021; Epub ahead of print. PMID: 34260813. [Full Text](#)

**BACKGROUND:** Hospitalized patients with COVID-19 have increased risks of venous (VTE) and arterial thromboembolism (ATE). Active cancer diagnosis and treatment are well-known risk factors; however, a risk assessment model (RAM) for VTE in patients with both cancer and COVID-19 is lacking. **METHODS:** Among patients with cancer in the CCC19 cohort study, we assessed the incidence of VTE and ATE within 90 days of COVID-19 associated hospitalization. A multivariable logistic regression model specifically for VTE was built using a priori determined clinical risk factors. A simplified RAM was derived and internally validated using bootstrap. **FINDINGS:** From 3/17/2020 to 11/30/2020, 2804 hospitalized patients were analyzed. The incidence of VTE and ATE was 7.6% and 3.9%, respectively. The incidence of VTE, but not ATE, was higher in patients receiving recent anti-cancer therapy. A simplified RAM for VTE was derived and named CoVID-TE (Cancer subtype high to very-high risk by original Khorana score +1, VTE history +2, ICU admission +2, D-dimer elevation +1, recent systemic anti-cancer Therapy +1, and non-Hispanic Ethnicity +1). The RAM stratified patients into two cohorts (low-risk, 0-2 points, n=1423 vs. high-risk, 3+ points, n=1034) where VTE occurred in 4.1% low-risk and 11.3% high-risk patients (c statistic 0.67, 95% CI 0.63-0.71). The RAM performed similarly well in subgroups of patients not on anticoagulant prior to admission and moderately ill patients not requiring direct ICU admission. **INTERPRETATION:** Hospitalized patients with cancer and



COVID-19 have elevated thrombotic risks. The CoVID-TE RAM for VTE prediction may help real-time data-driven decisions in this vulnerable population.

#### Hematology-Oncology

Yu KH, Hendifar AE, Alese OB, Draper A, Abdelrahim M, Burns E, **Khan G**, Cockrum P, Bhak RH, Nguyen C, DerSarkissian M, Duh MS, and Bahary N. Clinical Outcomes Among Patients With Metastatic Pancreatic Ductal Adenocarcinoma Treated With Liposomal Irinotecan. *Front Oncol* 2021; 11:678070. PMID: 34336666. [Full Text](#)

**BACKGROUND:** The NAPOLI-1 trial demonstrated that liposomal irinotecan in combination with fluorouracil (5-FU) and leucovorin (LV) prolonged survival with a manageable safety profile in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine-based therapy. Real-world data on clinical outcomes associated with liposomal irinotecan in NAPOLI-1-based regimens is needed to further substantiate this. **METHODS:** This real-world, retrospective chart review study included patients with mPDAC who received NAPOLI-1-based regimens from six academic centers in the United States. Liposomal irinotecan initiation defined the index date. Overall survival (OS) and progression-free survival (PFS) were assessed with Kaplan-Meier methodology. **RESULTS:** There were 374 patients evaluated; median age was 68 years, and 51% were female. Among 326 patients with baseline ECOG information, approximately 74% had ECOG score <2. Liposomal irinotecan was administered as a doublet with 5-FU in a NAPOLI-1-based regimen in the first line (1L; 16%), 2L (42%), and 3L+ (42%) of the metastatic setting. For patients treated in 1L, 2L, and 3L+, median [95% confidence interval (CI)] OS was 8.0 [5.1, 11.2], 7.3 [5.3, 8.8], and 4.6 [4.0, 5.7] months, and median [95% CI] PFS was 4.2 [2.2, 6.6], 3.0 [2.6, 3.7], and 2.0 [1.7, 2.2] months, respectively. **CONCLUSIONS:** Patients in a real-world setting treated with NAPOLI-1-based liposomal irinotecan doublet regimens at academic centers were older with poorer performance status compared to trial patients yet had similar outcomes and efficacy. Furthermore, liposomal irinotecan was frequently used in the 3L+ setting where no treatment has been approved and provided clinical benefit.

#### Hospital Medicine

Petty LA, Flanders SA, Vaughn VM, Ratz D, O'Malley M, Malani AN, Washer L, Kim T, Kocher KE, **Kaatz S**, Czilok T, McLaughlin E, Prescott HC, Chopra V, and Gandhi T. Risk Factors and Outcomes Associated with Community-Onset and Hospital-Acquired Co-infection in Patients Hospitalized for COVID-19: A Multi-Hospital Cohort Study. *Infect Control Hosp Epidemiol* 2021; Epub ahead of print.:1-28. PMID: 34308805. [Full Text](#)

**BACKGROUND:** We sought to determine the incidence of community-onset and hospital-acquired co-infection in patients hospitalized with COVID-19 and evaluate associated predictors and outcomes. **METHODS:** Multicenter retrospective cohort study of patients hospitalized for COVID-19, 3/2020 to 8/2020, across 38 Michigan hospitals assessed for prevalence, predictors, and outcomes of community-onset or hospital-acquired co-infection. In-hospital and 60-day mortality, readmission, discharge to long-term care facility (LTCF), and mechanical ventilation duration, were assessed for patients with vs. without co-infection. **RESULTS:** Of 2205 patients with COVID-19, 6.4% (N=141) had a co-infection (3.0% community-onset, 3.4% hospital-acquired). 64.9% of patients without co-infection received antibiotics. Community-onset co-infection predictors include admission from LTCF (OR 3.98, 95% CI 2.34-6.76, p<0.001) and admission to intensive care (OR 4.34, 95% CI 2.87-6.55, p<0.001). Hospital-acquired co-infection predictors include fever (OR 2.46, 95% CI 1.15-5.27, p=0.02) and advanced respiratory support (OR 40.72, 95% CI 13.49-122.93, p<0.001). Patients with (vs. without) community-onset co-infection had longer mechanical ventilation (OR 3.31, 95% CI 1.67-6.56,

p=0.001) and higher in-hospital (OR 1.90, 95% CI 1.06-3.40 p=0.03) and 60-day mortality (OR 1.86, 95% CI 1.05-3.29 p=0.03). Patients with (vs. without) hospital-acquired co-infection had higher discharge to LTCF (OR 8.48, 95%CI 3.30-21.76 p<0.001), in-hospital (OR 4.17, 95% CI 2.37-7.33, p=<.001) and 60-day mortality (OR 3.66, 95% CI 2.11-6.33, p=<.001).

**CONCLUSION:** Despite community-onset and hospital-acquired co-infection being uncommon, most patients hospitalized with COVID-19 received antibiotics. Admission from LTCF and to ICU were associated with increased risk of community-onset co-infection. Future work should prospectively validate predictors of COVID-19 co-infection to facilitate antibiotic reduction.

#### Infectious Diseases

**Al-Bizri LA, Vahia AT, Rizvi K, Bardossy AC, Robinson PK, Shelters RT, Klotz S, Starr PM, Reyes KQ, Suleyman G, and Alangaden GJ.** Effect of a urine culture stewardship initiative on urine culture utilization and catheter-associated urinary tract infections in intensive care units. *Infect Control Hosp Epidemiol* 2021; Epub ahead of print.:1-4. PMID: 34236024. [Full Text](#)

**OBJECTIVE:** Urine cultures have poor specificity for catheter-associated urinary tract infections (CAUTIs). We evaluated the effect of a urine-culture stewardship program on urine culture utilization and CAUTI in adult intensive care units (ICUs). **DESIGN:** A quasi-interventional study was performed from 2015 to 2017. **SETTING AND PATIENTS:** The study cohort comprised 21,367 patients admitted to the ICU at a teaching hospital. **INTERVENTION:** The urine culture stewardship program included monthly 1-hour discussions with ICU house staff emphasizing avoidance of "pan-culture" for sepsis workup and obtaining urine culture only if a urinary source of sepsis is suspected. The urine culture utilization rate metric (UCUR; ie, no. urine cultures/catheter days ×100) was utilized to measure the effect. Monthly UCUR, catheter utilization ratio (CUR), and CAUTI rate were reported on an interactive quality dashboard. To ensure safety, catheterized ICU patients (2015-2016) were evaluated for 30-day readmission for UTI. Time-series data and relationships were analyzed using Spearman correlation coefficients and regression analysis. **RESULTS:** Urine culture utilization decreased from 3,081 in 2015 to 2,158 in 2016 to 1,218 in 2017. CAUTIs decreased from 78 in 2015 to 60 in 2016 and 28 in 2017. Regression analysis over time showed significant decreases in UCUR (r, 0.917; P < .0001) and CAUTI rate (r, 0.657; P < .0001). The co-correlation between UCUR and CAUTI rate was (r, 0.625; P < .0001) compared to CUR and CAUTI rate (r, 0.523; P = .004). None of these patients was readmitted with a CAUTI. **CONCLUSIONS:** Urine culture stewardship program was effective and safe in reducing UC overutilization and was correlated with a decrease in CAUTIs. Addition of urine-culture stewardship to standard best practices could reduce CAUTI in ICUs.

#### Infectious Diseases

**Hoffert M, Passalacqua KD, Haftka-George A, Lanfranco OA, and Martin RA.** A Curriculum for Enhancing Physician Teaching Skills: The Value of Physician-Educator Partnerships. *J Med Educ Curric Dev* 2021; 8. PMID: Not assigned. [Full Text](#)

Developing as a physician requires an enormous amount of complex training, and quality of instruction greatly affects training outcomes. But while physicians are expected to teach trainees within the clinic, they often do not receive formal training in effective instructional practices. Providing faculty development programs is one way that institutions can help physicians develop teaching skills, but these programs often are developed without the input of educational specialists and not based in educational theory. In this methodology paper, we describe a 5-module curriculum that was developed in a cross-disciplinary collaboration between instructional designers and physician faculty. By merging educational and medical expertise and using adult learning theory with the Charlotte-Danielson educational framework, an essentials for clinical teaching educational endorsement program (ECTEEP) was created as a feature of the

institutional curriculum within a large, urban teaching hospital. Here we describe how the program was developed through a physician-educator partnership, outline the program's key content, and highlight essential aspects of successful implementation. The ECTEEP incorporates active learning approaches within an abbreviated format, distilling 5 critical aspects of effective teaching that are relevant to the clinical environment: cultural humility and safe learning environments, instruction practices for engaging learners, instruction and assessment strategies, receiving and giving feedback, and mentorship and coaching. A central feature of the program is that facilitators actively model the teaching behaviors they are conveying, which underscores the critical importance of facilitator preparation and skill. Our curriculum is offered here as a basic template for institutions that may want to establish a program for enhancing physician teaching skill.

#### Infectious Diseases

**Johnson CC, Coleman CM, Sitarik AR, Leon JE, Tibbetts RJ, Cook BC, Muma BK, Weinmann AJ, and Samuel LP.** SARS-CoV-2 RT-PCR positivity and antibody prevalence among asymptomatic hospital-based health care workers. *J Clin Virol* 2021; 140:104794. PMID: 34023573. [Full Text](#)

**BACKGROUND:** The level of asymptomatic infection with SARS-CoV-2 could be substantial and among health care workers (HCWs) a source of continuing transmission of the virus to patients and co-workers. **OBJECTIVES:** Measure the period prevalence of SARS-CoV-2 PCR positivity and seroprevalence of SARS-CoV-2 IgG antibodies among a random sample of asymptomatic health system hospital-based health care workers (HCWs) 6½ -15½ weeks after 4/5/2020, the peak of the first surge of COVID-19 admissions. **RESULTS:** Of 524 eligible and consented participants from four metropolitan hospitals, nasopharyngeal swabs were obtained from 439 (83.8 %) and blood from 374 (71.4 %). Using PCR nucleic acid-based amplification (NAAT) methods, the period prevalence of SARS-CoV-2 infection was 0.23 % (95 % confidence interval (CI) 0.01 %-1.28 %; 1/439) from 5/21/20-7/16/20. The seroprevalence of SARS-CoV-2 IgG antibodies from June 17-July 24, 2020 was 2.41 % (95 % CI 1.27 %-4.51 %; 9/374). Those who were reactive were younger (median age 36 versus 44 years;  $p = 0.050$ ), and those with self-reported Hispanic/Latino ethnicity had a higher seroprevalence (2/12 = 16.7 % versus 7/352 = 2.0 %;  $p = 0.051$ ). There were no significant differences by sex, race, residence, hospital, unit or job type. The one employee who was found to be PCR test positive in this study was also reactive for IgG antibodies, tested 27 days later. **CONCLUSIONS:** The period prevalence of PCR positivity to SARS-CoV-2 and IgG seroprevalence was unexpectedly low in asymptomatic HCWs after a peak in COVID-19 admissions and the establishment of state and institutional infection control policies, suggesting that routine screening tests while community prevalence is relatively low would produce a minimal yield.

#### Infectious Diseases

**Saffo Z, Guo W, Springer K, Maksimowicz-McKinnon K, Kak V, McKinnon JE, and Bhargava P.** The role of tocilizumab therapy in critically ill patients with severe acute respiratory syndrome coronavirus 2. *J Osteopath Med* 2021; 121(8):705-714. PMID: 34237804. [Full Text](#)

**CONTEXT:** Tocilizumab (TCZ), an interleukin-6 (IL-6) receptor antagonist, has been approved for use in rheumatoid arthritis and cytokine storm syndrome (CSS) associated with chimeric antigen receptor T cells treatment. Although TCZ is currently utilized in the treatment of critically ill coronavirus 2019 (COVID-19) patients, data on survival impact is minimal. **OBJECTIVES:** To assess the mortality rate of patients presenting with COVID-19 who received TCZ for suspected CSS. **METHODS:** This retrospective cohort study was conducted at Henry Ford Health System between March 10, 2020 and May 18, 2020. Data collection began in May 2020 and was

completed in June 2020. Patients included in the study required hospital admission and had positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction on nasopharyngeal swab. Eligibility criteria to receive TCZ, per hospital protocol, included any of the following: persistent fever, defined as 38.0 °C for at least 6 hours; a diagnosis of the acute respiratory distress syndrome (ARDS); serum ferritin  $\geq 1,000$  (ng/mL) or doubling within 24 hours; D-Dimer  $\geq 5$  (mg/L); serum lactate dehydrogenase  $\geq 500$  (IU/L); or interleukin-6 level  $\geq 5$  times the upper limit of normal. Dosing was initially determined by weight, then changed to a fixed 400 mg per hospital protocol. A comparator cohort was created from patients with COVID-19 and ARDS who did not receive TCZ. Patient survival was analyzed using the Kaplan-Meier method and compared by log rank test. A multivariable cox regression was applied to evaluate the association between TCZ and mortality. RESULTS: One hundred and thirty patients were evaluated in the study, 54 (41.5%) of whom received TCZ. Patients who received TCZ were younger (mean age, 63.8 vs. 69.4 years;  $p=0.0083$ ) and had higher body mass indices (mean, 33.9 vs. 30.4;  $p=0.005$ ). Of the comorbid conditions evaluated, heart disease was more common in the comparator group than the TCZ group (27 patients [35.5%] vs. 10 patients [18.5%];  $p=0.034$ ). A Kaplan-Meier survival curve demonstrated no difference in survival between TCZ and comparator patients (log rank  $p=0.495$ ). In the multivariable Cox regression model for mortality at 30 days, treatment with TCZ was not associated with decreased mortality (hazard ratio, 1.1; 95% confidence interval, 0.53-2.3;  $p=0.77$ ). Lower mean C-reactive protein (CRP) levels were demonstrated within 48 hours of disposition in the TCZ group (mean TCZ, 4.9 vs. mean comparator, 13.0;  $p<0.0001$ ). CONCLUSIONS: In this cohort study, no difference in survival was observed in critically ill patients treated with TCZ.

#### Infectious Diseases

**Shallal A**, Abada E, Fehmi Z, Kamatham S, Trak J, Fehmi O, Toma A, Farooqi S, Jang H, Kim S, Bandyopadhyay S, **Zervos M**, and Ali-Fehmi R. Human Papillomavirus Infection and Cervical Dysplasia in a Subset of Arab American Women. *Womens Health Rep (New Rochelle)* 2021; 2(1):273-278. PMID: 34318297. [Full Text](#)

Background: With limited health data on Arab Americans (AAs), we sought to describe the health-seeking behaviors, prevalence of abnormal cervical cytology and high-risk human papillomavirus (HPV) serotypes, and the relationship with socioeconomic factors among a subset of AA women. Methods: Retrospective observational cohort study of women undergoing routine cancer screening at the Arab-American Center for Economic and Social Services clinic. Data collected included demographics, tobacco use, gross monthly income, prior Papanicolaou (Pap) smear history, and results of cervical cytology and high-risk HPV testing. Results: Of 430 women, 74 (17%) reported that they had never had a Pap smear. Three hundred eighty-eight (90%) women had cervical cytology interpreted as "negative for intraepithelial lesion," the remaining 42 (10%) women had abnormal results. Thirteen (3%) women reported prior abnormal Pap smear, which was significantly associated with additional abnormal Pap smear on multivariable analyses (odds ratio 65.46; 95% confidence interval [CI] 17.01-338.62;  $p < 0.001$ ). One hundred twenty-five (29%) women were tested for high-risk HPV serotypes; 106 (91%) had negative results, 4 (3%) were positive for HPV-16, 7 (6%) were positive for other high-risk serotypes, and 8 results were not recorded. A negative HPV screen was significantly associated with a negative Pap smear (Fisher's exact test  $p = 0.006$ ). There was no significant association between abnormal cervical cytology and evaluated socioeconomic factors. Conclusions: Additional population based-studies to determine cervical dysplasia/cancer and HPV prevalence in women of Middle Eastern descent are needed.

### Infectious Diseases

**Yared N**, Malone M, Welo E, Mohammed I, Groene E, Flory M, Basta NE, Horvath KJ, and Kulasingam S. Challenges related to human papillomavirus (HPV) vaccine uptake in Minnesota: clinician and stakeholder perspectives. *Cancer Causes Control* 2021; Epub ahead of print. PMID: 34247291. [Full Text](#)

**BACKGROUND:** Human papillomavirus (HPV) vaccination rates among adolescents are increasing in Minnesota (MN) but remain below the Healthy People 2020 goal of 80% completion of the series. The goal of this study was to identify messaging and interventions impacting HPV vaccine uptake in MN through interviews with clinicians and key stakeholders. **METHODS:** We conducted semi-structured key participant interviews with providers and stakeholders involved in HPV vaccination efforts in MN between 2018 and 2019. Provider interview questions focused on messaging around the HPV vaccine and clinic-based strategies to impact HPV vaccine uptake. Stakeholder interview questions focused on barriers and facilitators at the organizational or state level, as well as initiatives and collaborations to increase HPV vaccination. Responses to interviews were recorded and transcribed. Thematic content analysis was used to identify themes from interviews. **RESULTS:** 14 clinicians and 13 stakeholders were interviewed. Identified themes were grouped into 2 major categories that dealt with messaging around the HPV vaccine, direct patient-clinician interactions and external messaging, and a third thematic category involving healthcare system-related factors and interventions. The messaging strategy identified as most useful was promoting the HPV vaccine for cancer prevention. The need for stakeholders to prioritize HPV vaccination uptake was identified as a key factor to increasing HPV vaccination rates. Multiple providers and stakeholders identified misinformation spread through social media as a barrier to HPV vaccine uptake. **CONCLUSION:** Emphasizing the HPV vaccine's cancer prevention benefits and prioritizing it among healthcare stakeholders were the most consistently cited strategies for promoting HPV vaccine uptake. Methods to combat the negative influence of misinformation about HPV vaccines in social media are an urgent priority.

### Internal Medicine

Abozenah M, Kadado AJ, **Aljamal A**, Sawalha K, Salerno C, Battisha A, Hernandez-Montfort J, and Lotfi A. Concurring hypertrophic cardiomyopathy and takotsubo cardiomyopathy: Assessment and management. *Heart Lung* 2021; 50(4):546-557. PMID: 33143911. [Full Text](#)

The prevalence of takotsubo cardiomyopathy (TCM) has been on the rise, but co-occurrence with hypertrophic cardiomyopathy (HOCM) remains rare. Although presenting patient demographics were similar to those in TCM, the potential for hemodynamic compromise was significantly compounded by the presence of underlying HOCM. Management was similar to standalone TCM, although use of inotropic agents and mechanical support appears to be more prevalent. Despite the increased potential for complications and the paucity of data regarding management, outcomes appear to be mostly favorable in both the hospitalization period and at follow-up. Interestingly, despite a new diagnosis of HOCM in about half the cases described, which signifies no significant left ventricular outflow tract (LVOT) gradient prior to TCM, half of those patients had a persistently elevated LVOT gradient after resolution of TCM. This poses a question of whether or not TCM can predispose to LVOT obstruction in HOCM patients even after its resolution.

### Internal Medicine

**Al-Bizri LA, Vahia AT, Rizvi K, Bardossy AC, Robinson PK, Shelters RT, Klotz S, Starr PM, Reyes KQ, Suleyman G, and Alangaden GJ.** Effect of a urine culture stewardship initiative on urine culture utilization and catheter-associated urinary tract infections in intensive care units. *Infect Control Hosp Epidemiol* 2021; Epub ahead of print.:1-4. PMID: 34236024. [Full Text](#)

**OBJECTIVE:** Urine cultures have poor specificity for catheter-associated urinary tract infections (CAUTIs). We evaluated the effect of a urine-culture stewardship program on urine culture utilization and CAUTI in adult intensive care units (ICUs). **DESIGN:** A quasi-interventional study was performed from 2015 to 2017. **SETTING AND PATIENTS:** The study cohort comprised 21,367 patients admitted to the ICU at a teaching hospital. **INTERVENTION:** The urine culture stewardship program included monthly 1-hour discussions with ICU house staff emphasizing avoidance of "pan-culture" for sepsis workup and obtaining urine culture only if a urinary source of sepsis is suspected. The urine culture utilization rate metric (UCUR; ie, no. urine cultures/catheter days  $\times 100$ ) was utilized to measure the effect. Monthly UCUR, catheter utilization ratio (CUR), and CAUTI rate were reported on an interactive quality dashboard. To ensure safety, catheterized ICU patients (2015-2016) were evaluated for 30-day readmission for UTI. Time-series data and relationships were analyzed using Spearman correlation coefficients and regression analysis. **RESULTS:** Urine culture utilization decreased from 3,081 in 2015 to 2,158 in 2016 to 1,218 in 2017. CAUTIs decreased from 78 in 2015 to 60 in 2016 and 28 in 2017. Regression analysis over time showed significant decreases in UCUR ( $r, 0.917$ ;  $P < .0001$ ) and CAUTI rate ( $r, 0.657$ ;  $P < .0001$ ). The co-correlation between UCUR and CAUTI rate was ( $r, 0.625$ ;  $P < .0001$ ) compared to CUR and CAUTI rate ( $r, 0.523$ ;  $P = .004$ ). None of these patients was readmitted with a CAUTI. **CONCLUSIONS:** Urine culture stewardship program was effective and safe in reducing UC overutilization and was correlated with a decrease in CAUTIs. Addition of urine-culture stewardship to standard best practices could reduce CAUTI in ICUs.

### Internal Medicine

**Bhasin A, Musa A, Massoud L, Razikeen A, Noori A, Ghandour A, Gelovani D, Afonso LC, Lieberman R, and Vaidya A.** Increasing Diversity in Cardiology: A Fellowship Director's Perspective. *Cureus* 2021; 13(7):e16344. PMID: 34306895. [Full Text](#)

**Background** Underrepresented-minorities (URM) remain few in number amongst practicing cardiologists and across cardiology fellowship training programs in the U.S. Increased diversity is needed across the entire field and is particularly necessary within graduate medical education cardiology fellowship training programs. **Objectives** This cross-sectional study was performed to identify which strategies were supported and implemented by cardiology fellowship program directors (PDs) to increase URM representation, to determine which entities hold the responsibility to increase diversity according to program directors, and to quantify URM representation in cardiology fellowship programs. **Methods** A 15-item survey was submitted to all American College of Graduate Medical Education (ACGME) accredited cardiology fellowship programs via electronic mail. **Results** Of 250 cardiology fellowship programs, 71 responses were received (28.4%). The number of URM faculty varied from 0-1 to more than six, and URM faculty held leadership roles in most programs (62.0%). A total of 16 respondents (22.5%) were URM program directors. Most respondents agreed that diversity was important to their training program (85.9%). The majority endorsed direct recruitment of URM applicants (60.6%), opportunities for applicants to connect with (54.9%) or be recruited by URM fellows (54.9%), holistic application review (67.6%), promoting mentorship by URM faculty (69.0%), URM faculty involvement in applicant interviewing (54.9%), and increased recruitment of URM faculty members (73.2%). Program directors allocated major responsibility to increase diversity to fellowship programs (71.8%), residency programs (63.3%), and medical schools (53.5%).

**Conclusions** This study found that most cardiology programs have URM faculty in leadership roles, and nearly a quarter of the surveyed program directors were URMs. Cardiology program directors endorsed and employed numerous strategies to increase diversity and URM representation in fellowship programs. Additionally, program directors held fellowship training programs most responsible for increasing URM representation in the field of cardiology.

#### Internal Medicine

**Hoffert M, Passalacqua KD, Haftka-George A, Lanfranco OA**, and Martin RA. A Curriculum for Enhancing Physician Teaching Skills: The Value of Physician-Educator Partnerships. *J Med Educ Curric Dev* 2021; 8. PMID: Not assigned. [Full Text](#)

Developing as a physician requires an enormous amount of complex training, and quality of instruction greatly affects training outcomes. But while physicians are expected to teach trainees within the clinic, they often do not receive formal training in effective instructional practices. Providing faculty development programs is one way that institutions can help physicians develop teaching skills, but these programs often are developed without the input of educational specialists and not based in educational theory. In this methodology paper, we describe a 5-module curriculum that was developed in a cross-disciplinary collaboration between instructional designers and physician faculty. By merging educational and medical expertise and using adult learning theory with the Charlotte-Danielson educational framework, an essentials for clinical teaching educational endorsement program (ECTEEP) was created as a feature of the institutional curriculum within a large, urban teaching hospital. Here we describe how the program was developed through a physician-educator partnership, outline the program's key content, and highlight essential aspects of successful implementation. The ECTEEP incorporates active learning approaches within an abbreviated format, distilling 5 critical aspects of effective teaching that are relevant to the clinical environment: cultural humility and safe learning environments, instruction practices for engaging learners, instruction and assessment strategies, receiving and giving feedback, and mentorship and coaching. A central feature of the program is that facilitators actively model the teaching behaviors they are conveying, which underscores the critical importance of facilitator preparation and skill. Our curriculum is offered here as a basic template for institutions that may want to establish a program for enhancing physician teaching skill.

#### Internal Medicine

Ofosu A, Mohan BP, **Ichkhanian Y**, Masadeh M, Febin J, Barakat M, Ramai D, Chandan S, Haiyeva G, Khan SR, Aghaie Meybodi M, Facciorusso A, Repici A, Wani S, Thosani N, and Khashab MA. Peroral endoscopic myotomy (POEM) vs pneumatic dilation (PD) in treatment of achalasia: A meta-analysis of studies with  $\geq 12$ -month follow-up. *Endosc Int Open* 2021; 9(7):E1097-e1107. PMID: 34222636. [Full Text](#)

**Background and study aims** Peroral endoscopic myotomy (POEM) is increasingly being used as the preferred treatment option for achalasia. The aim of this systematic review and meta-analysis was to compare the efficacy and safety of POEM versus pneumatic balloon dilation (PD). **Methods** We performed a comprehensive review of studies that reported clinical outcomes of POEM and PD for the treatment of achalasia. Measured outcomes included clinical success (improvement of symptoms based on a validated scale including an Eckardt score  $\leq 3$ ), adverse events, and post-treatment gastroesophageal reflux disease (GERD). **Results** Sixty-six studies (6268 patients) were included in the final analysis, of which 29 studies (2919 patients) reported on POEM and 33 studies (3050 patients) reported on PD and 4 studies (299 patients) compared POEM versus PD. Clinical success with POEM was superior to PD at 12, 24, and 36 months (92.9%, vs 76.9%  $P = 0.001$ ; 90.6% vs 74.8%,  $P = 0.004$ ; 88.4% vs 72.2%,

P =0.006, respectively). POEM was superior to PD in type I, II and III achalasia (92.7% vs 61%, P =0.01; 92.3% vs 80.3%, P =0.01; 92.3%v 41.9%, P =0.01 respectively) Pooled OR of clinical success at 12 and 24 months were significantly higher with POEM (8.97; P =0.001 & 5.64; P =0.006). Pooled OR of GERD was significantly higher with POEM (by symptoms: 2.95, P =0.02 and by endoscopic findings: 6.98, P =0.001). Rates of esophageal perforation (0.3% vs 0.6%, P =0.8) and significant bleeding (0.4% vs 0.7%, P =0.56) were comparable between POEM and PD groups. Conclusions POEM is more efficacious than PD in the treatment of patients with achalasia during short-term and long-term follow-up, albeit with higher risk of abnormal esophageal acid exposure.

#### Internal Medicine

**Ramireddy S, and Shakir A.** Syncope and Sarcoidosis: A Criss-Cross of Diagnoses. *Cureus* 2021; 13(7):e16367. PMID: 34306898. [Full Text](#)

Syncope has a broad range of differential diagnoses. Sarcoidosis, a multisystem inflammatory disorder characterized by the formation of noncaseating granulomas, is a rare but important diagnosis to consider while evaluating patients presenting with presyncopal or syncopal symptoms. Although sarcoidosis is most commonly known to affect the lungs, it is estimated that at least 25% of patients with sarcoidosis have myocardial involvement, with only 5% of these patients showing clinical symptoms. Here, we present the rare case of a Caucasian male patient diagnosed with cardiac sarcoidosis after presenting to the hospital with presyncope. The patient had an internal cardioverter-defibrillator placed during hospitalization and was initiated on prednisone and methotrexate in the outpatient setting. He exhibited clinical and radiographical improvement in the six-month follow-up period after treatment was initiated.

#### Neurology

**Kaur J, Fahmy LM, Davoodi-Bojd E, Zhang L, Ding G, Hu J, Zhang Z, Chopp M, and Jiang Q.** Waste Clearance in the Brain. *Front Neuroanat* 2021; 15:665803. PMID: 34305538. [Full Text](#)

Waste clearance (WC) is an essential process for brain homeostasis, which is required for the proper and healthy functioning of all cerebrovascular and parenchymal brain cells. This review features our current understanding of brain WC, both within and external to the brain parenchyma. We describe the interplay of the blood-brain barrier (BBB), interstitial fluid (ISF), and perivascular spaces within the brain parenchyma for brain WC directly into the blood and/or cerebrospinal fluid (CSF). We also discuss the relevant role of the CSF and its exit routes in mediating WC. Recent discoveries of the glymphatic system and meningeal lymphatic vessels, and their relevance to brain WC are highlighted. Controversies related to brain WC research and potential future directions are presented.

#### Neurology

Lipp MM, Hickey AJ, Langer R, and **LeWitt PA.** A technology evaluation of CVT-301 (Inbrija): an inhalable therapy for treatment of Parkinson's disease. *Expert Opin Drug Deliv* 2021; Epub ahead of print. PMID: 34311641. [Full Text](#)

**INTRODUCTION:** The most widely used pharmacological treatment for Parkinson's disease is levodopa, the precursor for dopamine formation in the brain. With time, the effectiveness of levodopa declines, and patients experience motor fluctuations, or OFF periods. A levodopa formulation administered via a capsule-based oral inhaler provides a new delivery mechanism for levodopa that provides rapid relief of OFF periods. **AREAS COVERED:** CVT-301 is a dry powder formulation designed to supply levodopa to the systemic circulation via pulmonary absorption. The technology, pharmacokinetics, efficacy, and safety data of this formulation are



presented. EXPERT OPINION: Oral inhalation is a novel method of administration for levodopa that bypasses the gastrointestinal tract, allowing levodopa to enter the systemic circulation rapidly and more reliably than oral medications. Gastrointestinal dysfunction, a common feature of Parkinson's disease, can lead to impaired absorption of oral medications. Pulmonary delivery rapidly elevates levodopa plasma concentrations to provide relief of OFF periods for patients receiving oral levodopa.

### Neurology

Nogueira RG, Abdalkader M, Qureshi MM, Frankel MR, Mansour OY, Yamagami H, Qiu Z, Farhoudi M, Siegler JE, Yaghi S, Raz E, Sakai N, Ohara N, Piotin M, Mechtouff L, Eker O, Chalumeau V, Kleinig TJ, Pop R, Liu J, Winters HS, Shang X, Vasquez AR, Blasco J, Arenillas JF, Martinez-Galdamez M, Brehm A, Psychogios MN, Lylyk P, Haussen DC, Al-Bayati AR, Mohammaden MH, Fonseca L, Luís Silva M, Montalverne F, Renieri L, Mangiafico S, Fischer U, Gralla J, Frei D, Chugh C, Mehta BP, Nagel S, Mohlenbruch M, Ortega-Gutierrez S, Farooqui M, Hassan AE, Taylor A, Lapergue B, Consoli A, Campbell BC, Sharma M, Walker M, Van Horn N, Fiehler J, Nguyen HT, Nguyen QT, Watanabe D, Zhang H, Le HV, Nguyen VQ, Shah R, Devlin T, Khandelwal P, Linfante I, Izzath W, Lavados PM, Olavarría VV, Sampaio Silva G, de Carvalho Sousa AV, Kirmani J, Bendszus M, Amano T, Yamamoto R, Doijiri R, Tokuda N, Yamada T, Terasaki T, Yazawa Y, Morris JG, Griffin E, Thornton J, Lavoie P, Matouk C, Hill MD, Demchuk AM, Killer-Oberpfalzer M, Nahab F, Altschul D, Ramos-Pachón A, Pérez de la Ossa N, Kikano R, Boisseau W, Walker G, Cordina SM, Puri A, Luisa Kuhn A, Gandhi D, Ramakrishnan P, Novakovic-White R, **Chebl A**, Kargiotis O, Czap A, Zha A, Masoud HE, Lopez C, Ozretic D, Al-Mufti F, Zie W, Duan Z, Yuan Z, Huang W, Hao Y, Luo J, Kalousek V, Bourcier R, Guile R, Hetts S, Al-Jehani HM, AlHazzani A, Sadeghi-Hokmabadi E, Teleb M, Payne J, Lee JS, Hong JM, Sohn SI, Hwang YH, Shin DH, Roh HG, Edgell R, Khatri R, Smith A, Malik A, Liebeskind D, Herial N, Jabbour P, Magalhaes P, Ozdemir AO, Aykac O, Uwatoko T, Dembo T, Shimizu H, Sugiura Y, Miyashita F, Fukuda H, Miyake K, Shimbo J, Sugimura Y, Beer-Furlan A, Joshi K, Catanese L, Abud DG, Neto OG, Mehrpour M, Al Hashmi A, Saqqur M, Mostafa A, Fifi JT, Hussain S, John S, Gupta R, Sivan-Hoffmann R, Reznik A, Sani AF, Geyik S, Akil E, Churojana A, Ghoreishi A, Saadatnia M, Sharifipour E, Ma A, Faulder K, Wu T, Leung L, Malek A, Voetsch B, Wakhloo A, Rivera R, Barrientos Iman DM, Pikula A, Lioutas VA, Thomalla G, Birnbaum L, Machi P, Bernava G, McDermott M, Kleindorfer D, Wong K, Patterson MS, Fiorot JA, Jr., Huded V, Mack W, Tenser M, Eskey C, Multani S, Kelly M, Janardhan V, Cornett O, Singh V, Murayama Y, Mokin M, Yang P, Zhang X, Yin C, Han H, Peng Y, Chen W, Crosa R, Frudit ME, Pandian JD, Kulkarni A, Yagita Y, Takenobu Y, Matsumaru Y, Yamada S, Kono R, Kanamaru T, Yamazaki H, Sakaguchi M, Todo K, Yamamoto N, Sonoda K, Yoshida T, Hashimoto H, Nakahara I, Cora E, Volders D, Ducroux C, Shoamanesh A, Ospel J, Kaliaev A, Ahmed S, Rashid U, Rebello LC, Pereira VM, Fahed R, Chen M, Sheth SA, Palaiodimou L, Tsvigoulis G, Chandra R, Koyfman F, Leung T, Khosravani H, Dharmadhikari S, Frisullo G, Calabresi P, Tsiskaridze A, Lobjanidze N, Grigoryan M, Czlonkowska A, de Sousa DA, Demeestere J, Liang C, Sangha N, Lutsep HL, Ayo-Martín Ó, Cruz-Culebras A, Tran AD, Young CY, Cordonnier C, Caparros F, De Lecinana MA, Fuentes B, Yavagal D, Jovin T, Spelle L, Moret J, Khatri P, Zaidat O, Raymond J, Martins S, and Nguyen T. Global impact of COVID-19 on stroke care. *Int J Stroke* 2021; 16(5):573-584. PMID: 33459583. [Full Text](#)

BACKGROUND: The COVID-19 pandemic led to profound changes in the organization of health care systems worldwide. AIMS: We sought to measure the global impact of the COVID-19 pandemic on the volumes for mechanical thrombectomy, stroke, and intracranial hemorrhage hospitalizations over a three-month period at the height of the pandemic (1 March-31 May 2020) compared with two control three-month periods (immediately preceding and one year prior). METHODS: Retrospective, observational, international study, across 6 continents, 40 countries,

and 187 comprehensive stroke centers. The diagnoses were identified by their ICD-10 codes and/or classifications in stroke databases at participating centers. RESULTS: The hospitalization volumes for any stroke, intracranial hemorrhage, and mechanical thrombectomy were 26,699, 4002, and 5191 in the three months immediately before versus 21,576, 3540, and 4533 during the first three pandemic months, representing declines of 19.2% (95%CI, -19.7 to -18.7), 11.5% (95%CI, -12.6 to -10.6), and 12.7% (95%CI, -13.6 to -11.8), respectively. The decreases were noted across centers with high, mid, and low COVID-19 hospitalization burden, and also across high, mid, and low volume stroke/mechanical thrombectomy centers. High-volume COVID-19 centers (-20.5%) had greater declines in mechanical thrombectomy volumes than mid- (-10.1%) and low-volume (-8.7%) centers ( $p < 0.0001$ ). There was a 1.5% stroke rate across 54,366 COVID-19 hospitalizations. SARS-CoV-2 infection was noted in 3.9% (784/20,250) of all stroke admissions. CONCLUSION: The COVID-19 pandemic was associated with a global decline in the volume of overall stroke hospitalizations, mechanical thrombectomy procedures, and intracranial hemorrhage admission volumes. Despite geographic variations, these volume reductions were observed regardless of COVID-19 hospitalization burden and pre-pandemic stroke/mechanical thrombectomy volumes.

### Neurology

Sun YV, Li C, Hui Q, Huang Y, Barbano R, Rodriguez R, Malaty IA, Reich S, Bambarger K, Holmes K, Jankovic J, **Patel NJ**, Roze E, Vidailhet M, Berman BD, LeDoux MS, Espay AJ, Agarwal P, Pirio-Richardson S, Frank SA, Ondo WG, Saunders-Pullman R, Chouinard S, Natividad S, Berardelli A, Pantelyat AY, Brashear A, Fox SH, Kasten M, Krämer UM, Neis M, Bäumer T, Loens S, Borsche M, Zittel S, Maurer A, Gelderblom M, Volkmann J, Odorfer T, Kühn AA, Borngreber F, König IR, Cruchaga C, Cotton AC, Kilic-Berkmen G, Freeman A, Factor SA, Scorr L, Bremner JD, Vaccarino V, Quyyumi AA, Klein C, Perlmutter JS, Lohmann K, and Jinnah HA. A Multi-center Genome-wide Association Study of Cervical Dystonia. *Mov Disord* 2021; Epub ahead of print. PMID: 34320236. [Full Text](#)

BACKGROUND: Several monogenic causes for isolated dystonia have been identified, but they collectively account for only a small proportion of cases. Two genome-wide association studies have reported a few potential dystonia risk loci; but conclusions have been limited by small sample sizes, partial coverage of genetic variants, or poor reproducibility. OBJECTIVE: To identify robust genetic variants and loci in a large multicenter cervical dystonia cohort using a genome-wide approach. METHODS: We performed a genome-wide association study using cervical dystonia samples from the Dystonia Coalition. Logistic and linear regressions, including age, sex, and population structure as covariates, were employed to assess variant- and gene-based genetic associations with disease status and age at onset. We also performed a replication study for an identified genome-wide significant signal. RESULTS: After quality control, 919 cervical dystonia patients compared with 1491 controls of European ancestry were included in the analyses. We identified one genome-wide significant variant (rs2219975, chromosome 3, upstream of COL8A1, P-value  $3.04 \times 10^{-8}$ ). The association was not replicated in a newly genotyped sample of 473 cervical dystonia cases and 481 controls. Gene-based analysis identified DENND1A to be significantly associated with cervical dystonia (P-value  $1.23 \times 10^{-6}$ ). One low-frequency variant was associated with lower age-at-onset ( $16.4 \pm 2.9$  years, P-value =  $3.07 \times 10^{-8}$ , minor allele frequency = 0.01), located within the GABBR2 gene on chromosome 9 (rs147331823). CONCLUSION: The genetic underpinnings of cervical dystonia are complex and likely consist of multiple distinct variants of small effect sizes. Larger sample sizes may be needed to provide sufficient statistical power to address the presumably multi-genetic etiology of cervical dystonia. © 2021 International Parkinson and Movement Disorder Society.

## Neurology

Zafar SF, Rosenthal ES, Jing J, Ge W, Tabaeizadeh M, **Nour HA**, Shoukat M, Sun H, Javed F, Kassa S, Edhi M, Bordbar E, Gallagher J, Moura V, Jr., Ghanta M, Shao YP, An S, Sun J, Cole AJ, and Westover MB. Automated Annotation of Epileptiform Burden and Its Association with Outcomes. *Ann Neurol* 2021; 90(2):300-311. PMID: 34231244. [Full Text](#)

**OBJECTIVE:** This study was undertaken to determine the dose-response relation between epileptiform activity burden and outcomes in acutely ill patients. **METHODS:** A single center retrospective analysis was made of 1,967 neurologic, medical, and surgical patients who underwent >16 hours of continuous electroencephalography (EEG) between 2011 and 2017. We developed an artificial intelligence algorithm to annotate 11.02 terabytes of EEG and quantify epileptiform activity burden within 72 hours of recording. We evaluated burden (1) in the first 24 hours of recording, (2) in the 12-hours epoch with highest burden (peak burden), and (3) cumulatively through the first 72 hours of monitoring. Machine learning was applied to estimate the effect of epileptiform burden on outcome. Outcome measure was discharge modified Rankin Scale, dichotomized as good (0-4) versus poor (5-6). **RESULTS:** Peak epileptiform burden was independently associated with poor outcomes ( $p < 0.0001$ ). Other independent associations included age, Acute Physiology and Chronic Health Evaluation II score, seizure on presentation, and diagnosis of hypoxic-ischemic encephalopathy. Model calibration error was calculated across 3 strata based on the time interval between last EEG measurement (up to 72 hours of monitoring) and discharge: (1) <5 days between last measurement and discharge, 0.0941 (95% confidence interval [CI] = 0.0706-0.1191); 5 to 10 days between last measurement and discharge, 0.0946 (95% CI = 0.0631-0.1290); >10 days between last measurement and discharge, 0.0998 (95% CI = 0.0698-0.1335). After adjusting for covariates, increase in peak epileptiform activity burden from 0 to 100% increased the probability of poor outcome by 35%. **INTERPRETATION:** Automated measurement of peak epileptiform activity burden affords a convenient, consistent, and quantifiable target for future multicenter randomized trials investigating whether suppressing epileptiform activity improves outcomes. *ANN NEUROL* 2021;90:300-311.

## Neurosurgery

Barekatain Y, Ackroyd JJ, Yan VC, Khadka S, Wang L, Chen KC, Poral AH, Tran T, Georgiou DK, Arthur K, Lin YH, Satani N, Ballato ES, Behr EI, **deCarvalho AC**, Verhaak RGW, de Groot J, Huse JT, Asara JM, Kalluri R, and Muller FL. Homozygous MTAP deletion in primary human glioblastoma is not associated with elevation of methylthioadenosine. *Nat Commun* 2021; 12(1):4228. PMID: 34244484. [Full Text](#)

Homozygous deletion of methylthioadenosine phosphorylase (MTAP) in cancers such as glioblastoma represents a potentially targetable vulnerability. Homozygous MTAP-deleted cell lines in culture show elevation of MTAP's substrate metabolite, methylthioadenosine (MTA). High levels of MTA inhibit protein arginine methyltransferase 5 (PRMT5), which sensitizes MTAP-deleted cells to PRMT5 and methionine adenosyltransferase 2A (MAT2A) inhibition. While this concept has been extensively corroborated in vitro, the clinical relevance relies on exhibiting significant MTA accumulation in human glioblastoma. In this work, using comprehensive metabolomic profiling, we show that MTA secreted by MTAP-deleted cells in vitro results in high levels of extracellular MTA. We further demonstrate that homozygous MTAP-deleted primary glioblastoma tumors do not significantly accumulate MTA in vivo due to metabolism of MTA by MTAP-expressing stroma. These findings highlight metabolic discrepancies between in vitro models and primary human tumors that must be considered when developing strategies for precision therapies targeting glioblastoma with homozygous MTAP deletion.

### Neurosurgery

Kim RB, Scoville JP, Karsy M, **Lim S**, Jensen RL, and Menacho ST. Work relative value units and perioperative outcomes in patients undergoing brain tumor surgery. *Neurosurg Rev* 2021; Epub ahead of print. PMID: 34236568. [Request Article](#)

The work relative value unit (wRVU) is a commonly cited surrogate for surgical complexity; however, it is highly susceptible to subjective interpretation and external forces. Our objective was to evaluate whether wRVU is associated with perioperative outcomes, including complications, after brain tumor surgery. The 2006-2014 American College of Surgeons National Surgical Quality Improvement Program database was queried to identify patients  $\geq 18$  years who underwent brain tumor resection. Patients were categorized into approximate quintiles based on total wRVU. The relationship between wRVU and several perioperative outcomes was assessed with univariate and multivariate analyses. Subgroup analyses were performed using a Current Procedural Terminology code common to all wRVU groups. The 16,884 patients were categorized into wRVU ranges 0-30.83 (4664 patients), 30.84-34.58 (2548 patients), 34.59-38.04 (3147 patients), 38.05-45.38 (3173 patients), and  $\geq 45.39$  (3352 patients). In multivariate logistic regression analysis, increasing wRVU did not predict more 30-day postoperative complications, except respiratory complications and need for blood transfusion. Linear regression analysis showed that wRVU was poorly correlated with operative duration and length of stay. On multivariate analysis of the craniectomy subgroup, wRVU was not associated with overall or respiratory complications. The highest wRVU group was still associated with greater risk of requiring blood transfusion (OR 3.01,  $p < 0.001$ ). Increasing wRVU generally did not correlate with 30 days postoperative complications in patients undergoing any surgery for brain tumor resection; however, the highest wRVU groups may be associated with greater risk of respiratory complications and need for transfusion. These finding suggests that wRVU may be a poor surrogate for case complexity.

### Neurosurgery

**Macki M, Anand SK, Hamilton T, Lim S, Mansour T, Bazydlo M, Schultz L, Abdulhak MM, Khalil JG, Park P, Aleem I, Easton R, Schwalb JM, Nerenz D, and Chang V.** Analysis of Factors associated with Return to Work After Lumbar Surgery up to 2-years follow-up: A Michigan Spine Surgery Improvement Collaborative (MSSIC) Study. *Spine (Phila Pa 1976)* 2021; Epub ahead of print. PMID: 34265812. [Full Text](#)

**STUDY DESIGN:** Michigan Spine Surgery Improvement Collaborative (MSSIC) prospectively collects data on all patients undergoing operations for degenerative and/or deformity indications. **OBJECTIVE:** We aimed to identify which factors are significantly associated with return-to-work after lumbar surgery at long-term follow-up. **SUMMARY OF BACKGROUND DATA:** Prior publications have created a clinically relevant predictive model for return-to-work, wherein education, gender, race, comorbidities, and preoperative symptoms increased likelihood of return-to-work at 3months after lumbar surgery. We sought to determine if these trends 1) persisted at 1 year and 2years postoperatively; or 2) differed among preoperatively employed versus unemployed patients. **METHODS:** MSSIC was queried for all patients undergoing lumbar operations (2014-2019). All patients intended to return-to-work postoperatively. Patients were followed for up to 2years postoperatively. Measures of association were calculated with multivariable generalized estimating equations (GEE). **RESULTS:** Return-to-work increased from 63% (3542/5591) at 90days postoperatively to 75% (3143/4147) at 1 year and 74% (2133/2866) at 2 years postoperatively. Following GEE, neither clinical nor surgical variables predicted return-to-work at all three time intervals: 90days, 1 year, and 2years postoperatively. Only socioeconomic factors reached statistical significance at all follow-up points. Preoperative

employment followed by insurance status had the greatest associations with return-to-work. In a sub-analysis of patients who were preoperatively employed, insurance was the only factor with significant associations with return-to-work at all three follow-up intervals. The return-to-work rates among unemployed patients at baseline increased from 29% (455/1100) at 90days, 44% (495/608) at 1 year, and 46% (366/426) at 2years postoperatively. The only two significant factors associated with return-to-work at all three follow-up intervals were Medicaid, as compared to private insurance, and male gender. **CONCLUSION:** In patients inquiring about long-term return-to-work after lumbar surgery, insurance status represents the important determinant of employment status. Level of Evidence: 2.

#### Neurosurgery

**Zervos TM, Asmaro K, and Air EL.** In Reply: Contemporary Analysis of Minimal Clinically Important Difference in the Neurosurgical Literature. *Neurosurgery* 2021; Epub ahead of print. PMID: 34293157. [Full Text](#)

#### Nursing

**Al-Bizri LA, Vahia AT, Rizvi K, Bardossy AC, Robinson PK, Shelters RT, Klotz S, Starr PM, Reyes KQ, Suleyman G, and Alangaden GJ.** Effect of a urine culture stewardship initiative on urine culture utilization and catheter-associated urinary tract infections in intensive care units. *Infect Control Hosp Epidemiol* 2021; Epub ahead of print.:1-4. PMID: 34236024. [Full Text](#)

**OBJECTIVE:** Urine cultures have poor specificity for catheter-associated urinary tract infections (CAUTIs). We evaluated the effect of a urine-culture stewardship program on urine culture utilization and CAUTI in adult intensive care units (ICUs). **DESIGN:** A quasi-interventional study was performed from 2015 to 2017. **SETTING AND PATIENTS:** The study cohort comprised 21,367 patients admitted to the ICU at a teaching hospital. **INTERVENTION:** The urine culture stewardship program included monthly 1-hour discussions with ICU house staff emphasizing avoidance of "pan-culture" for sepsis workup and obtaining urine culture only if a urinary source of sepsis is suspected. The urine culture utilization rate metric (UCUR; ie, no. urine cultures/catheter days  $\times$ 100) was utilized to measure the effect. Monthly UCUR, catheter utilization ratio (CUR), and CAUTI rate were reported on an interactive quality dashboard. To ensure safety, catheterized ICU patients (2015-2016) were evaluated for 30-day readmission for UTI. Time-series data and relationships were analyzed using Spearman correlation coefficients and regression analysis. **RESULTS:** Urine culture utilization decreased from 3,081 in 2015 to 2,158 in 2016 to 1,218 in 2017. CAUTIs decreased from 78 in 2015 to 60 in 2016 and 28 in 2017. Regression analysis over time showed significant decreases in UCUR ( $r$ , 0.917;  $P$  < .0001) and CAUTI rate ( $r$ , 0.657;  $P$  < .0001). The co-correlation between UCUR and CAUTI rate was ( $r$ , 0.625;  $P$  < .0001) compared to CUR and CAUTI rate ( $r$ , 0.523;  $P$  = .004). None of these patients was readmitted with a CAUTI. **CONCLUSIONS:** Urine culture stewardship program was effective and safe in reducing UC overutilization and was correlated with a decrease in CAUTIs. Addition of urine-culture stewardship to standard best practices could reduce CAUTI in ICUs.

#### Obstetrics, Gynecology and Women's Health Services

Wahid M, Dar SA, Jawed A, Mandal RK, Akhter N, Khan S, Khan F, Jogiah S, Rai AK, and **Rattan R.** Microbes in gynecologic cancers: Causes or consequences and therapeutic potential. *Semin Cancer Biol* 2021; Epub ahead of print. PMID: 34302959. [Full Text](#)

Gynecologic cancers, starting in the reproductive organs of females, include cancer of cervix, endometrium, ovary commonly and vagina and vulva rarely. The changes in the composition of microbiome in gut and vagina affect immune and metabolic signaling of the host cells resulting in chronic inflammation, angiogenesis, cellular proliferation, genome instability, epithelial barrier

breach and metabolic dysregulation that may lead to the onset or aggravated progression of gynecologic cancers. While microbiome in gynecologic cancers is just at horizon, certain significant microbiome signature associations have been found. Cervical cancer is accompanied with high loads of human papillomavirus, Fusobacteria and Sneathia species; endometrial cancer is reported to have presence of Atopobium vaginae and Porphyromonas species and significantly elevated levels of Proteobacteria and Firmicutes phylum bacteria, with Chlamydia trachomatis, Lactobacillus and Mycobacterium reported in ovarian cancer. Balancing microbiome composition in gynecologic cancers has the potential to be used as a therapeutic target. For example, the Lactobacillus species may play an important role in blocking adhesions of incurative pathogens to vaginal epithelium by lowering the pH, producing bacteriocins and employing competitive exclusions. The optimum or personalized balance of the microbiota can be maintained using pre- and probiotics, and fecal microbiota transplantations loaded with specific bacteria. Current evidence strongly suggest that a healthy microbiome can train and trigger the body's immune response to attack various gynecologic cancers. Furthermore, microbiome modulations can potentially contribute to improvements in immuno-oncology therapies.

#### Obstetrics, Gynecology and Women's Health Services

**Yahya JB, Zhu S, Burmeister C, Hijaz MY, and Elshaikh MA.** Matched-pair Analysis for Survival Endpoints Between Women With Early-stage Uterine Carcinosarcoma and Uterine Serous Carcinoma. *Am J Clin Oncol* 2021; Epub ahead of print. PMID: 34265785. [Full Text](#)

**OBJECTIVE:** The objective of this study was to compare survival endpoints between women with uterine carcinosarcoma and those with uterine serous carcinoma utilizing matching analysis. **METHODS:** Patients with stages I to II who underwent hysterectomy at our institution were included in this analysis. Patients with carcinosarcoma were then matched to patients with serous carcinoma based on stage, and adjuvant management received (observation, radiation treatment alone, chemotherapy alone, or combined modality with radiotherapy and chemotherapy. Recurrence-free survival, disease-specific survival, and overall survival were calculated for the 2 groups. **RESULTS:** A total of 134 women were included (67 women with carcinosarcoma and 67 with serous carcinoma, matched 1:1). There was no statistically significant difference between the 2 groups regarding 5-year recurrence-free survival (59% vs. 62%), disease-specific survival (66% vs. 67%), or overall survival (53% vs. 57%), respectively. The only independent predictor of shorter recurrence-free survival for the entire cohort was the lack of adjuvant combined modality therapy, while lower uterine segment involvement was the only independent predictor for shorter disease-specific survival. Lack of lymph node dissection and lack of adjuvant combined modality therapy were independent predictors of shorter overall survival. **DISCUSSION:** When matched based on stage and adjuvant treatment, our study suggests that there is no statistically significant difference in survival endpoints between women with early-stage carcinosarcoma and serous carcinoma. Adjuvant combined modality treatment is an independent predictor of longer recurrence-free survival and overall survival.

#### Orthopedics/Bone and Joint Center

**Jildeh TR, Abbas MJ,** Hengy MH, O'Brien H, Gani GS, and Okoroha KR. Informed Consent for the Orthopaedic Surgeon. *JBJS Rev* 2021; 9(7). PMID: 34270504. [Full Text](#)

In the United States, orthopaedic surgeons have a legal obligation to obtain informed consent from patients before performing surgery; it is a process that includes a signed written document. There are specific legal requirements that vary somewhat by state but generally include disclosure and documentation of the diagnosis, an explanation of the recommended procedure, a conversation about the risks and benefits of the procedure, and a discussion about alternative

treatments. Inadequate disclosure of risks and alternatives is associated with increased indemnity risk. Studies have shown that many consent processes and forms are suboptimal.

Orthopedics/Bone and Joint Center

**Montgomery ZA, Yedulla NR, Koolmees D, Battista E, Parsons Iii TW, and Day CS.** Are orthopaedic providers willing to work overtime to address COVID-19-related patient backlogs and financial deficits? *Bone Jt Open* 2021; 2(7):562-568. PMID: 34320326. [Full Text](#)

AIMS: COVID-19-related patient care delays have resulted in an unprecedented patient care backlog in the field of orthopaedics. The objective of this study is to examine orthopaedic provider preferences regarding the patient care backlog and financial recovery initiatives in response to the COVID-19 pandemic. METHODS: An orthopaedic research consortium at a multi-hospital tertiary care academic medical system developed a three-part survey examining provider perspectives on strategies to expand orthopaedic patient care and financial recovery. Section 1 asked for preferences regarding extending clinic hours, section 2 assessed surgeon opinions on expanding surgical opportunities, and section 3 questioned preferred strategies for departmental financial recovery. The survey was sent to the institution's surgical and nonoperative orthopaedic providers. RESULTS: In all, 73 of 75 operative (n = 55) and nonoperative (n = 18) providers responded to the survey. A total of 92% of orthopaedic providers (n = 67) were willing to extend clinic hours. Most providers preferred extending clinic schedule until 6pm on weekdays. When asked about extending surgical block hours, 96% of the surgeons (n = 53) were willing to extend operating room (OR) block times. Most surgeons preferred block times to be extended until 7pm (63.6%, n = 35). A majority of surgeons (53%, n = 29) believe that over 50% of their surgical cases could be performed at an ambulatory surgery centre (ASC). Of the strategies to address departmental financial deficits, 85% of providers (n = 72) were willing to work extra hours without a pay cut. CONCLUSION: Most orthopaedic providers are willing to help with patient care backlogs and revenue recovery by working extended hours instead of having their pay reduced. These findings provide insights that can be incorporated into COVID-19 recovery strategies. Level of Evidence: III Cite this article: *Bone Jt Open* 2021;2(7):562-568.

Orthopedics/Bone and Joint Center

**Moutzouros V, and Jildeh TR.** Hybrid Remnant-Sparing Anterior Cruciate Ligament Repair-Reconstruction. *Arthrosc Tech* 2021; 10(7):e1717-e1721. PMID: 34336569. [Full Text](#)

In anterior cruciate ligament (ACL) reconstruction, the remnant ACL is often debrided in an effort to improve visualization of patient anatomy and reduce surgical difficulty. However, retention of the tibial remnant of a torn ACL theoretically portends several advantages. These include preservation of knee proprioception and mechanoreceptors, an enhanced biological environment for healing, and accelerated revascularization and ligamentization of the graft. Despite these advantages, it is not a widely adopted practice and the optimal technique is still subject to debate. The purpose of this technical note is to describe our preferred technique for performing hybrid ACL reconstruction with remnant incorporation.

Orthopedics/Bone and Joint Center

Muscatelli SR, **Charters MA**, and Hallstrom BR. Time for an Update? A Look at Current Guidelines for Venous Thromboembolism Prophylaxis After Hip and Knee Arthroplasty and Hip Fracture. *Arthroplast Today* 2021; 10:105-107. PMID: 34337116. [Full Text](#)

Venous thromboembolism is a well-established complication of total hip and knee arthroplasty and hip fracture surgery. Clinical practice guidelines have been proposed to help clinicians

provide prophylaxis against this risk. However, most guidelines reference data that are becoming outdated because of new advances in perioperative protocols. Recent data would suggest that aspirin may be appropriate for most patients after total hip and knee replacement and a more potent chemoprophylaxis for higher risk patients. Low-molecular-weight heparin remains the recommended choice after hip fracture surgery, although there is a paucity of recent literature in this patient population. There are randomized trials currently underway in the arthroplasty population that may guide clinicians in the appropriate choice of chemoprophylaxis. These studies should inform updates to the current clinical practice guidelines.

#### Orthopedics/Bone and Joint Center

Pahuta MA, **Fisk F**, Versteeg AL, Fisher CG, Sahgal A, Gokaslan ZL, Reynolds J, Laufer I, Lazary A, Rhines LD, Boriani S, Bettegowda C, and Dea N. Calculating Utilities from the Spine Oncology Study Group Outcomes Questionnaire: A Necessity for Economic and Decision Analysis. *Spine (Phila Pa 1976)* 2021; Epub ahead of print. PMID: 34334684. [Full Text](#)

**STUDY DESIGN:** General population utility valuation study. **OBJECTIVE:** To develop a technique for calculating utilities from the Spine Oncology Study Group Outcomes Questionnaire v2.0 (SOSGOQ2.0). **SUMMARY OF BACKGROUND DATA:** The ability to calculate quality-adjusted life-years (QALYs) for metastatic spine disease would enhance treatment decision making and facilitate economic analysis. QALYs are calculated using utilities. **METHODS:** Using a hybrid concept-retention and factorial analysis shortening approach, we first shortened the SOSGOQ2.0 to eight items (SOSGOQ-8D). This was done to lessen the cognitive burden of the utility valuation exercise. A general population sample of 2730 adults was then asked to evaluate 12 choice sets based on SOSGOQ-8D health states in a Discrete Choice Experiment. A utility scoring rubric was then developed using a mixed multinomial-logit regression model. **RESULTS:** We were able to reduce the SOSGOQ2.0 to an SOSGOQ-8D with a mean error of 0.003 and mean absolute error of 3.078 compared to the full questionnaire. The regression model demonstrated good predictive performance and was used to develop a utility scoring rubric. Regression results revealed that participants did not regard all SOSGOQ-8D items as equally important. **CONCLUSION:** We provide a simple technique for converting the SOSGOQ2.0 to utilities. The ability to evaluate QALYs in metastatic spine disease will facilitate economic analysis and patient counselling. We also quantify the importance of individual SOSGOQ-8D items. Clinicians should heed these findings and offer treatments that maximize function in the most important items. Level of Evidence: 3.

#### Orthopedics/Bone and Joint Center

**Ruder MC, Zuel R, Diefenbach BJ, and Bey MJ.** Quantifying shoulder activity after rotator cuff repair: Technique and preliminary results. *J Orthop Res* 2021; Epub ahead of print. PMID: 34191325. [Full Text](#)

Repair tissue healing after rotator cuff repair remains a significant clinical problem, and excessive shoulder activity after surgical repair is believed to contribute to re-tears. In contrast, small animal studies have demonstrated that complete removal of activity impairs tendon healing and have advocated for an "appropriate" level of activity, but in humans the appropriate amount of shoulder activity to enhance healing is not known. As an initial step toward understanding the relationship between postoperative shoulder activity and repair tissue healing, the objectives of this study were to assess the precision, accuracy, and feasibility of a wrist-worn triaxial accelerometer for measuring shoulder activity. Following assessments of precision ( $\pm 0.002$  g) and accuracy ( $\pm 0.006$  g), feasibility was assessed by measuring 1 week of shoulder activity in 14 rotator cuff repair patients and 8 control subjects. Shoulder activity was reported in terms of volume (mean acceleration, activity count, mean activity index, active time)



and intensity (intensity gradient). Patients had significantly less volume ( $p \leq .03$ ) and intensity ( $p = .01$ ) than controls. Time post-surgery was significantly associated with the volume ( $p \leq .05$  for mean acceleration, activity count, and mean activity index) and intensity ( $p = .03$ ) of shoulder activity, but not active time ( $p = .08$ ). These findings indicate this approach has the accuracy and precision necessary to continuously monitor shoulder activity with a wrist-worn sensor. The preliminary data demonstrate the ability to discriminate between healthy control subjects and patients recovering from rotator cuff repair and provide support for using a wearable sensor to monitor changes over time in shoulder activity.

Orthopedics/Bone and Joint Center

**Shaw JH, Lindsay-Rivera KG, Buckley PJ, Weir RM, Banka TR, and Davis JJ.** Minimal Clinically Important Difference in Robotic-Assisted Total Knee Arthroplasty Versus Standard Manual Total Knee Arthroplasty. *J Arthroplasty* 2021; 36(7s):S233-s241. PMID: 33692001. [Full Text](#)

**BACKGROUND:** The purpose of this study was to determine whether robotic total knee arthroplasty (R-TKA) demonstrated evidence of improvement in minimal clinically important difference (MCID) in early (<4 weeks) and intermittent (4-8 month) patient-reported outcomes compared with manual total knee arthroplasty (M-TKA). **METHODS:** A prospectively collected database was reviewed of 1160 consecutive patients undergoing R-TKA or M-TKA from December 2017 to October 2019. Primary outcomes consisted of Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS-JR) and Patient-Reported Outcomes Measurement Information System Global Health Measures of Physical Health (PH) and Mental Health (MH). Statistical analysis included MCID via the distribution method. **RESULTS:** Univariate analysis demonstrated conflicting results for early MCID achievement favoring M-TKA (4-week KOOS-JR,  $P = .03$ ) for the multisurgeon cohort, but favored R-TKA (4-week Patient-Reported Outcomes Measurement Information System-PH,  $P = .04$ ) in the single-surgeon analysis, and the remaining outcome scores were similar. Ultimately, multivariate analysis demonstrated similar 4-week and 6-month MCID achievement in all measures. Lower preoperative scores consistently achieved MCID at a higher rate in M-TKA, although in R-TKA, the higher baseline scores improved at a rate comparable with those with lower scores in all but the short-term postoperative KOOS-JR. **CONCLUSION:** R-TKA demonstrated comparable MCID achievement to M-TKA across the larger cohort. Single-surgeon comparison did show some early benefit. Confounding variables such as surgical technique, implant fixation, and responsiveness of an outcome measure may be as important as simply what tools are used during surgery. Such granular data should be sought out in future studies.

Orthopedics/Bone and Joint Center

**Tramer JS, Patel R, Kuhlmann NA, and Muh SJ.** Simultaneous, Ipsilateral Distal Biceps and Distal Triceps Rupture in Healthy Weight Lifter: A Case Report. *JBJS Case Connect* 2021; 11(3). PMID: 34252056. [Full Text](#)

**CASE:** A 38-year-old weight lifter presented with a complete distal biceps rupture with retraction and a near complete ipsilateral distal triceps tear sustained during the bench press exercise. The tendons were fixed operatively using a simultaneous posterior and anterolateral approach to the elbow. **CONCLUSION:** Simultaneous, ipsilateral distal biceps and distal triceps tendon injury is a rare occurrence that leads to significant functional loss. Repair of distal biceps rupture using a single-incision technique with a cortical button and distal triceps using a double-row suture anchor repair was successful in restoring functional anatomy to our patient.

Orthopedics/Bone and Joint Center

**Yedulla NR, Faraj MT, Koolmees DS, Battista EB, Montgomery ZA, and Day CS.** Assessing Orthopedic Patient Preferences for Mandated Virtual Care During the COVID-19 Pandemic and Elective Virtual Care in Non-Pandemic Circumstances. *Orthopedics* 2021; 44(4):e471-e476. PMID: 34292825. [Request Article](#)

The purpose of this study was to compare orthopedic patient preferences for mandated virtual care during the coronavirus disease 2019 (COVID-19) pandemic and elective virtual care during non-pandemic circumstances. An orthopedic virtual care questionnaire was administered to adult orthopedic patients undergoing their first orthopedic virtual visit between March 15, 2020, and May 18, 2020. The questionnaire had 13 items rated on a 1-to-5 Likert scale ("strongly agree" to "strongly disagree"). Responses were compared using Kruskal-Wallis and nonparametric Wilcoxon rank-sum tests. Patients showed higher preferences for mandated virtual care during the pandemic when compared with elective virtual care during non-pandemic circumstances ( $2.25 \pm 1.31$  vs  $4.10 \pm 1.25$ ,  $P < .0001$ ) and also preferred virtual visits in other specialties compared with orthopedics ( $2.17 \pm 1.35$  vs  $2.79 \pm 1.42$ ,  $P < .0001$ ). Patients older than 50 years were more likely to view virtual care as the best option during the pandemic ( $2.06 \pm 1.25$  vs  $2.48 \pm 1.35$ ,  $P < .0165$ ) and equally as effective as in-person visits in non-pandemic circumstances ( $2.45 \pm 1.36$  vs  $2.83 \pm 1.18$ ,  $P < .0150$ ). Female patients were more likely to pursue future orthopedic virtual visits ( $2.61 \pm 1.37$  vs  $3.07 \pm 1.45$ ,  $P < .0203$ ) and view their virtual visit as equally effective as an in-person visit ( $2.47 \pm 1.33$  vs  $2.87 \pm 1.18$ ,  $P < .0181$ ). Orthopedic patient preference for mandated virtual care during the COVID-19 pandemic seems to be higher than for elective virtual care during non-pandemic circumstances, and older and female patients appear to favor virtual care. [*Orthopedics*. 2021;44(4):e471-e476.].

Orthopedics/Bone and Joint Center

**Yu CC, Fidai M, Washington T, Bartol S, and Graziano G.** Oral- is as Effective as Intravenous Tranexamic Acid at Reducing Blood Loss in Thoracolumbar Spinal Fusions: A Prospective Randomized Trial. *Spine (Phila Pa 1976)* 2021; Epub ahead of print. PMID: 34224510. [Full Text](#)

**STUDY DESIGN:** A prospective randomized trial at a university affiliated tertiary medical center between February 2017 and March 2020. **OBJECTIVE:** Compare perioperative blood loss in patients undergoing elective posterior thoracolumbar fusion who were treated with IV versus PO TXA. **SUMMARY OF BACKGROUND DATA:** The use of antifibrinolytic agents such as tranexamic acid (TXA) to decrease operative blood loss and allogenic blood transfusions is well documented in the literature. While evidence supports the use of intravenous (IV) and topical formulations of TXA in spine surgery, the use of oral (PO) TXA has not been studied. **METHODS:** 261 patients undergoing thoracolumbar fusion were randomized to receive 1.95g of PO TXA 2hours preoperatively or 2g IV TXA (1g before incision and 1g before wound closure) intraoperatively. The sample was further stratified into 3 categories based on number of levels fused (1-2 level fusions, 3-5, and >5). The primary outcome was the reduction of hemoglobin. Secondary outcomes included calculated blood loss, drain output, postoperative transfusion, complications, and length of hospital stay. Equivalence analysis was performed with a two one-sided test (TOST). **RESULTS:** 137 patients received IV and 124 received PO TXA. The average age was  $62 \pm 13$  years (Mean  $\pm$  SD), including 141 females and 120 males. Revision cases comprised of 67% of the total sample. Patient demographic factors were similar between groups except for weight, BMI, and preoperative platelet count. The mean reduction of hemoglobin was similar between IV and PO groups (3.56 vs. 3.28g/dL, respectively;  $P = 0.002$ , equivalence). IV TXA group had a higher transfusion rate compared to PO TXA group (22 patients [19%] vs. 12 patients [10%];  $P = 0.03$ ). In addition, IV group had longer length of stay (LOS) than PO group (4.4 vs. 3.7 days;  $P = 0.02$ ). **CONCLUSION:** Patients treated with IV and PO TXA experienced

the same perioperative blood loss after small and large spinal fusions. In subgroup analysis, the intermediate (3-5 level) spinal fusions had less blood loss with PO TXA than IV TXA. Given its lower cost, PO TXA represents a superior alternative to IV TXA in patients undergoing elective posterior thoracolumbar fusion and may improve healthcare cost-efficiency in the studied population. Level of Evidence: 1.

Orthopedics/Bone and Joint Center

Zhou Y, Chen C, Cheng M, Alshahrani Y, **Franovic S, Lau E**, Xu G, Ni G, Cavanaugh JM, **Muh S**, and Lemos S. Comparison of machine learning methods in sEMG signal processing for shoulder motion recognition. *Biomed Signal Process Control* 2021; 68. PMID: Not assigned.

[Request Article](#)

Machine learning (ML) methods have been previously applied and compared in pattern recognition of hand and elbow motions based on surface electromyographic (sEMG) signals. However, there are only a few studies that have investigated the ML methods for shoulder motion pattern recognition. This study compared the efficiency of ML algorithms, including support vector machine (SVM), logistic regression (LR), and artificial neural network (ANN) in processing sEMG signals for shoulder motion pattern recognition. This study also investigated the effects of sliding time window epoch on the recognition accuracy. Eighteen healthy subjects were recruited for this study, their EMG signals were collected from twelve muscles during performing activities of daily living (ADL) motions including drinking, pushing forward/pulling backward, and abduction/adduction. The 80 % of recorded sEMG datasets were used for model training to build the ML models and 20 % were used for model validation and determination of the accuracy of ML algorithms in motion pattern recognition. The influence of sliding time window sizes was studied for algorithm optimization. Statistical analysis was performed to determine the difference in the accuracy of ML methods. Results showed that there was a significant difference among the three machine learning methods and different sliding time window sizes. There was not a significant difference in overlapping time. The highest accuracy was  $97.41 \pm 1.8$  % using the SVM method with a sliding time window of 270 ms. Machine learning techniques provided a quick approach for shoulder motion pattern recognition. The better classifier for pattern recognition of shoulder motion was SVM.

Orthopedics/Bone and Joint Center

**Ziedas A, Abed V, Swantek A, Cross A, Chaides S, Rahman T, and Makhni EC.** Social Determinants of Health Influence Access to Care and Outcomes in Patients Undergoing Anterior Cruciate Ligament Reconstruction: A Systematic Review. *Arthroscopy* 2021; Epub ahead of print. PMID: 34252555. [Full Text](#)

**PURPOSE:** To investigate the impact social determinants of health (SDOH) have on accessing orthopedic treatment following an anterior cruciate ligament injury, as well as patient-reported and surgical outcomes following anterior cruciate ligament reconstruction (ACLR). **METHODS:** A systematic search of the PubMed, MEDLINE, Epub Ahead of Print, Embase, and Web of Science databases was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to identify studies that reported at least one SDOH and its effect on patient-reported outcomes or surgical outcomes following anterior cruciate ligament reconstruction. Our search identified 937 studies. After eliminating 273 duplicates, two authors screened 664 articles based on title and abstract. Following this initial screen, 76 studies were evaluated for data extraction. Studies were categorized based on the social determinant(s) of health reported. **RESULTS:** Twenty-two articles published between 2002 and 2020 were included in this study, encompassing 15 retrospective cohort studies, 3 prospective cohort studies, 3 cross-sectional studies, and 1 case-control study from 9 journals

across 3 countries. Of these papers, 9 articles investigated race/ethnicity, 8 investigated insurance status, 4 investigated income, 5 investigated education level, 2 investigated employment status, and 5 investigated socioeconomic status. Reported outcomes included time to treatment, concomitant knee injury, patient-reported outcome measurement scores, postoperative complications, need for additional surgery, and postoperative healthcare utilization. **CONCLUSION:** Certain SDOH, including Black race, Hispanic ethnicity, public health insurance, and lower socioeconomic status contribute to a delay in access to care, which may result in increased severity of concomitant knee injuries encountered at the time of anterior cruciate ligament reconstruction and inferior outcomes. **STUDY DESIGN:** Level III, systematic review of level I-III evidence.

#### Otolaryngology – Head and Neck Surgery

Calderón-Garcidueñas L, Rajkumar RP, Stommel EW, Kulesza R, **Mansour Y**, Rico-Villanueva A, Flores-Vázquez JO, Brito-Aguilar R, Ramírez-Sánchez S, García-Alonso G, Chávez-Franco DA, Luévano-Castro SC, García-Rojas E, Revueltas-Ficachi P, Villarreal-Ríos R, and Mukherjee PS. Brainstem Quadruple Aberrant Hyperphosphorylated Tau, Beta-Amyloid, Alpha-Synuclein and TDP-43 Pathology, Stress and Sleep Behavior Disorders. *Int J Environ Res Public Health* 2021; 18(13). PMID: 34206224. [Full Text](#)

Quadruple aberrant hyperphosphorylated tau (p- $\tau$ ), amyloid- $\beta$  peptide, alpha-synuclein and TDP-43 brainstem and supratentorial pathology are documented in forensic  $\leq 40$ y autopsies in Metropolitan Mexico City (MMC), and p- $\tau$  is the major aberrant protein. Post-traumatic stress disorder (PTSD) is associated with an elevated risk of subsequent dementia, and rapid eye movement sleep behavior disorder (RBD) is documented in PD, AD, Lewy body dementia and ALS. This study aimed to identify an association between PTSD and potential pRBD in Mexico. An anonymous online survey of 4502 urban college-educated adults,  $29.3 \pm 10.3$  years; MMC, n = 1865; non-MMC, n = 2637, measured PTSD symptoms using the Impact of Event Scale-Revised (IES-R) and pRBD symptoms using the RBD Single-Question. Over 50% of the participants had IES-R scores  $\geq 33$  indicating probable PTSD. pRBD was identified in 22.6% of the participants across Mexico and 32.7% in MMC residents with PTSD. MMC subjects with PTSD had an OR 2.6218 [2.5348, 2.7117] of answering yes to the pRBD. PTSD and pRBD were more common in women. This study showed an association between PTSD and pRBD, strengthening the possibility of a connection with misfolded proteinopathies in young urbanites. We need to confirm the RBD diagnosis using an overnight polysomnogram. Mexican women are at high risk for stress and sleep disorders.

#### Otolaryngology – Head and Neck Surgery

**Craig JR, Cheema AJ, Dunn RT, Vemuri S, and Peterson EL.** Extrasinus Complications From Odontogenic Sinusitis: A Systematic Review. *Otolaryngol Head Neck Surg* 2021; Epub ahead of print. PMID: 34253072. [Full Text](#)

**OBJECTIVE:** Odontogenic sinusitis (ODS) can cause infectious orbital, intracranial, and osseous complications. Diagnosis and management of complicated ODS have not been discussed in recent sinusitis guidelines. The purpose of this systematic review was to describe epidemiological and clinical features, as well as management strategies of complicated ODS. **DATA SOURCES:** PubMed, EMBASE, and Cochrane Library. **REVIEW METHODS:** A systematic review was performed to describe various features of complicated ODS. All complicated ODS studies were included in qualitative analysis, but studies were only included in quantitative analysis if they reported specific patient-level data. **RESULTS:** Of 1126 studies identified, 75 studies with 110 complicated ODS cases were included in qualitative analysis, and 47 studies with 62 orbital and intracranial complications were included in quantitative analyses.

About 70% of complicated ODS cases were orbital complications. Only 23% of complicated ODS studies were published in otolaryngology journals. Regarding ODS-related orbital and intracranial complications, about 80% occurred in adults, and 75% were male. Complicated ODS occurred most commonly from apical periodontitis of maxillary molars. There were no relationships between sinusitis extent and orbital or intracranial complications. High rates of anaerobic and  $\alpha$ -hemolytic streptococcal bacteria were identified in complicated ODS. Management generally included systemic antibiotics covering aerobic and anaerobic bacteria, and surgical interventions were generally performed to address both the complications (orbital and/or intracranial) and possible infectious sources (dentition and sinuses). **CONCLUSION:** ODS should be considered in all patients with infectious extrasinus complications. Multidisciplinary management between otolaryngologists, dental specialists, ophthalmologists, and neurosurgeons should be considered to optimize outcomes.

#### Otolaryngology – Head and Neck Surgery

**Gardinier JD.** The Diminishing Returns of Mechanical Loading and Potential Mechanisms that Desensitize Osteocytes. *Curr Osteoporos Rep* 2021; Epub ahead of print. PMID: 34216359. [Full Text](#)

Adaptation to mechanical loading is critical to maintaining bone mass and offers therapeutic potential to preventing age-related bone loss and osteoporosis. However, increasing the duration of loading is met with "diminishing returns" as the anabolic response quickly becomes saturated. As a result, the anabolic response to daily activities and repetitive bouts of loading is limited by the underlying mechanisms that desensitize and render bone unresponsive at the cellular level. Osteocytes are the primary cells that respond to skeletal loading and facilitate the overall anabolic response. Although many of osteocytes' signaling mechanisms activated in response to loading are considered anabolic in nature, several of them can also render osteocytes insensitive to further stimuli and thereby creating a negative feedback loop that limits osteocytes' overall response. The purpose of this review is to examine the potential mechanisms that may contribute to the loss of mechanosensitivity. In particular, we examined the inactivation/desensitization of ion channels and signaling molecules along with the potential role of endocytosis and cytoskeletal reorganization. The significance in defining the negative feedback loop is the potential to identify unique targets for enabling osteocytes to maintain their sensitivity. In doing so, we can begin to cultivate new strategies that capitalize on the anabolic nature of daily activities that repeatedly load the skeleton.

#### Otolaryngology – Head and Neck Surgery

**Grewal JS, Law RH, Williams AM, Wertz AG, and Chang SS.** Does insurance type influence overall survival in patients with laryngeal squamous cell carcinoma? *Am J Otolaryngol* 2021; 42(4):102959. PMID: 33667796. [Full Text](#)

**OBJECTIVE:** Patients with head and neck cancer with Medicaid or no insurance present at a more advanced stage and have lower survival. This study is one of the first to examine the relationship between specific insurance types and overall survival for laryngeal squamous cell carcinoma patients. **STUDY DESIGN:** Retrospective chart review. **SETTING:** Henry Ford Cancer Institute. **SUBJECTS AND METHODS:** A retrospective database review was performed using the Henry Ford Virtual Data Warehouse Tumor Registry. Six hundred and fifty patients diagnosed with laryngeal squamous cell carcinoma were identified. Insurance groups analyzed were fee for service, health maintenance organization, Henry Ford Medical Group - a managed care type insurance, Medicare and Medicaid/uninsured. Cox proportional hazards and Kaplan-Meier curves were generated to analyze overall survival and display survival differences respectively. **RESULTS:** The uninsured group had the lowest median survival time of

29.8 months (95% CI: 20.3-44.8) and the highest HR of 1.85 (95% CI 1.16-2.93) as compared to the HMO group at  $p < 0.001$ . Patients with fee for service insurance had longer overall survival compared to the other insurance types. Patients with fee for service insurance also had a high proportion of patients with advanced stage disease, but a younger mean age. Henry Ford Medical Group had a higher mean age and no statistically significant difference in survival when compared to fee for service. ( $p = 0.999$ ) After controlling for socioeconomic status, insurance type remains a significant predictor of overall survival. CONCLUSIONS: Fee for service had the highest overall survival of the different insurance types, but it was only statistically significant when compared to the Medicaid/uninsured group.

#### Otolaryngology – Head and Neck Surgery

**Law RH, Ahmed AM, Van Harn M, and Craig JR.** Middle turbinate resection is unlikely to cause empty nose syndrome in first year postoperatively. *Am J Otolaryngol* 2021; 42(4):102931. PMID: 33550027. [Full Text](#)

**PURPOSE:** Empty nose syndrome (ENS) is characterized by nasal dryness, crusting, and paradoxical nasal obstruction most commonly after inferior turbinate resection. ENS has also been reported to occur after middle turbinate resection (MTR), and concern for causing ENS is a possible reason surgeons preserve the MT during endoscopic sinus surgery (ESS). The objective was to determine whether MTR during ESS led to ENS. **MATERIALS AND METHODS:** This was a prospective case series of 95 consecutive patients that underwent bilateral subtotal MTR during ESS with either Draf IIB or Draf III frontal sinusotomies, for chronic rhinosinusitis with or without nasal polyps, and frontal sinus inverted papillomas. Demographic data and postoperative Empty Nose Syndrome 6-item Questionnaire (ENS6Q) scores were obtained. Nasal crusting was also documented on last postoperative nasal endoscopy. **RESULTS:** Pathologies included chronic rhinosinusitis with nasal polyps (69), without nasal polyps (12), and inverted papillomas (14). Fifty-six patients underwent subtotal MTRs during ESS with Draf IIB, and 39 with Draf III. Mean follow-up was 19.4 months (range 12-49). Mean postoperative ENS6Q score was 2.1. Only 2.1% had ENS6Q scores  $\geq 11$ , and 6.3% had nasal crusting at last follow-up. None of the patients with ENS6Q scores  $\geq 11$  had nasal crusting at last follow-up. There were no significant differences in outcomes between ages, genders, surgery types, or pathologies. **CONCLUSIONS:** Patients who underwent bilateral subtotal MTR during ESS were unlikely to develop ENS by at least 1 year postoperatively, based on patients rarely experiencing ENS6Q scores  $\geq 11$  or persistent nasal crusting.

#### Otolaryngology – Head and Neck Surgery

Macias D, Hand BN, Maurer S, Balliet W, Ellis MA, Pipkorn P, Huang AT, Nilsen ML, Ruggiero KJ, **Williams AM**, Marsh CH, Li H, Rhoten BA, Sterba KR, and Graboyes EM. Factors Associated With Risk of Body Image-Related Distress in Patients With Head and Neck Cancer. *JAMA Otolaryngol Head Neck Surg* 2021; Epub ahead of print. PMID: 34236423. [Full Text](#)

**IMPORTANCE:** Body image-related distress (BID) is common among head and neck cancer (HNC) survivors and associated with significant morbidity. Risk factors for HNC-related BID remain poorly characterized because prior research has used outcome measures that fail to fully capture BID as experienced by HNC survivors. **OBJECTIVE:** To assess the association of demographic and oncologic characteristics with HNC-related BID using the Inventory to Measure and Assess imaGe disturbance-Head & Neck (IMAGE-HN), a validated, multidomain, patient-reported outcome measure of HNC-related BID. **DESIGN, SETTING, AND PARTICIPANTS:** This cross-sectional study assessed 301 adult survivors of surgically managed HNC at 4 academic medical centers. **MAIN OUTCOMES AND MEASURES:** The primary outcome measure was IMAGE-HN scores, for which higher scores reflect more severe HNC-

related BID. Multivariable linear regression analyses were performed to evaluate the association of patient characteristics with IMAGE-HN global and 4 subdomain (other-oriented appearance concerns, personal dissatisfaction with appearance, distress with functional impairments, and social avoidance) scores. RESULTS: Of the 301 participants (212 [70.4%] male; mean [SD] age, 65.3 [11.7] years), 181 (60.1%) underwent free flap reconstruction. Graduation from college ( $\beta = -9.6$ ; 95% CI, -17.5 to -1.7) or graduate school ( $\beta = -12.6$ ; 95% CI, -21.2 to -3.8) was associated with lower IMAGE-HN social avoidance scores compared with less than a high school education. Compared with paid work, unemployment was associated with higher IMAGE-HN other-oriented appearance ( $\beta = 10.7$ ; 95% CI, 2.0-19.3), personal dissatisfaction with appearance ( $\beta = 12.5$ ; 95% CI, 1.2-23.7), and global ( $\beta = 8.0$ ; 95% CI, 0.6-15.4) scores. Compared with no reconstruction, free flap reconstruction was associated with higher IMAGE-HN global scores ( $\beta = 11.5$ ; 95% CI, 7.9-15.0) and all subdomain scores (other-oriented appearance:  $\beta = 13.1$ ; 95% CI, 8.6-17.6; personal dissatisfaction with appearance:  $\beta = 15.4$ ; 95% CI, 10.0-20.7; distress with functional impairment:  $\beta = 12.8$ ; 95% CI, 8.1-17.4; and social avoidance and isolation:  $\beta = 10.2$ ; 95% CI, 5.8-14.6). Higher IMAGE-HN distress with functional impairment scores were found in those who received surgery and adjuvant radiation ( $\beta = 7.8$ ; 95% CI, 2.9-12.7) or chemoradiotherapy ( $\beta = 6.5$ ; 95% CI, 1.8-11.3) compared with surgery alone. The multivariable regression model accounted for a modest proportion of variance in IMAGE-HN global ( $R^2 = 0.18$ ) and subdomain scores ( $R^2 = 0.20$  for other-oriented appearance, 0.14 for personal dissatisfaction with appearance, 0.21 for distress with functional impairment, and 0.13 for social avoidance and isolation). CONCLUSIONS AND RELEVANCE: In this cross-sectional study, factors associated with risk of HNC-related BID included free flap reconstruction, lower educational attainment, unemployment, and multiple treatment modalities. These characteristics explain a modest proportion of variance in IMAGE-HN scores, suggesting that other characteristics may be the major risk factors for HNC-related BID and should be explored in future studies.

#### Otolaryngology – Head and Neck Surgery

Surna MV, Jacobowitz O, Chang J, Koutsourelakis I, Smith D, Alkan U, D'Agostino M, Boon M, Heiser C, Hoff P, Huntley C, Kent D, Kominsky A, Lewis R, Maurer JT, Ravesloot M, Soose R, Steffen A, Weaver E, **Williams AM**, Woodson T, **Yaremchuk K**, and Ishman SL. Improving outcomes of hypoglossal nerve stimulation therapy: current practice, future directions and research gaps. Proceedings of the 2019 International Sleep Surgery Society Research Forum. *J Clin Sleep Med* 2021; Epub ahead of print. PMID: 34279214. [Full Text](#)

Hypoglossal nerve stimulation (HGNS) has evolved as a novel and effective therapy for patients with moderate-to-severe obstructive sleep apnea (OSA). Despite positive published outcomes of HGNS, there exist uncertainties regarding proper patient selection, surgical technique, and the reporting of outcomes and individual factors that impact therapy effectiveness. According to current guidelines, this therapy is indicated for select patients, and recommendations are based on the Stimulation Therapy for Apnea Reduction (STAR) trial. Ongoing research and physician experiences continuously improve methods to optimize the therapy. An understanding of the way in which airway anatomy, OSA phenotypes, individual health status, psychological conditions and comorbid sleep disorders influence the effectiveness of HGNS is essential to improve outcomes and expand therapy indications. This manuscript presents discussions on current evidence, future directions, and research gaps for HGNS therapy from the 10th International Surgical Sleep Society expert research panel.

#### Pathology and Laboratory Medicine

Ahmed A, Naji A, **Zhang J, Raoufi M, Alhamar M, Salgia R, and Mullins K.** Mantle Cell Lymphoma Presenting as Diarrhea in a Liver Transplant Recipient. *ACG Case Rep J* 2021; 8(7):e00635. PMID: 34307713. [Full Text](#)

We present a 63-year-old man with a medical history of hepatocellular carcinoma who underwent orthotopic liver transplant 10 years prior on long-term immunosuppressive therapy. The patient presented to the clinic with diarrhea, and the workup revealed mantle cell lymphoma. Mantle cell lymphoma is an extremely rare finding in transplanted livers. It is essential to include mantle cell lymphoma, along with a broad differential, during the workup of diarrhea in post-transplant patients.

#### Pathology and Laboratory Medicine

**Arora K, Rodgers S, Alkhatib Y, Onwubiko IN, Padmanabhan A, and Otrrock ZK.** P-selectin expression assay in a repeatedly serotonin-release assay-negative patient with heparin-induced thrombocytopenia. *Blood Coagul Fibrinolysis* 2021; Epub ahead of print. PMID: 34261860. [Full Text](#)

Heparin-induced thrombocytopenia (HIT) is an immune complication of heparin therapy caused by antibodies to complexes of platelet factor 4 (PF4) and heparin. Pathogenic antibodies to PF4/heparin bind and activate platelets to propagate a hypercoagulable state culminating in life-threatening thrombosis. The serotonin-release assay (SRA) is considered the gold-standard test to diagnose HIT. However, the sensitivity of the SRA was questioned with reported cases of clinical diagnosis of HIT and negative SRA. Herein, we present the utility of platelet factor 4-dependent P-selectin expression assay (PEA) in diagnosing HIT in a patient with thrombocytopenia and recurrent thrombosis who repeatedly tested negative with SRA.

#### Pathology and Laboratory Medicine

Hsiao CJ, Patel AGM, Fasanya HO, Stoffel MR, Beal SG, **Winston-McPherson GN**, Campbell ST, Cotten SW, Crews BO, Kuan K, Lapedis CJ, Mathias PC, Peck Palmer OM, and Greene DN. The Lines That Held Us: Assessing Racial and Socioeconomic Disparities in SARS-CoV-2 Testing. *J Appl Lab Med* 2021; Epub ahead of print. PMID: 34240171. [Full Text](#)

**BACKGROUND:** Racial disparities in SARS-CoV-2 prevalence are apparent. Race is a sociocultural construct, necessitating investigation into how sociocultural factors contribute. **METHODS:** This cross-sectional study linked laboratory data of adult patients between February 29 and May 15, 2020 with socio-demographics variables from the 2018 American Community Survey (ACS). Medical sites included healthcare organizations in Michigan, New York, North Carolina, California, Florida, Pennsylvania, and Washington. Race was treated as a proxy for racism and not biological essentialism. Laboratory data included patient age, sex, race, ethnicity, test result, test location, and residential ZIP code. ACS data included economic and educational variables contributing to an SES Index, population density, proportion Medicaid, and racial composition for corresponding ZIP code. Associations between race/socioeconomic variables and test results were examined using odds ratios (OR). **RESULTS:** Of 126 452 patients [mean (SD) age 51.9 (18.4) years; 52 747 (41.7%) men; 68 856 (54.5%) White and 27 805 (22.0%) Black], 18 905 (15.0%) tested positive. Of positive tests, 5238 (SD 27.7%) were White and 7223 (SD 38.2%) were Black. Black race increased the odds of a positive test; this finding was consistent across sites [OR 2.11 (95% CI 1.95-2.29)]. When subset by race, higher SES increased the odds of a positive test for White patients [OR 1.10 (95% CI 1.05-1.16)] but decreased the odds for Black patients [OR 0.92 (95% CI 0.86-0.99)]. Black patients, but not White patients, who tested positive overwhelmingly resided in more densely populated areas.



CONCLUSIONS: Black race was associated with SARS-CoV-2 positivity and the relationship between SES and test positivity differed by race, suggesting the impact of socioeconomic status on test positivity is race-specific.

#### Pathology and Laboratory Medicine

**Johnson CC, Coleman CM, Sitarik AR, Leon JE, Tibbetts RJ, Cook BC, Muma BK, Weinmann AJ, and Samuel LP.** SARS-CoV-2 RT-PCR positivity and antibody prevalence among asymptomatic hospital-based health care workers. *J Clin Virol* 2021; 140:104794. PMID: 34023573. [Full Text](#)

BACKGROUND: The level of asymptomatic infection with SARS-CoV-2 could be substantial and among health care workers (HCWs) a source of continuing transmission of the virus to patients and co-workers. OBJECTIVES: Measure the period prevalence of SARS-CoV-2 PCR positivity and seroprevalence of SARS-CoV-2 IgG antibodies among a random sample of asymptomatic health system hospital-based health care workers (HCWs) 6½ -15½ weeks after 4/5/2020, the peak of the first surge of COVID-19 admissions. RESULTS: Of 524 eligible and consented participants from four metropolitan hospitals, nasopharyngeal swabs were obtained from 439 (83.8 %) and blood from 374 (71.4 %). Using PCR nucleic acid-based amplification (NAAT) methods, the period prevalence of SARS-CoV-2 infection was 0.23 % (95 % confidence interval (CI) 0.01 %-1.28 %; 1/439) from 5/21/20-7/16/20. The seroprevalence of SARS-CoV-2 IgG antibodies from June 17-July 24, 2020 was 2.41 % (95 % CI 1.27 %-4.51 %; 9/374). Those who were reactive were younger (median age 36 versus 44 years;  $p = 0.050$ ), and those with self-reported Hispanic/Latino ethnicity had a higher seroprevalence ( $2/12 = 16.7\%$  versus  $7/352 = 2.0\%$ ;  $p = 0.051$ ). There were no significant differences by sex, race, residence, hospital, unit or job type. The one employee who was found to be PCR test positive in this study was also reactive for IgG antibodies, tested 27 days later. CONCLUSIONS: The period prevalence of PCR positivity to SARS-CoV-2 and IgG seroprevalence was unexpectedly low in asymptomatic HCWs after a peak in COVID-19 admissions and the establishment of state and institutional infection control policies, suggesting that routine screening tests while community prevalence is relatively low would produce a minimal yield.

#### Pathology and Laboratory Medicine

Rundle AG, **Sadasivan SM, Chitale DA, Gupta NS, Williamson SR,** Kryvenko ON, **Chen Y, Bobbitt K,** Tang D, and **Rybicki BA.** Racial differences in the systemic inflammatory response to prostate cancer. *PLoS One* 2021; 16(7):e0252951. PMID: 34242232. [Full Text](#)

Systemic inflammation may increase risk for prostate cancer progression, but the role it plays in prostate cancer susceptibility is unknown. From a cohort of over 10,000 men who had either a prostate biopsy or transurethral resection that yielded a benign finding, we analyzed 517 incident prostate cancer cases identified during follow-up and 373 controls with one or more white blood cell tests during a follow-up period between one and 18 years. Multilevel, multivariable longitudinal models were fit to two measures of systemic inflammation, neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR), to determine NLR and MLR trajectories associated with increased risk for prostate cancer. For both measures, we found no significant differences in the trajectories by case/control status, however in modeling NLR trajectories there was a significant interaction between race (white or Black and case-control status). In race specific models, NLR and MLR values were consistently higher over time among white controls than white cases while case-control differences in NLR and MLR trajectories were not apparent among Black men. When cases were classified as aggressive as compared to non-aggressive, the case-control differences in NLR and MLR values over time among white men were most apparent for non-aggressive cases. For NLR among white men, significant

case-control differences were observed for the entire duration of observation for men who had inflammation in their initial prostate specimen. It is possible that, among white men, monitoring of NLR and MLR trajectories after an initial negative biopsy may be useful in monitoring prostate cancer risk.

#### Pathology and Laboratory Medicine

**Zarbo RJ.** Management Systems to Structure Continuous Quality Improvement. *Am J Clin Pathol* 2021; Epub ahead of print. PMID: 34273147. [Request Article](#)

**OBJECTIVES:** This review describes the processes and effectiveness of the primary management systems that structure and sustain consistent behaviors and result in a transformed culture of continuous quality improvement (CQI) from top to bottom throughout the Henry Ford medical laboratory enterprise. **METHODS:** Through a 17-year focus to achieve a functional CQI enterprise, quality management systems were developed and continuously improved by teams of laboratory leaders, managers, and quality specialists to coordinate and standardize human efforts, and provide actionable knowledge and data to engage improvement efforts at all levels of work. Lean and ISO 15189 discipline and requirements were addressed in annual management review of functionality and effectiveness to close gaps and further refine the management systems. **RESULTS:** Improvements in the use and effectiveness of 4 management systems are illustrated. **CONCLUSIONS:** The 4 primary management systems that provide structure and support transformation to a culture of CQI are the team leader, Plan-Do-Check-Act problem-solving, deviation management, and daily management systems. These management systems are designed to deepen the effectiveness of the continuous improvement culture by helping managers understand variation in the work they oversee and providing guidance for more effective employee engagement in the daily processes of quality improvement.

#### Podiatry

**Seidel GK,** Jamal SA, Weidert E, Carington F, Andary MT, Millis SR, and **Loder BG.** Predictive Outcome Modeling of Preoperative Clinical Symptoms and Electrodiagnostic Data in Tarsal Tunnel Surgery. *J Brachial Plex Peripher Nerve Inj* 2021; 16(1):e37-e45. PMID: 34335869. [Full Text](#)

**Background** The relationship between tarsal tunnel syndrome (TTS), electrodiagnostic (Edx) findings, and surgical outcome is unknown. Analysis of TTS surgical release outcome patient satisfaction and comparison to Edx nerve conduction studies (NCSs) is important to improve outcome prediction when deciding who would benefit from TTS release. **Methods** Retrospective study of 90 patients over 7 years that had tarsal tunnel (TT) release surgery with outcome rating and preoperative tibial NCS. Overall, 64 patients met study inclusion criteria with enough NCS data to be classified into one of the following three groups: (1) probable TTS, (2) peripheral polyneuropathy, or (3) normal. Most patients had preoperative clinical provocative testing including diagnostic tibial nerve injection, tibial Phalen's sign, and/or Tinel's sign and complaints of plantar tibial neuropathic symptoms. Outcome measure was percentage of patient improvement report at surgical follow-up visit. **Results** Patient-reported improvement was 92% in the probable TTS group (n = 41) and 77% of the non-TTS group (n = 23). Multivariate modeling revealed that three out of eight variables predicted improvement from surgical release, NCS consistent with TTS (p = 0.04), neuropathic symptoms (p = 0.045), and absent Phalen's test (p = 0.001). The R<sup>2</sup> was 0.21 which is a robust result for this outcome measurement process. **Conclusion** The best predictors of improvement in patients with TTS release were found in patients that had preoperative Edx evidence of tibial neuropathy in the TT and tibial

nerve plantar symptoms. Determining what factors predict surgical outcome will require prospective evaluation and evaluation of patients with other nonsurgical modalities.

#### Public Health Sciences

**Craig JR, Cheema AJ, Dunn RT, Vemuri S, and Peterson EL.** Extrasinus Complications From Odontogenic Sinusitis: A Systematic Review. *Otolaryngol Head Neck Surg* 2021; Epub ahead of print. PMID: 34253072. [Full Text](#)

**OBJECTIVE:** Odontogenic sinusitis (ODS) can cause infectious orbital, intracranial, and osseous complications. Diagnosis and management of complicated ODS have not been discussed in recent sinusitis guidelines. The purpose of this systematic review was to describe epidemiological and clinical features, as well as management strategies of complicated ODS. **DATA SOURCES:** PubMed, EMBASE, and Cochrane Library. **REVIEW METHODS:** A systematic review was performed to describe various features of complicated ODS. All complicated ODS studies were included in qualitative analysis, but studies were only included in quantitative analysis if they reported specific patient-level data. **RESULTS:** Of 1126 studies identified, 75 studies with 110 complicated ODS cases were included in qualitative analysis, and 47 studies with 62 orbital and intracranial complications were included in quantitative analyses. About 70% of complicated ODS cases were orbital complications. Only 23% of complicated ODS studies were published in otolaryngology journals. Regarding ODS-related orbital and intracranial complications, about 80% occurred in adults, and 75% were male. Complicated ODS occurred most commonly from apical periodontitis of maxillary molars. There were no relationships between sinusitis extent and orbital or intracranial complications. High rates of anaerobic and  $\alpha$ -hemolytic streptococcal bacteria were identified in complicated ODS. Management generally included systemic antibiotics covering aerobic and anaerobic bacteria, and surgical interventions were generally performed to address both the complications (orbital and/or intracranial) and possible infectious sources (dentition and sinuses). **CONCLUSION:** ODS should be considered in all patients with infectious extrasinus complications. Multidisciplinary management between otolaryngologists, dental specialists, ophthalmologists, and neurosurgeons should be considered to optimize outcomes.

#### Public Health Sciences

**Johnson CC, Coleman CM, Sitarik AR, Leon JE, Tibbetts RJ, Cook BC, Muma BK, Weinmann AJ, and Samuel LP.** SARS-CoV-2 RT-PCR positivity and antibody prevalence among asymptomatic hospital-based health care workers. *J Clin Virol* 2021; 140:104794. PMID: 34023573. [Full Text](#)

**BACKGROUND:** The level of asymptomatic infection with SARS-CoV-2 could be substantial and among health care workers (HCWs) a source of continuing transmission of the virus to patients and co-workers. **OBJECTIVES:** Measure the period prevalence of SARS-CoV-2 PCR positivity and seroprevalence of SARS-CoV-2 IgG antibodies among a random sample of asymptomatic health system hospital-based health care workers (HCWs) 6½ -15½ weeks after 4/5/2020, the peak of the first surge of COVID-19 admissions. **RESULTS:** Of 524 eligible and consented participants from four metropolitan hospitals, nasopharyngeal swabs were obtained from 439 (83.8 %) and blood from 374 (71.4 %). Using PCR nucleic acid-based amplification (NAAT) methods, the period prevalence of SARS-CoV-2 infection was 0.23 % (95 % confidence interval (CI) 0.01 %-1.28 %; 1/439) from 5/21/20-7/16/20. The seroprevalence of SARS-CoV-2 IgG antibodies from June 17-July 24, 2020 was 2.41 % (95 % CI 1.27 %-4.51 %; 9/374). Those who were reactive were younger (median age 36 versus 44 years;  $p = 0.050$ ), and those with self-reported Hispanic/Latino ethnicity had a higher seroprevalence (2/12 = 16.7 % versus 7/352 = 2.0 %;  $p = 0.051$ ). There were no significant differences by sex, race, residence, hospital, unit

or job type. The one employee who was found to be PCR test positive in this study was also reactive for IgG antibodies, tested 27 days later. CONCLUSIONS: The period prevalence of PCR positivity to SARS-CoV-2 and IgG seroprevalence was unexpectedly low in asymptomatic HCWs after a peak in COVID-19 admissions and the establishment of state and institutional infection control policies, suggesting that routine screening tests while community prevalence is relatively low would produce a minimal yield.

#### Public Health Sciences

**Law RH, Ahmed AM, Van Harn M, and Craig JR.** Middle turbinate resection is unlikely to cause empty nose syndrome in first year postoperatively. *Am J Otolaryngol* 2021; 42(4):102931. PMID: 33550027. [Full Text](#)

**PURPOSE:** Empty nose syndrome (ENS) is characterized by nasal dryness, crusting, and paradoxical nasal obstruction most commonly after inferior turbinate resection. ENS has also been reported to occur after middle turbinate resection (MTR), and concern for causing ENS is a possible reason surgeons preserve the MT during endoscopic sinus surgery (ESS). The objective was to determine whether MTR during ESS led to ENS. **MATERIALS AND METHODS:** This was a prospective case series of 95 consecutive patients that underwent bilateral subtotal MTR during ESS with either Draf IIB or Draf III frontal sinusotomies, for chronic rhinosinusitis with or without nasal polyps, and frontal sinus inverted papillomas. Demographic data and postoperative Empty Nose Syndrome 6-item Questionnaire (ENS6Q) scores were obtained. Nasal crusting was also documented on last postoperative nasal endoscopy. **RESULTS:** Pathologies included chronic rhinosinusitis with nasal polyps (69), without nasal polyps (12), and inverted papillomas (14). Fifty-six patients underwent subtotal MTRs during ESS with Draf IIB, and 39 with Draf III. Mean follow-up was 19.4 months (range 12-49). Mean postoperative ENS6Q score was 2.1. Only 2.1% had ENS6Q scores  $\geq 11$ , and 6.3% had nasal crusting at last follow-up. None of the patients with ENS6Q scores  $\geq 11$  had nasal crusting at last follow-up. There were no significant differences in outcomes between ages, genders, surgery types, or pathologies. **CONCLUSIONS:** Patients who underwent bilateral subtotal MTR during ESS were unlikely to develop ENS by at least 1 year postoperatively, based on patients rarely experiencing ENS6Q scores  $\geq 11$  or persistent nasal crusting.

#### Public Health Sciences

**Macki M, Anand SK, Hamilton T, Lim S, Mansour T, Bazydlo M, Schultz L, Abdulhak MM, Khalil JG, Park P, Aleem I, Easton R, Schwalb JM, Nerenz D, and Chang V.** Analysis of Factors associated with Return to Work After Lumbar Surgery up to 2-years follow-up: A Michigan Spine Surgery Improvement Collaborative (MSSIC) Study. *Spine (Phila Pa 1976)* 2021; Epub ahead of print. PMID: 34265812. [Full Text](#)

**STUDY DESIGN:** Michigan Spine Surgery Improvement Collaborative (MSSIC) prospectively collects data on all patients undergoing operations for degenerative and/or deformity indications. **OBJECTIVE:** We aimed to identify which factors are significantly associated with return-to-work after lumbar surgery at long-term follow-up. **SUMMARY OF BACKGROUND DATA:** Prior publications have created a clinically relevant predictive model for return-to-work, wherein education, gender, race, comorbidities, and preoperative symptoms increased likelihood of return-to-work at 3 months after lumbar surgery. We sought to determine if these trends 1) persisted at 1 year and 2 years postoperatively; or 2) differed among preoperatively employed versus unemployed patients. **METHODS:** MSSIC was queried for all patients undergoing lumbar operations (2014-2019). All patients intended to return-to-work postoperatively. Patients were followed for up to 2 years postoperatively. Measures of association were calculated with multivariable generalized estimating equations (GEE). **RESULTS:** Return-to-work increased

from 63% (3542/5591) at 90 days postoperatively to 75% (3143/4147) at 1 year and 74% (2133/2866) at 2 years postoperatively. Following GEE, neither clinical nor surgical variables predicted return-to-work at all three time intervals: 90 days, 1 year, and 2 years postoperatively. Only socioeconomic factors reached statistical significance at all follow-up points. Preoperative employment followed by insurance status had the greatest associations with return-to-work. In a sub-analysis of patients who were preoperatively employed, insurance was the only factor with significant associations with return-to-work at all three follow-up intervals. The return-to-work rates among unemployed patients at baseline increased from 29% (455/1100) at 90 days, 44% (495/608) at 1 year, and 46% (366/426) at 2 years postoperatively. The only two significant factors associated with return-to-work at all three follow-up intervals were Medicaid, as compared to private insurance, and male gender. **CONCLUSION:** In patients inquiring about long-term return-to-work after lumbar surgery, insurance status represents the important determinant of employment status. Level of Evidence: 2.

#### Public Health Sciences

Rundle AG, **Sadasivan SM, Chitale DA, Gupta NS, Williamson SR**, Kryvenko ON, **Chen Y, Bobbitt K**, Tang D, and **Rybicki BA**. Racial differences in the systemic inflammatory response to prostate cancer. *PLoS One* 2021; 16(7):e0252951. PMID: 34242232. [Full Text](#)

Systemic inflammation may increase risk for prostate cancer progression, but the role it plays in prostate cancer susceptibility is unknown. From a cohort of over 10,000 men who had either a prostate biopsy or transurethral resection that yielded a benign finding, we analyzed 517 incident prostate cancer cases identified during follow-up and 373 controls with one or more white blood cell tests during a follow-up period between one and 18 years. Multilevel, multivariable longitudinal models were fit to two measures of systemic inflammation, neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR), to determine NLR and MLR trajectories associated with increased risk for prostate cancer. For both measures, we found no significant differences in the trajectories by case/control status, however in modeling NLR trajectories there was a significant interaction between race (white or Black and case-control status). In race specific models, NLR and MLR values were consistently higher over time among white controls than white cases while case-control differences in NLR and MLR trajectories were not apparent among Black men. When cases were classified as aggressive as compared to non-aggressive, the case-control differences in NLR and MLR values over time among white men were most apparent for non-aggressive cases. For NLR among white men, significant case-control differences were observed for the entire duration of observation for men who had inflammation in their initial prostate specimen. It is possible that, among white men, monitoring of NLR and MLR trajectories after an initial negative biopsy may be useful in monitoring prostate cancer risk.

#### Public Health Sciences

**Saffo Z, Guo W, Springer K, Maksimowicz-McKinnon K, Kak V, McKinnon JE, and Bhargava P**. The role of tocilizumab therapy in critically ill patients with severe acute respiratory syndrome coronavirus 2. *J Osteopath Med* 2021; 121(8):705-714. PMID: 34237804. [Full Text](#)

**CONTEXT:** Tocilizumab (TCZ), an interleukin-6 (IL-6) receptor antagonist, has been approved for use in rheumatoid arthritis and cytokine storm syndrome (CSS) associated with chimeric antigen receptor T cells treatment. Although TCZ is currently utilized in the treatment of critically ill coronavirus 2019 (COVID-19) patients, data on survival impact is minimal. **OBJECTIVES:** To assess the mortality rate of patients presenting with COVID-19 who received TCZ for suspected CSS. **METHODS:** This retrospective cohort study was conducted at Henry Ford Health System between March 10, 2020 and May 18, 2020. Data collection began in May 2020 and was

completed in June 2020. Patients included in the study required hospital admission and had positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction on nasopharyngeal swab. Eligibility criteria to receive TCZ, per hospital protocol, included any of the following: persistent fever, defined as 38.0 °C for at least 6 hours; a diagnosis of the acute respiratory distress syndrome (ARDS); serum ferritin  $\geq 1,000$  (ng/mL) or doubling within 24 hours; D-Dimer  $\geq 5$  (mg/L); serum lactate dehydrogenase  $\geq 500$  (IU/L); or interleukin-6 level  $\geq 5$  times the upper limit of normal. Dosing was initially determined by weight, then changed to a fixed 400 mg per hospital protocol. A comparator cohort was created from patients with COVID-19 and ARDS who did not receive TCZ. Patient survival was analyzed using the Kaplan-Meier method and compared by log rank test. A multivariable cox regression was applied to evaluate the association between TCZ and mortality. RESULTS: One hundred and thirty patients were evaluated in the study, 54 (41.5%) of whom received TCZ. Patients who received TCZ were younger (mean age, 63.8 vs. 69.4 years;  $p=0.0083$ ) and had higher body mass indices (mean, 33.9 vs. 30.4;  $p=0.005$ ). Of the comorbid conditions evaluated, heart disease was more common in the comparator group than the TCZ group (27 patients [35.5%] vs. 10 patients [18.5%];  $p=0.034$ ). A Kaplan-Meier survival curve demonstrated no difference in survival between TCZ and comparator patients (log rank  $p=0.495$ ). In the multivariable Cox regression model for mortality at 30 days, treatment with TCZ was not associated with decreased mortality (hazard ratio, 1.1; 95% confidence interval, 0.53-2.3;  $p=0.77$ ). Lower mean C-reactive protein (CRP) levels were demonstrated within 48 hours of disposition in the TCZ group (mean TCZ, 4.9 vs. mean comparator, 13.0;  $p<0.0001$ ). CONCLUSIONS: In this cohort study, no difference in survival was observed in critically ill patients treated with TCZ.

#### Public Health Sciences

**Santarossa S**, Hill AB, **Sitarik AR**, **Mackenzie T**, **Hawkins S**, **Scher K**, **Sohaski A**, **Baseer M**, **Dombrowski R**, **Plum A**, and **Joseph CLM**. Food insecurity in Detroit: Exploring the relationship between patient-reported food insecurity and proximity to healthful grocery stores. *Public Health Nutr* 2021; Epub ahead of print.:1-24. PMID: 34325766. [Full Text](#)

**OBJECTIVE:** The objective of the current study was to determine if patients of a large health care system in Detroit who self-identify as food insecure live further away from healthy grocery stores compared to food secure patients. Secondly, we explored whether food insecurity and distance to healthy grocery stores is related to ecological measures of vehicle availability in the area of residence. **DESIGN:** A secondary data analysis which uses baseline data from a pilot intervention/feasibility study. **SETTING:** Detroit, Michigan, USA. **PARTICIPANTS:** Patients of Henry Ford Health System were screened for food insecurity to determine eligibility for a pilot intervention/feasibility study (i.e., Henry's Groceries for Health), conducted through a collaboration with Gleaners Community Foodbank of Southeastern Michigan. Only patients residing in Detroit city limits (including Highland Park and Hamtramck) were included in the secondary analysis. Of the 1,100 patients included in the analysis, 336 (31%) were food insecure. **RESULTS:** After accounting for sociodemographic factors associated with food insecurity, we did not find evidence that food insecure patients lived further away from healthier grocery stores, nor was this modified by ecological measures of vehicle access. However, some neighborhoods were identified as having a significantly higher risk of food insecurity. **CONCLUSIONS:** Food insecure patients in Detroit are perhaps limited by social and political determinants and not their immediate neighborhood geography or physical access to healthy grocery stores. Future research should explore the complexity in linkages between household socioeconomic factors, sociocultural dynamics, and the neighborhood food environment.

### Public Health Sciences

**Yahya JB, Zhu S, Burmeister C, Hijaz MY, and Elshaikh MA.** Matched-pair Analysis for Survival Endpoints Between Women With Early-stage Uterine Carcinosarcoma and Uterine Serous Carcinoma. *Am J Clin Oncol* 2021; Epub ahead of print. PMID: 34265785. [Full Text](#)

**OBJECTIVE:** The objective of this study was to compare survival endpoints between women with uterine carcinosarcoma and those with uterine serous carcinoma utilizing matching analysis. **METHODS:** Patients with stages I to II who underwent hysterectomy at our institution were included in this analysis. Patients with carcinosarcoma were then matched to patients with serous carcinoma based on stage, and adjuvant management received (observation, radiation treatment alone, chemotherapy alone, or combined modality with radiotherapy and chemotherapy. Recurrence-free survival, disease-specific survival, and overall survival were calculated for the 2 groups. **RESULTS:** A total of 134 women were included (67 women with carcinosarcoma and 67 with serous carcinoma, matched 1:1). There was no statistically significant difference between the 2 groups regarding 5-year recurrence-free survival (59% vs. 62%), disease-specific survival (66% vs. 67%), or overall survival (53% vs. 57%), respectively. The only independent predictor of shorter recurrence-free survival for the entire cohort was the lack of adjuvant combined modality therapy, while lower uterine segment involvement was the only independent predictor for shorter disease-specific survival. Lack of lymph node dissection and lack of adjuvant combined modality therapy were independent predictors of shorter overall survival. **DISCUSSION:** When matched based on stage and adjuvant treatment, our study suggests that there is no statistically significant difference in survival endpoints between women with early-stage carcinosarcoma and serous carcinoma. Adjuvant combined modality treatment is an independent predictor of longer recurrence-free survival and overall survival.

### Pulmonary and Critical Care Medicine

Berry LL, **Awdish RLA**, Letchuman S, and Steffensen KD. Trust-Based Partnerships Are Essential - and Achievable - in Health Care Service. *Mayo Clin Proc* 2021; 96(7):1896-1906. PMID: 34090685. [Full Text](#)

When people think about trust in the context of health care, they typically focus on whether patients trust the competence of doctors and other health professionals. But for health care to reach its full potential as a service, trust must also include the notion of partnership, whereby patients see their clinicians as reliable, caring, shared decision-makers who provide ongoing "healing" in its broadest sense. Four interrelated service-quality concepts are central to fostering trust-based partnerships in health care: empathetic creativity, discretionary effort, seamless service, and fear mitigation. Health systems and institutions that prioritize trust-based partnerships with patients have put these concepts into practice using several concrete approaches: investing in organizational culture; hiring health professionals for their values, not just their skills; promoting continuous learning; attending to the power of language in all care interactions; offering patients "go-to" sources for timely assistance; and creating systems and structures that have trust built into their very design. It is in the real-world implementation of trust-based partnership that health care can reclaim its core mission.

### Pulmonary and Critical Care Medicine

**Hamam MS, Klausner HA, France J, Tang A**, Swor RA, Paxton JH, O'Neil BJ, Brent C, Neumar RW, Dunne RB, **Reddi S**, and **Miller JB**. Prehospital Tibial Intraosseous Drug Administration is Associated with Reduced Survival Following Out of Hospital Cardiac Arrest: A study for the CARES Surveillance Group. *Resuscitation* 2021; Epub ahead of print. PMID: 34237357. [Full Text](#)

**BACKGROUND:** Recent reports have questioned the efficacy of intraosseous (IO) drug administration for out-of-hospital cardiac arrest (OHCA) resuscitation. Our aim was to determine whether prehospital administration of resuscitative medications via the IO route was associated with lower rates of return of spontaneous circulation (ROSC) and survival to hospital discharge than peripheral intravenous (IV) infusion in the setting of OHCA. **METHODS:** We obtained data on all OHCA patients receiving prehospital IV or IO drug administration from the three most populous counties in Michigan over three years. Data was from the Michigan Cardiac Arrest Registry to Enhance Survival (CARES) database. The association between route of drug administration and outcomes was tested using a matched propensity score analysis. **RESULTS:** From a total of 10,626 OHCA patients, 6869 received parenteral drugs during their prehospital resuscitation (37.8% by IO) and were included in analysis. Unadjusted outcomes were lower in patients with IO vs. IV access: 18.3% vs. 23.8% for ROSC ( $p < 0.001$ ), 3.2% vs. 7.6% for survival to hospital discharge ( $p < 0.001$ ), and 2.0% vs. 5.8% for favorable neurological function ( $p < 0.001$ ). After adjustment, IO route remained associated with lower odds of sustained ROSC (OR 0.72, 95% CI 0.63-0.81,  $p < 0.001$ ), hospital survival (OR 0.48, 95% CI 0.37-0.62,  $p < 0.001$ ), and favorable neurological outcomes (OR 0.42, 95% CI 0.30-0.57,  $p < 0.001$ ). **CONCLUSION:** In this cohort of OHCA patients, the use of prehospital IO drug administration was associated with unfavorable clinical outcomes.

### Radiation Oncology

McFarlane MR, Hochstedler KA, Laucis AM, Sun Y, Chowdhury A, Matuszak MM, Hayman J, Bergsma D, Boike T, Kestin L, **Movsas B**, Grills I, Dominello M, Dess RT, Schonewolf C, Spratt DE, Pierce L, Paximadis P, Jolly S, and Schipper M. Predictors of Pneumonitis after Conventionally Fractionated Radiotherapy for Locally Advanced Lung Cancer. *Int J Radiat Oncol Biol Phys* 2021; Epub ahead of print. PMID: 34314815. [Full Text](#)

**PURPOSE/OBJECTIVES:** Multiple factors influence the risk of developing pneumonitis after radiotherapy (RT) for lung cancer, but few resources exist to guide clinicians in predicting risk in an individual patient treated with modern techniques. We analyzed toxicity data from a state-wide consortium to develop an integrated pneumonitis risk model. **MATERIALS/METHODS:** All patients ( $n=1302$ ) received conventionally fractionated RT for stage II-III non-small cell lung cancer (NSCLC) between April 2012 and July 2019. Pneumonitis occurring within six months of treatment was graded by local practitioners and prospectively collected from 27 academic and community clinics participating in a state-wide quality consortium. Pneumonitis was modeled as either Grade  $\geq 2$  (G2+) or as Grade  $\geq 3$  (G3+). Logistic regression models were fit to quantify univariable associations with dose and clinical factors and stepwise AIC based modeling was utilized to build multivariable prediction models. **RESULTS:** The overall rate of pneumonitis of any grade in the six months following RT was 16% (208 cases). 7% (94 cases) were G2+ and <1% (11 cases) were G3+. Adjusting for incomplete follow-up, estimated rates for G2+ and G3+ were 14% and 2%, respectively. In univariate analyses, gEUD, V5, V10, V20, V30, and Mean Lung Dose (MLD) were positively associated with G2+ pneumonitis risk, while current smoking status was associated with lower odds of pneumonitis. G2+ pneumonitis risk of  $\geq 22\%$  was independently predicted by MLD of  $\geq 20$  Gy, V20 of  $\geq 35\%$ , and V5 of  $\geq 75\%$ . In multivariate analyses, the lung V5 metric remained a significant predictor of G2+ pneumonitis even when controlling for MLD, despite their close correlation. For G3+ pneumonitis, MLD and V20 were statistically significant predictors. Number of comorbidities was an independent predictor of G3+, but not G2+ pneumonitis. **CONCLUSIONS:** We present an analysis of pneumonitis risk after definitive RT for lung cancer using a large, prospective dataset. We incorporate comorbidity burden, smoking status, and dosimetric parameters in an integrated risk model. These data may guide clinicians in assessing pneumonitis risk in individual patients.



### Radiation Oncology

Skinner H, Hu C, Tsakiridis T, Santana-Davila R, Lu B, Erasmus JJ, **Doemer AJ**, Videtic GMM, Coster J, Yang AX, Lee RY, Werner-Wasik M, Schaner PE, McCormack SE, Esparaz BT, McGarry RC, Bazan J, Struve T, Paulus R, and Bradley JD. Addition of Metformin to Concurrent Chemoradiation in Patients With Locally Advanced Non-Small Cell Lung Cancer: The NRG-LU001 Phase 2 Randomized Clinical Trial. *JAMA Oncol* 2021; Epub ahead of print. PMID: 34323922. [Full Text](#)

**IMPORTANCE:** Non-small cell lung cancer (NSCLC) has relatively poor outcomes. Metformin has significant data supporting its use as an antineoplastic agent. **OBJECTIVE:** To compare chemoradiation alone vs chemoradiation and metformin in stage III NSCLC. **DESIGN, SETTING, AND PARTICIPANTS:** The NRG-LU001 randomized clinical trial was an open-label, phase 2 study conducted from August 24, 2014, to December 15, 2016. Patients without diabetes who were diagnosed with unresectable stage III NSCLC were stratified by performance status, histology, and stage. The setting was international and multi-institutional. This study examined prespecified endpoints, and data were analyzed on an intent-to-treat basis. Data were analyzed from February 25, 2019, to March 6, 2020. **INTERVENTIONS:** Chemoradiation and consolidation chemotherapy with or without metformin. **MAIN OUTCOMES AND MEASURES:** The primary outcome was 1-year progression-free survival (PFS), designed to detect 15% improvement in 1-year PFS from 50% to 65% (hazard ratio [HR], 0.622). Secondary end points included overall survival, time to local-regional recurrence, time to distant metastasis, and toxicity per Common Terminology Criteria for Adverse Events, version 4.03. **RESULTS:** A total of 170 patients were enrolled, with 167 eligible patients analyzed after exclusions (median age, 64 years [interquartile range, 58-72 years]; 97 men [58.1%]; 137 White patients [82.0%]), with 81 in the control group and 86 in the metformin group. Median follow-up was 27.7 months (range, 0.03-47.21 months) among living patients. One-year PFS rates were 60.4% (95% CI, 48.5%-70.4%) in the control group and 51.3% (95% CI, 39.8%-61.7%) in the metformin group (HR, 1.15; 95% CI, 0.77-1.73; P = .24). Clinical stage was the only factor significantly associated with PFS on multivariable analysis (HR, 1.79; 95% CI, 1.19-2.69; P = .005). One-year overall survival was 80.2% (95% CI, 69.3%-87.6%) in the control group and 80.8% (95% CI, 70.2%-87.9%) in the metformin group. There were no significant differences in local-regional recurrence or distant metastasis at 1 or 2 years. No significant difference in adverse events was observed between treatment groups. **CONCLUSIONS AND RELEVANCE:** In this randomized clinical trial, the addition of metformin to concurrent chemoradiation was well tolerated but did not improve survival among patients with unresectable stage III NSCLC. **TRIAL REGISTRATION:** ClinicalTrials.gov Identifier: NCT02186847.

### Radiation Oncology

**Snyder KC, Cunningham J, Huang Y, Zhao B, Dolan J, Wen N, Chetty IJ, Shah MM, and Siddiqui SM.** Dosimetric Evaluation of Fractionated Stereotactic Radiation Therapy for Skull Base Meningiomas Using HyperArc and Multicriteria Optimization. *Adv Radiat Oncol* 2021; 6(4):100663. PMID: 33997481. [Full Text](#)

**PURPOSE:** Treatment planning of skull based meningiomas can be difficult due to the irregular shaped target volumes and proximity to critical optic structures. This study evaluated the use of HyperArc (HA) radiosurgery optimization and delivery in conjunction with multicriteria optimization (MCO) to create conformal and efficient treatment plans for conventionally fractionated radiation therapy to difficult base-of-skull (BOS) lesions. **METHODS AND MATERIALS:** Twelve patients with BOS meningioma were retrospectively planned with HA-specific optimization algorithm, stereotactic normal tissue objective (SRS-NTO), and conventional automatic normal tissue objective to evaluate normal brain sparing (mean dose

and V20 Gy). MCO was used on both SRS-NTO and automatic normal tissue objective plans to further decrease organ-at-risk doses and target dose maximum to within clinically acceptable constraints. Delivery efficiency was evaluated based on planned monitor units. RESULTS: The SRS-NTO in HA can be used to improve the mid- and low-dose spread to normal brain tissue in the irradiation of BOS meningiomas. Improvement in normal brain sparing can be seen in larger, more irregular shaped lesions and less so in smaller spherical targets. MCO can be used in conjunction with the SRS-NTO to reduce target dose maximum and dose to organ at risk without sacrificing the gain in normal brain sparing. CONCLUSIONS: HA can be beneficial both in treatment planning by using the SRS-NTO and in delivery efficiency through the decrease in monitor units and automated delivery.

#### Radiation Oncology

**Yahya JB, Zhu S, Burmeister C, Hijaz MY, and Elshaikh MA.** Matched-pair Analysis for Survival Endpoints Between Women With Early-stage Uterine Carcinosarcoma and Uterine Serous Carcinoma. *Am J Clin Oncol* 2021; Epub ahead of print. PMID: 34265785. [Full Text](#)

OBJECTIVE: The objective of this study was to compare survival endpoints between women with uterine carcinosarcoma and those with uterine serous carcinoma utilizing matching analysis. METHODS: Patients with stages I to II who underwent hysterectomy at our institution were included in this analysis. Patients with carcinosarcoma were then matched to patients with serous carcinoma based on stage, and adjuvant management received (observation, radiation treatment alone, chemotherapy alone, or combined modality with radiotherapy and chemotherapy. Recurrence-free survival, disease-specific survival, and overall survival were calculated for the 2 groups. RESULTS: A total of 134 women were included (67 women with carcinosarcoma and 67 with serous carcinoma, matched 1:1). There was no statistically significant difference between the 2 groups regarding 5-year recurrence-free survival (59% vs. 62%), disease-specific survival (66% vs. 67%), or overall survival (53% vs. 57%), respectively. The only independent predictor of shorter recurrence-free survival for the entire cohort was the lack of adjuvant combined modality therapy, while lower uterine segment involvement was the only independent predictor for shorter disease-specific survival. Lack of lymph node dissection and lack of adjuvant combined modality therapy were independent predictors of shorter overall survival. DISCUSSION: When matched based on stage and adjuvant treatment, our study suggests that there is no statistically significant difference in survival endpoints between women with early-stage carcinosarcoma and serous carcinoma. Adjuvant combined modality treatment is an independent predictor of longer recurrence-free survival and overall survival.

#### Rehabilitation Services/Physical Therapy/Occupational Health

**Seidel GK, Jamal SA, Weidert E, Carington F, Andary MT, Millis SR, and Loder BG.** Predictive Outcome Modeling of Preoperative Clinical Symptoms and Electrodiagnostic Data in Tarsal Tunnel Surgery. *J Brachial Plex Peripher Nerve Inj* 2021; 16(1):e37-e45. PMID: 34335869. [Full Text](#)

Background The relationship between tarsal tunnel syndrome (TTS), electrodiagnostic (Edx) findings, and surgical outcome is unknown. Analysis of TTS surgical release outcome patient satisfaction and comparison to Edx nerve conduction studies (NCSs) is important to improve outcome prediction when deciding who would benefit from TTS release. Methods Retrospective study of 90 patients over 7 years that had tarsal tunnel (TT) release surgery with outcome rating and preoperative tibial NCS. Overall, 64 patients met study inclusion criteria with enough NCS data to be classified into one of the following three groups: (1) probable TTS, (2) peripheral polyneuropathy, or (3) normal. Most patients had preoperative clinical provocative testing including diagnostic tibial nerve injection, tibial Phalen's sign, and/or Tinel's sign and

complaints of plantar tibial neuropathic symptoms. Outcome measure was percentage of patient improvement report at surgical follow-up visit. Results Patient-reported improvement was 92% in the probable TTS group ( n = 41) and 77% of the non-TTS group ( n = 23). Multivariate modeling revealed that three out of eight variables predicted improvement from surgical release, NCS consistent with TTS ( p = 0.04), neuropathic symptoms ( p = 0.045), and absent Phalen's test ( p = 0.001). The R (2) was 0.21 which is a robust result for this outcome measurement process. Conclusion The best predictors of improvement in patients with TTS release were found in patients that had preoperative Edx evidence of tibial neuropathy in the TT and tibial nerve plantar symptoms. Determining what factors predict surgical outcome will require prospective evaluation and evaluation of patients with other nonsurgical modalities.

#### Research Administration

Gleichgerrcht E, Munsell BC, Alhusaini S, Alvim MKM, Bargalló N, Bender B, Bernasconi A, Bernasconi N, Bernhardt B, Blackmon K, Caligiuri ME, Cendes F, Concha L, Desmond PM, Devinsky O, Doherty CP, Domin M, Duncan JS, Focke NK, Gambardella A, Gong B, Guerrini R, Hatton SN, Kälviäinen R, Keller SS, Kochunov P, Kotikalapudi R, Kreilkamp BAK, Labate A, Langner S, Larivière S, Lenge M, Lui E, Martin P, Mascalchi M, Meletti S, O'Brien TJ, Pardoe HR, Pariente JC, Xian Rao J, Richardson MP, Rodríguez-Cruces R, Rüber T, Sinclair B, **Soltanian-Zadeh H**, Stein DJ, Striano P, Taylor PN, Thomas RH, Elisabetta Vaudano A, Vivash L, von Podewills F, Vos SB, Weber B, Yao Y, Lin Yasuda C, Zhang J, Thompson PM, Sisodiya SM, McDonald CR, and Bonilha L. Artificial intelligence for classification of temporal lobe epilepsy with ROI-level MRI data: A worldwide ENIGMA-Epilepsy study. *Neuroimage Clin* 2021; 31:102765. PMID: 34339947. [Full Text](#)

Artificial intelligence has recently gained popularity across different medical fields to aid in the detection of diseases based on pathology samples or medical imaging findings. Brain magnetic resonance imaging (MRI) is a key assessment tool for patients with temporal lobe epilepsy (TLE). The role of machine learning and artificial intelligence to increase detection of brain abnormalities in TLE remains inconclusive. We used support vector machine (SV) and deep learning (DL) models based on region of interest (ROI-based) structural (n = 336) and diffusion (n = 863) brain MRI data from patients with TLE with ("lesional") and without ("non-lesional") radiographic features suggestive of underlying hippocampal sclerosis from the multinational (multi-center) ENIGMA-Epilepsy consortium. Our data showed that models to identify TLE performed better or similar (68-75%) compared to models to lateralize the side of TLE (56-73%, except structural-based) based on diffusion data with the opposite pattern seen for structural data (67-75% to diagnose vs. 83% to lateralize). In other aspects, structural and diffusion-based models showed similar classification accuracies. Our classification models for patients with hippocampal sclerosis were more accurate (68-76%) than models that stratified non-lesional patients (53-62%). Overall, SV and DL models performed similarly with several instances in which SV mildly outperformed DL. We discuss the relative performance of these models with ROI-level data and the implications for future applications of machine learning and artificial intelligence in epilepsy care.

#### Research Administration

Kemp SB, Pasca di Magliano M, and **Crawford HC**. Myeloid cell mediated immune suppression in pancreatic cancer. *Cell Mol Gastroenterol Hepatol* 2021; Epub ahead of print. PMID: 34303882. [Full Text](#)

Pancreatic ductal adenocarcinoma (PDA), the most common pancreatic cancer, is a nearly-universally lethal malignancy. PDA is characterized by extensive infiltration of immunosuppressive myeloid cells, including tumor-associated macrophages (TAMs) and

myeloid-derived suppressor cells (MDSCs). Myeloid cells in the tumor microenvironment (TME) inhibit cytotoxic T cell responses promoting carcinogenesis. Immune checkpoint therapy has not been effective in PDA, most likely due to this robust immune suppression, making it critical to elucidate mechanisms behind this phenomenon. Here, we review myeloid cell infiltration and cellular crosstalk in PDA progression and highlight current therapeutic approaches to target myeloid cell-driven immune suppression.

### Rheumatology

**Saffo Z, Guo W, Springer K, Maksimowicz-McKinnon K, Kak V, McKinnon JE, and Bhargava P.** The role of tocilizumab therapy in critically ill patients with severe acute respiratory syndrome coronavirus 2. *J Osteopath Med* 2021; 121(8):705-714. PMID: 34237804. [Full Text](#)

CONTEXT: Tocilizumab (TCZ), an interleukin-6 (IL-6) receptor antagonist, has been approved for use in rheumatoid arthritis and cytokine storm syndrome (CSS) associated with chimeric antigen receptor T cells treatment. Although TCZ is currently utilized in the treatment of critically ill coronavirus 2019 (COVID-19) patients, data on survival impact is minimal. OBJECTIVES: To assess the mortality rate of patients presenting with COVID-19 who received TCZ for suspected CSS. METHODS: This retrospective cohort study was conducted at Henry Ford Health System between March 10, 2020 and May 18, 2020. Data collection began in May 2020 and was completed in June 2020. Patients included in the study required hospital admission and had positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction on nasopharyngeal swab. Eligibility criteria to receive TCZ, per hospital protocol, included any of the following: persistent fever, defined as 38.0 °C for at least 6 hours; a diagnosis of the acute respiratory distress syndrome (ARDS); serum ferritin  $\geq 1,000$  (ng/mL) or doubling within 24 hours; D-Dimer  $\geq 5$  (mg/L); serum lactate dehydrogenase  $\geq 500$  (IU/L); or interleukin-6 level  $\geq 5$  times the upper limit of normal. Dosing was initially determined by weight, then changed to a fixed 400 mg per hospital protocol. A comparator cohort was created from patients with COVID-19 and ARDS who did not receive TCZ. Patient survival was analyzed using the Kaplan-Meier method and compared by log rank test. A multivariable cox regression was applied to evaluate the association between TCZ and mortality. RESULTS: One hundred and thirty patients were evaluated in the study, 54 (41.5%) of whom received TCZ. Patients who received TCZ were younger (mean age, 63.8 vs. 69.4 years;  $p=0.0083$ ) and had higher body mass indices (mean, 33.9 vs. 30.4;  $p=0.005$ ). Of the comorbid conditions evaluated, heart disease was more common in the comparator group than the TCZ group (27 patients [35.5%] vs. 10 patients [18.5%];  $p=0.034$ ). A Kaplan-Meier survival curve demonstrated no difference in survival between TCZ and comparator patients (log rank  $p=0.495$ ). In the multivariable Cox regression model for mortality at 30 days, treatment with TCZ was not associated with decreased mortality (hazard ratio, 1.1; 95% confidence interval, 0.53-2.3;  $p=0.77$ ). Lower mean C-reactive protein (CRP) levels were demonstrated within 48 hours of disposition in the TCZ group (mean TCZ, 4.9 vs. mean comparator, 13.0;  $p<0.0001$ ). CONCLUSIONS: In this cohort study, no difference in survival was observed in critically ill patients treated with TCZ.

### Sleep Medicine

Gurubhagavatula I, Barger LK, Barnes CM, Basner M, Boivin DB, Dawson D, **Drake CL**, Flynn-Evans EE, Mysliwiec V, Patterson PD, Reid KJ, Samuels C, Shattuck NL, Kazmi U, Carandang G, Heald JL, and Dongen H. Guiding principles for determining work shift duration and addressing the effects of work shift duration on performance, safety, and health: guidance from the American Academy of Sleep Medicine and the Sleep Research Society. *J Clin Sleep Med* 2021; Epub ahead of print. PMID: 34180805. [Full Text](#)

Risks associated with fatigue that accumulates during work shifts have historically been managed through working time arrangements that specify fixed maximum durations of work shifts and minimum durations of time off. By themselves, such arrangements are not sufficient to curb risks to performance, safety, and health caused by misalignment between work schedules and the biological regulation of waking alertness and sleep. Science-based approaches for determining shift duration and mitigating associated risks, while addressing operational needs, require: 1) a recognition of the factors contributing to fatigue and fatigue-related risks; 2) an understanding of evidence-based countermeasures that may reduce fatigue and/or fatigue-related risks; and 3) an informed approach to selecting workplace-specific strategies for managing work hours. We propose a series of guiding principles to assist stakeholders with designing a shift duration decision-making process that effectively balances the need to meet operational demands with the need to manage fatigue-related risks.

### Sleep Medicine

Gurubhagavatula I, Barger LK, Barnes CM, Basner M, Boivin DB, Dawson D, **Drake CL**, Flynn-Evans EE, Mysliwiec V, Patterson PD, Reid KJ, Samuels C, Shattuck NL, Kazmi U, Carandang G, Heald JL, and Van Dongen HPA. Guiding Principles For Determining Work Shift Duration And Addressing The Effects Of Work Shift Duration On Performance, Safety, And Health. *Sleep* 2021; Epub ahead of print. PMID: 34263305. [Full Text](#)

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### Sleep Medicine

Janse van Rensburg DC, Jansen van Rensburg A, Fowler PM, Bender AM, Stevens D, Sullivan KO, Fullagar HHK, Alonso JM, Biggins M, Claassen-Smithers A, Collins R, Dohi M, Driller MW, Dunican IC, Gupta L, Halson SL, Lastella M, Miles KH, Nedelec M, Page T, Roach G, Sargent C, **Singh M**, Vincent GE, Vitale JA, and Botha T. Managing Travel Fatigue and Jet Lag in Athletes: A Review and Consensus Statement. *Sports Med* 2021; Epub ahead of print.:1-22. PMID: 34263388. [Full Text](#)

Athletes are increasingly required to travel domestically and internationally, often resulting in travel fatigue and jet lag. Despite considerable agreement that travel fatigue and jet lag can be a real and impactful issue for athletes regarding performance and risk of illness and injury, evidence on optimal assessment and management is lacking. Therefore 26 researchers and/or clinicians with knowledge in travel fatigue, jet lag and sleep in the sports setting, formed an expert panel to formalise a review and consensus document. This manuscript includes definitions of terminology commonly used in the field of circadian physiology, outlines basic information on the human circadian system and how it is affected by time-givers, discusses the causes and consequences of travel fatigue and jet lag, and provides consensus on recommendations for managing travel fatigue and jet lag in athletes. The lack of evidence

restricts the strength of recommendations that are possible but the consensus group identified the fundamental principles and interventions to consider for both the assessment and management of travel fatigue and jet lag. These are summarised in travel toolboxes including strategies for pre-flight, during flight and post-flight. The consensus group also outlined specific steps to advance theory and practice in these areas.

### Surgery

Arbeille P, Zuj KA, Macias BR, Ebert DJ, Laurie SS, Sargsyan AE, Martin DS, Lee SMC, **Dulchavsky SA**, Stenger MB, and Hargens AR. Lower body negative pressure reduces jugular and portal vein volumes, and counteracts the cerebral vein velocity elevation during long-duration spaceflight. *J Appl Physiol (1985)* 2021; Epub ahead of print. PMID: 34323592. [Full Text](#)

**PURPOSE:** Cephalad fluid shifts in space have been hypothesized to cause the spaceflight-associated neuro-ocular syndrome (SANS) by increasing the intracranial-ocular translaminar pressure gradient. Lower body negative pressure (LBNP) can be used to shift upper-body blood and other fluids towards the legs during spaceflight. We hypothesized that microgravity would increase jugular vein volume (JVvol), portal vein cross-sectional area (PV), and intracranial venous blood velocity (MCV) and that 25mmHg LBNP application would return these variables towards preflight levels. **METHODS:** Data were collected from 14 subjects (11 male) before and during long-duration ISS spaceflights. Ultrasound measures of JVvol, PV, and MCV were acquired while seated and supine before flight and early during spaceflight at days 45 (FD45) and late (FD150) with and without LBNP. **RESULTS:** JVvol increased from preflight supine and seated postures ( $46 \pm 48$  % and  $646 \pm 595$  % on FD45 and  $43 \pm 43$  % and  $702 \pm 631$  % on FD150,  $p < 0.05$ ), MCV increased from preflight supine  $44 \pm 31$  % on FD45 and  $115 \pm 116$  % on FD150 ( $p < 0.05$ ), PV increased from preflight supine and seated ( $51 \pm 56$  % and  $100 \pm 74$  %) on FD150 ( $p < 0.05$ ). Inflight 25mmHg LBNP restored JVvol, and MCV to preflight supine and PV to preflight seated level. **CONCLUSIONS:** Elevated JVvol confirms the sustained neck-head blood engorgement inflight, while increased PV area supports the fluid shift at the splanchnic level. Also, MCV increased potentially due to reduced lumen diameter. LBNP, returning variables to preflight levels, may be an effective countermeasure.

### Surgery

Benz C, Smith J, Mani R, Musunuru T, He J, and **Okereke I**. Dysphagia Secondary to Intraluminal Choriocarcinoma of the Gastroesophageal Junction. *Am J Gastroenterol* 2021; Epub ahead of print. PMID: 34283820. [Full Text](#)

### Surgery

Bergquist JR, Thiels CA, Shubert CR, **Ivanics T**, Habermann EB, Vege SS, Grotz TE, Cleary SP, Smoot RL, Kendrick ML, Nagorney DM, and Truty MJ. Perception versus reality: A National Cohort Analysis of the surgery-first approach for resectable pancreatic cancer. *Cancer Med* 2021; Epub ahead of print. PMID: 34289264. [Full Text](#)

**INTRODUCTION:** Although surgical resection is necessary, it is not sufficient for long-term survival in pancreatic ductal adenocarcinoma (PDAC). We sought to evaluate survival after up-front surgery (UFS) in anatomically resectable PDAC in the context of three critical factors: (A) margin status; (B) CA19-9; and (C) receipt of adjuvant chemotherapy. **METHODS:** The National Cancer Data Base (2010-2015) was reviewed for clinically resectable (stage 0/I/II) PDAC patients. Surgical margins, pre-operative CA19-9, and receipt of adjuvant chemotherapy were evaluated. Patient overall survival was stratified based on these factors and their respective combinations. Outcomes after UFS were compared to equivalently staged patients after

neoadjuvant chemotherapy on an intention-to-treat (ITT) basis. RESULTS: Twelve thousand and eighty-nine patients were included (n = 9197 UFS, n = 2892 ITT neoadjuvant). In the UFS cohort, only 20.4% had all three factors (median OS = 31.2 months). Nearly 1/3rd (32.7%) of UFS patients had none or only one factor with concomitant worst survival (median OS = 14.7 months). Survival after UFS decreased with each failing factor (two factors: 23 months, one factor: 15.5 months, no factors: 7.9 months) and this persisted after adjustment. Overall survival was superior in the ITT-neoadjuvant cohort (27.9 vs. 22 months) to UFS. CONCLUSION: Despite the perceived benefit of UFS, only 1-in-5 UFS patients actually realize maximal survival when known factors highly associated with outcomes are assessed. Patients are proportionally more likely to do worst, rather than best after UFS treatment. Similarly staged patients undergoing ITT-neoadjuvant therapy achieve survival superior to the majority of UFS patients. Patients and providers should be aware of the false perception of 'optimal' survival benefit with UFS in anatomically resectable PDAC.

#### Surgery

**Kitajima T, Moonka D, Yeddula S, Collins K, Rizzari M, Yoshida A, Abouljoud MS, and Nagai S.** Reply. *Liver Transpl* 2021; Epub ahead of print. PMID: 33786986. [Full Text](#)

#### Surgery

Mohan N, and **Okereke I.** Commentary: The behavior of leaders. *J Thorac Cardiovasc Surg* 2021; Epub ahead of print. PMID: 34304891. [Full Text](#)

#### Urology

Dielubanza EJ, Enemchukwu EA, and **Atiemo HO.** Workforce Diversity in Female Pelvic Medicine and Reconstructive Surgery: An analysis of the American Urological Association Census Data. *Urology* 2021; Epub ahead of print. PMID: 34274388. [Full Text](#)

OBJECTIVE: To describe the current state of workforce diversity in Female Pelvic Medicine and Reconstructive Surgery (FPMRS) using the 2014-2019 American Urological Association (AUA) census data. MATERIALS: We evaluated FPMRS workforce diversity using the AUA census data from 2014 to 2019. Underrepresented in medicine (URiM) groups were categorized as individuals who self-identified as non-Hispanic Black/African American, Hispanic, Multiracial, and Other. The FPMRS workforce was then compared to the overall urologic workforce and the other urologic subspecialties (oncology, pediatric urology, and endourology) and assessed by AUA section. RESULTS: In 2019, 602 urologists self-identified as FPMRS providers. Of these 12.4% (n=74) were categorized as URiM urologists compared to 8% of the overall urologic workforce. Women who represent 9.9% of all urologists were overrepresented in FPMRS workforce (46.5%). FPMRS had the largest proportion of URiM and women urologists when compared to the other subspecialty areas. CONCLUSION: The FPMRS urologic subspecialty has the highest percentage of women and URiM urologists compared to all other urologic subspecialty areas. Engagement initiatives and targeted programs may offer insights into this trend. Further research is required to determine the impact of such programs in attracting URiM and women to FPMRS.

#### Urology

**Jamil M, Hanna R, Sood A, Corsi N, Modonutti D, Keeley J, Etta P, Novara G, Patel A, Rogers C, and Abdollah F.** Renal Tumor Size and Presence Of Synchronous Lung Metastasis At Time Of Diagnosis: Implications For Chest Imaging. *Urology* 2021; Epub ahead of print. PMID: 34284011. [Full Text](#)

**OBJECTIVE:** To quantify synchronous lung metastasis risk based on renal tumor size and determine a renal tumor size threshold to determine when chest imaging is warranted. **METHODS:** We assessed 253,838 patients diagnosed with a renal tumor who underwent staging chest imaging between 2010-2016 within the National Cancer Database. Patients were stratified by renal tumor size in 10 mm increments, and synchronous lung metastasis risk was calculated for each category. Logistic regression analyses were used to test the relationship between renal tumor size and presence of synchronous lung metastasis after adjusting to all available covariables. **RESULTS:** Overall, 14,524 out of 253,838 (5.7%) patients had evidence of synchronous lung metastasis. Median (IQR) tumor size for patients with versus without sLM was 90 mm (65 - 115) vs. 40 mm (25 - 60), respectively. The incidence of synchronous lung metastasis was low for renal tumors <40 mm, without significant change, based on tumor size. Conversely, synchronous lung metastasis increased proportionally to renal tumor size for lesions ≥40 mm. In our cohort, 47% of patients (120,386/253,838) had a renal tumor <40 mm, and 0.9% (1,135/120,386) of these had patients had synchronous lung metastasis. Only 8% (1,135/14,524) of patients with synchronous lung metastasis had a renal tumor <40 mm. **CONCLUSION:** The risk of synchronous lung metastasis increased proportionally to renal tumor size; however, the risk was low for tumors <40 mm. These findings suggest that there may be minimal utility of performing screening chest imaging for patients with renal tumors <40 mm.

#### Urology

**Jamil ML, Wurst H, Robinson P, Rubinfeld I, Suleyman G, Pollak E, and Dabaja AA.** URINARY CATHETER ALLEVIATION NAVIGATOR PROTOCOL (UCANP): OVERVIEW OF PROTOCOL AND REVIEW OF INITIAL EXPERIENCE. *Am J Infect Control* 2021; Epub ahead of print. PMID: 34273463. [Full Text](#)

**BACKGROUND:** Given the associated morbidity, mortality, and financial consequences of catheter associated urinary tract infections (CAUTIs), efforts should be made to mitigate the risk. We sought to describe, and report results for a post-catheter removal bladder management protocol focused on decreasing catheter reinsertion, catheter days, and overall CAUTI risk. **METHODS:** This was a quality improvement initiative implemented over a 3-month period at a single urban, tertiary health care center. Patients with an indwelling urinary catheter deemed eligible for removal were followed and cared for according to the study protocol. Rates of catheter reinsertion, catheter days and assessment of CAUTI risk were compared between cohorts. **RESULTS:** A total of 173 patients were eligible for protocol enrollment. Catheter reinsertion rate was 16% during the pilot, compared to 21% and 27% for the historical cohorts, ( $p = 0.02$ ). The mean number of catheter days during the study was 1.4 days, compared to 9.5 and 5.6 days in the historical cohorts ( $p=0.004$ ). Catheter hours (OR 1.010 95% CI 1.005 - 1.015  $p <0.0001$ .) was a predictor of catheter reinsertion during the pilot. **CONCLUSIONS:** Our protocol resulted in a reduction of catheter reinsertion rates and number of catheter days. Expansion of this protocol to a larger patient cohort is required.

#### Urology

**Kachroo N, Raffee S, Elshatanoufy S, and Atiemo H.** High uterosacral ligament hysteropexy for the management of pelvic organ prolapse. *Int Braz J Urol* 2021; 47(4):902-904. PMID: 33848087. [Full Text](#)

#### Urology

Walker SR, Abdelsalam R, Ghosh S, Livingstone J, **Palanisamy N**, Boutros PC, Yip SM, Lees-Miller SP, and Bismar TA. Decreased ATM Protein Expression Is Substantiated with PTEN Loss in Defining Aggressive Phenotype of Prostate Cancer Associated with Lethal Disease. *Eur Urol Open Sci* 2021; 29:93-101. PMID: 34337539. [Full Text](#)



**BACKGROUND:** Ataxia Telangiectasia Mutated (ATM) serine/threonine protein kinase is a known tumor suppressor, involved in DNA damage repair. It has prognostic and predictive therapeutic implications and is associated with aggressive prostate cancer (PCa). **OBJECTIVE:** To investigate the prognostic value of ATM protein expression in PCa patients and assessed the combined value of ATM, ERG, and PTEN status. **DESIGN SETTING AND PARTICIPANTS:** This study consisted of 303 patients with incidental, locally advanced, and castrate-resistant PCa by transurethral resection of the prostate (TURP). **OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS:** TURP samples from 303 PCa patients were assessed by immunohistochemistry (IHC for ATM, ERG, and PTEN). Individual and combined marker status were correlated with International Society of Urological Pathology Gleason grade group, overall survival (OS), and PCa-specific mortality (PCSM). **RESULTS AND LIMITATIONS:** Decreased ATM expression (negative/weak intensity) occurred in 164/303 (54.1%) patients, and was associated with shorter OS and higher PCSM ( $p = 0.015$  and  $p = 0.001$ , respectively). Negative/weak ATM expression was significantly associated with PCSM with a hazard ratio of 2.09 (95% confidence interval 1.34-3.27,  $p = 0.001$ ). Assessment of Combined ATM/PTEN expression showed improved prognostic power to predict OS and PCSM, independent of Gleason grade groups. **CONCLUSIONS:** Decreased ATM protein expression is associated with poor outcomes in advanced PCa patients. Patients with combined low ATM/PTEN negative expression are at the highest risk for reduced OS and PCSM. Assessing the combined status of ATM/PTEN by IHC in PCa patients may aid in risk stratification relative to OS and PCSM. Moreover, since ATM plays an integral role in DNA damage response pathways, future studies will enhance our understanding of how outcomes of patients with altered ATM and PTEN expression can be improved further with poly-ADP ribose polymerase inhibitors (PARPi), combinations of PARPi and androgen receptor-targeted therapies, as well as platinum-based chemotherapies. **PATIENT SUMMARY:** Lower ATM intensity is associated with increased cancer-specific mortality in prostate cancer patients. Patients with lower ATM and PTEN negative expression showed decreased overall survival and increased cancer mortality compared with controls.

## Conference Abstracts

### Administration

**Penning DH, Cazacu S, Jevtovic-Todorovic V, Kalkanis S, Lewis M, and Brodie C.** Neuron-glia crosstalk mediate the neurotoxic effects of ketamine via extracellular vesicles. *GLIA* 2021; 69(SUPPL 1):E302-E303.

Background: General anesthetics (GA) are associated with neurodevelopmental abnormalities including cell death, cognitive and behavioral changes. There is now powerful evidence for non-cell autonomous mechanisms in almost every pathological condition in the brain, especially relevant to glial cells, mainly astrocytes and microglia, that exhibit structural and functional contacts with neurons. These interactions were recently reported to occur via the secretion of extracellular vesicles (EVs). Here, we employed primary human neural cells to analyze ketamine effects focusing on the functions of glial cells and their polarization/differentiation state. We also explored the roles of extracellular vesicles (EVs) and different components of the BDNF pathway. Methods: Ketamine effects were analyzed on human neuronal and glial cell proliferation and apoptosis and astrocytic (A1/A2) and microglial (M1/M2) cell activation were analyzed. The impact of the neuron-glia cell interactions in the neurotoxic effects of ketamine was analyzed using transwell co-cultures. The role of the brain-derived neurotrophic factor (BDNF) pathway, was analyzed using RT-PCR, ELISA western blot and gene silencing. EVs secreted by ketamine-treated cells were isolated, characterized and analyzed for their effects in neuron-glia cell interactions. Data were analyzed using analysis of variance or a Student's t test with correction for data sets with unequal variances. Results: Ketamine induced neuronal and oligodendrocytic cell apoptosis and promoted the expression of proinflammatory astrocytes (A1) and microglia (M1) phenotypes. Astrocytes and microglia enhanced the neurotoxic effects of ketamine on neuronal cells, whereas neurons increased oligodendrocyte cell death. Ketamine modulated different components in the BDNF pathway: decreasing BDNF secretion in neurons and astrocytes while increasing the expression of p75 in neurons and oligodendrocytes. In addition, ketamine treatment increased the lncRNA BDNF-AS levels and the secretion of pro-BDNF secretion. We found an important role of EVs secreted by ketamine-treated astrocytes in neuronal cell death by delivering BDNF-AS. Conclusions: Ketamine neurotoxicity involves both autonomous and non-cell autonomous mechanisms and components of the BDNF pathway expressed by neurons and glial cells represent major regulators of ketamine effects. We demonstrated for the first time a role of EVs as important mediators of ketamine effects by the delivery of specific non-coding RNAs. These results may contribute to a better understanding of cellular and molecular mechanisms underlying ketamine neurotoxic effects in humans and to the development of potential approaches to decrease its neurodevelopmental impact.

### Administration

Weiss MS, Jiang L, Townsel C, **Caldwell MT**, Fenner D, and Marsh EE. Trends in Emergency Department Visits among Reproductive Age Women in the United States, 2006-2018. *Reprod Sci* 2021; 28(SUPPL 1):308A-308A.

### Anesthesiology

**Penning DH, Cazacu S, Jevtovic-Todorovic V, Kalkanis S, Lewis M, and Brodie C.** Neuron-glia crosstalk mediate the neurotoxic effects of ketamine via extracellular vesicles. *GLIA* 2021; 69(SUPPL 1):E302-E303.

Background: General anesthetics (GA) are associated with neurodevelopmental abnormalities including cell death, cognitive and behavioral changes. There is now powerful evidence for non-cell autonomous mechanisms in almost every pathological condition in the brain, especially

relevant to glial cells, mainly astrocytes and microglia, that exhibit structural and functional contacts with neurons. These interactions were recently reported to occur via the secretion of extracellular vesicles (EVs). Here, we employed primary human neural cells to analyze ketamine effects focusing on the functions of glial cells and their polarization/differentiation state. We also explored the roles of extracellular vesicles (EVs) and different components of the BDNF pathway. Methods: Ketamine effects were analyzed on human neuronal and glial cell proliferation and apoptosis and astrocytic (A1/A2) and microglial (M1/M2) cell activation were analyzed. The impact of the neuron-glial cell interactions in the neurotoxic effects of ketamine was analyzed using transwell co-cultures. The role of the brain-derived neurotrophic factor (BDNF) pathway, was analyzed using RT-PCR, ELISA western blot and gene silencing. EVs secreted by ketamine-treated cells were isolated, characterized and analyzed for their effects in neuron-glia cell interactions. Data were analyzed using analysis of variance or a Student's t test with correction for data sets with unequal variances. Results: Ketamine induced neuronal and oligodendrocytic cell apoptosis and promoted the expression of proinflammatory astrocytes (A1) and microglia (M1) phenotypes. Astrocytes and microglia enhanced the neurotoxic effects of ketamine on neuronal cells, whereas neurons increased oligodendrocyte cell death. Ketamine modulated different components in the BDNF pathway: decreasing BDNF secretion in neurons and astrocytes while increasing the expression of p75 in neurons and oligodendrocytes. In addition, ketamine treatment increased the lncRNA BDNF-AS levels and the secretion of pro-BDNF secretion. We found an important role of EVs secreted by ketamine-treated astrocytes in neuronal cell death by delivering BDNF-AS. Conclusions: Ketamine neurotoxicity involves both autonomous and non-cell autonomous mechanisms and components of the BDNF pathway expressed by neurons and glial cells represent major regulators of ketamine effects. We demonstrated for the first time a role of EVs as important mediators of ketamine effects by the delivery of specific non-coding RNAs. These results may contribute to a better understanding of cellular and molecular mechanisms underlying ketamine neurotoxic effects in humans and to the development of potential approaches to decrease its neurodevelopmental impact.

### Gastroenterology

Fernandez M, Cristina Segovia M, Dijkstra G, Herlenius G, Testro A, Sharkey L, Braun F, Rumbo C, Lacaille F, Friend P, **Jafri S**, Vilca Melendez H, Horslen S, Schiano T, Zanfi C, Solar H, Ramisch D, Mazariegos G, and Gondolesi G. The effect of the COVID-19 pandemic in intestinal rehabilitation and transplant patients, initial results of an international survey. *Transplantation* 2021; 105(7 SUPPL 1):S11-S12.

Introduction: On January 30, 2020 the World Health Organization (WHO) declared the 2019-CoV outbreak in China as a global public health emergency and subsequently, a pandemic on March 11th. It was considered that intestinal failure and intestinal transplant patients might have a higher risk of severe complications from the COVID-19 disease, multidisciplinary intestinal failure teams had to adapt their clinical approaches in order to keep this vulnerable group of patients as safe as possible during the pandemic; but data was lacking. Therefore, in order to improve our knowledge, we designed a voluntary, international survey aiming to address the impact of the COVID-19 disease in intestinal failure and transplant patients worldwide. Patient and Methods: A retrospective, observational, multicenter survey was sent to all centers registered at the Intestinal Rehabilitation and Transplant Association (IRTA). The survey contained three modules: the 1st one consisted of 14 questions about the hospital's activity during the COVID-19 pandemic. The 2nd one, contained 43 questions, was about intestinal failure patient management and outcome and the 3rd one (52 questions) focused on intestinal transplant patients. We used the Google Form platform. We aim to present the preliminary results of the first module. Statistical analysis was performed with the IBM SPSS Statistic version 25.0® program. Results: 13/42 (41%) centers responded; including centers from

France, Netherlands, Italy, United States, UK, Sweden, Germany and Argentina. Only 2 centers reported moratorium on intestinal (IT) or multivisceral transplant (MVT), with a mean of 3 months ( $\pm 4$ ) [Table 1]. Since the pandemic started, 2 institutions reported 4 patients with intestinal rehabilitation or on TPN diagnosed with COVID-19 while 7 centers hospitals claimed to have had 9 patients post-IT/MTV affected by the disease. While 7 centers had their routine follow up and 'protocol biopsies' in the post-IT/MTV affected, none reported higher rates of rejection or complications. At the same time, 8 centers (77%) were affected by a mean of 15% decrease in referrals for new evaluations of intestinal failure or transplantation (compared to 2019) [Figure 1]. All centers adapted to utilizing telemedicine to follow up on IT/MVT patients

Conclusions: Many aspects of healthcare have been impacted by the COVID-19 pandemic. The survey showed that the number of affected patients has been lower than expected, the reduced number of centers required transient moratorium of their activity, but a secondary observation was that despite the availability of telemedicine, and probably related to the lockdown, there has been a significant reduction in the referrals for evaluation of intestinal failure and transplant patients, that may have the deleterious effect of the delay of treatment in health care system.

#### Gastroenterology

**Gordon SC**, Trivedi P, Bowlus C, Michael G, Goel A, Gulamhusein A, Levy C, Neff G, Stanca C, Thorburn D, Bacon B, Borg B, Doerffel Y, Forman L, Freilich B, Gheorghe L, Gonzalez MS, Harrison S, Huang J, Jeong S-H, Kim SU, Lake J, Odin J, Tak WY, Tobias H, Vierling JM, Yang K, Steinberg A, Choi Y-J, McWherter C, and Mayo MJ. Efficacy, safety, and tolerability of seladelpar in patients with compensated liver cirrhosis due to primary biliary cholangitis (PBC): a pooled analysis of phase 2 and phase 3 studies. *J Hepatol* 2021; 75:S686-S687.

#### Gastroenterology

**Ichkhanian Y, Ichkhanian Y, Beltran N, Nagai S, and Jafri S.** Role of surveillance biopsy frequency post intestine transplant: A tertiary care experience. *Transplantation* 2021; 105(7 SUPPL 1):S14.

Background: With only 81 intestine transplant (IT) in the U.S. in 2019, the literature on this type of solid organ transplant remains scarce. Frequent surveillance biopsy is required on the first month post IT due to high-risk of acute rejection, however, the frequency of surveillance biopsy 1-month post IT is often determined by the physician and the institutions' preference. Aims: Report IT outcomes and clinical impact of surveillance biopsy at a single tertiary care center. Methods: This is a retrospective review of patients that underwent IT during the time-period between 08/2010 and 03/2020. Primary outcome was the correlation between increased protocol biopsies and mortality. Secondary outcomes included correlation between increased protocol biopsies and hospital re-admissions, length of hospital stay, and rate of biopsy proven rejection detection. Kaplan-Meier curves was used to perform the survival analysis at 6-month, 1-year, and 2-years post-transplant. Results: A total of 35 patients (mean age  $47.6 \pm 12.9$  years, F 22 (63%) underwent IT for: ischemic bowel 11 (31%), Chron's disease 9 (25%), neuroendocrine tumor 6 (17%), trauma 3 (9%) and 'others' 6 (17%), of which 14 (40%) were part of multivisceral organ transplant. During the first-year posttransplant, the median number of biopsies was 12 (IQR 6-30), with evidence of definite acute graft rejection in 40%, 27%, and 41% at the 1-3, 3-6, and 6-12 post IT time intervals, respectively. During the duration of the study, the mortality rate was 18/35 (51%) at a median time of 37 (12-60) months post IT, and a total of 8/35 (23%) patients underwent enterectomy at a median time of 12 (8-36) months post IT (Table 1). In general, there was survival benefit for patients who had a total number of biopsies of  $\geq 10$  as compared to  $< 10$  biopsies at the time interval of 6-months post IT, ( $p=0.008$ ) (Table 2). There was a non-significant trend with longer median length of hospital stay in patients with greater number of biopsies. Conclusion: Our results indicate evidence of

survival benefit of increased protocol biopsies. Studies with larger sample sizes are required to validate our results.

### Gastroenterology

Jafri S, **Jafri S**, Segovia M, and Weiner J. A multicenter evaluation of the diagnosis, management and outcomes of adenovirus enteritis infection following intestine or multivisceral transplant. *Transplantation* 2021; 105(7 SUPPL 1):S81.

Introduction: Adenovirus Enteritis (AE) is a unique infection which can complicate patient course following intestine and multivisceral transplantation. Solid organ transplant patients have an increased risk for infection and intestine and multivisceral patients are unique in that they often develop inflammation from rejection in the intestine which might predispose to infection. Methods: We reviewed patients who received an intestine transplant at three academic transplant centers between 2010 and 2020 for demographic, laboratory and clinical data. Results: Five patients were identified with diagnosis of adenovirus enteritis. Three patients (60%) had isolated intestine transplant while two underwent multivisceral transplantation. Reason for transplant included trauma, volvulus, intestinal atresia and visceral neuropathy. All patients received induction with anti-thymocyte globulin (80%) or basiliximab. The initial diagnosis of infection occurred at a mean of 26.8 months following transplant (range 2-68 months). Diagnosis was by polymerase chain reaction (PCR) measurement in plasma (80%), intestine or stool. Cidofovir was used in 100% of cases as primary management. 40% of patients had reduction of immunosuppression at the time of diagnosis while the remainder did not. 60% of patients had rejection within a month prior to diagnosis. No patients had recurrent rejection in the month following treatment. Two patients had recurrent infection. No patients had graft loss or death within 6 months of infection. Two patients had enterectomy at a mean of 29.5 months after infection (range 22-37 months) Three patients died at a mean of 32 months following diagnosis (range 8-51 months). Conclusion: We present a series of five cases of adult patients with AE following intestinal and multivisceral transplant. AE may arise due to immunosuppression, vascular compromise of the transplanted organ, or a combination of factors. Our study supported rejection as a risk factor for infection. Graft loss or death was not seen within 6 months following infection.

### Gastroenterology

Janssen HLA, Lampertico P, Chen C-H, Heo J, Fournier C, Ahn SH, Tsang TYO, Coffin CS, Huang Y-H, Reggiani GM, Hui AJ, Elkhatab M, Chen C-Y, **Jafri S-M**, Tan S, Zhao Y, Suri V, Flaherty JF, Gaggar A, Brainard D, Chuang W-L, Agarwal K, Gane E, and Lim Y-S. Switching from tenofovir disoproxil fumarate and/or other oral antivirals to tenofovir alafenamide in virally suppressed CHB patients with moderate or severe renal impairment or ESRD on HD: final week 96 efficacy and safety results from a phase 2 study. *J Hepatol* 2021; 75:S756-S757.

### Gastroenterology

Montano-Loza AJ, Ronca V, Ebadi M, Hansen B, Hirschfield G, Elwir S, Alsaed M, Milkiewicz P, Janik MK, Marschall H-U, Burza MA, Efe C, Caliskan AR, Harputluoglu M, Kabacam G, Terrabuio DR, Onofrio F, Pares A, Llovet LP, Akyildiz M, Arikan C, Manns MP, Taubert R, Weber A-L, Schiano T, Hayde B, Czubkowski P, Socha P, Oldak N, Akamatsu N, Tanaka A, Levy C, Martin EF, Goel A, Sedki M, Jankowska I, Ikegami T, Rodriguez M, Sterneck M, Weiler-Normann C, Schramm C, Donato MF, Lohse AW, Andrade RJ, Bonder A, Patwardhan V, Van Hoek B, Biewenga M, Kremer AE, Ueda Y, Deneau M, Pedersen M, Mayo MJ, Floreani A, Burra P, Secchi MF, Beretta-Piccoli BT, Sciveres M, Maggiore G, **Jafri S-M**, Debray D, Girard M, Lacaille F, Lytvyak E, Mason AL, Heneghan M, and Oo YH. Multicentre international evaluation of autoimmune hepatitis and liver transplantation: disease recurrence is associated with

recipient features, type of immunosuppression and impaired outcomes. *J Hepatol* 2021; 75:S193-S194.

#### Gastroenterology

Qasawa A, **Beltran N**, **Nagai S**, **Muszkat Y**, and **Jafri S**. Quality of trace mineral monitoring and replacement for patients on teduglutide for short bowel syndrome. *Transplantation* 2021; 105(7 SUPPL 1):S71.

Introduction: We evaluated serum levels of trace minerals including zinc, copper, and selenium in patients with short bowel syndrome (SBS) taking teduglutide. We worked to see if trace mineral values were being monitored and corrected. Methods: We performed a retrospective review to identify patients with SBS on teduglutide. We obtained data for two years following initiation for monitoring of serum levels for zinc, copper, and selenium. We identified if supplementation was needed and initiated with improvement. Results: Of the 148 patients evaluated for SBS, 19 were on teduglutide. Mean age was 53 years (range 28-76), 79% female, 63% Caucasian, 16% Black. 31.6% (n=19), 42.1% (n=19), and 42.1% (n=19) never had any screening of zinc, copper, and selenium respectively over the two year period. At baseline, 15.8% (n=19), 10.5% (n=19), and 10.5% (n=19) of patients had screening for zinc, copper, and selenium respectively. Of those checked no patients had a mineral deficiency at baseline. At 6 months, 31.6% (n=19), 31.6% (n=19), and 26.3% (n=19) had screening for zinc, copper, and selenium respectively. There were documented deficiencies of zinc (33.3%), copper (33.3%) and selenium (20%) in those checked at 6 months. Of those with documented deficiencies there was replacement in 62.5% of patients. Less patients were being monitored at 12 months, 18 months and 24 months respectively (Table 1). Conclusion: This study indicates that there is a lack of trace mineral monitoring in patients taking teduglutide for SBS. In those being monitored there was a clear pattern of deficiencies being found by 6 months after initiation requiring repletion. Without adequate monitoring, it is difficult to know if patients are deficient in trace minerals and if supplementation is needed. Thorough monitoring is crucial to avoiding ongoing deficiencies.

#### Hematology-Oncology

Ajani J, El Hajbi F, Cunningham D, Alsina M, Thuss-Patience P, Scagliotti G, Van den Eynde M, **Rybkin I**, Shen L, Kato K, Kim S, D'Alonzo S, Yu W, Tao A, and Van Cutsem E. O-15 Randomized, phase 3 study of second-line tislelizumab vs chemotherapy in advanced or metastatic esophageal squamous cell carcinoma (RATIONALE 302) in the overall population and Europe/North America subgroup. *Ann Oncol* 2021; 32:S225.

Background: The global Phase 3 study RATIONALE 302 (NCT03430843) evaluated the efficacy and safety of second-line tislelizumab, an anti-PD-1 antibody, in patients with advanced or metastatic esophageal squamous cell carcinoma (ESCC). Here, we report data from the overall and Europe/North America (EU/NA) populations. Methods: Eligible adult patients had disease progression during or after first-line systemic therapy,  $\geq 1$  evaluable lesion per RECIST v1.1 and an Eastern Cooperative Oncology Group performance score (ECOG PS) of  $\leq 1$ . Patients were randomized (1:1) to receive tislelizumab 200 mg intravenously Q3W or investigator-chosen chemotherapy (paclitaxel, docetaxel, or irinotecan) and treated until disease progression, intolerable toxicity, or withdrawal. Stratification factors included chemotherapy option, region, and ECOG PS. The primary endpoint was overall survival (OS) in all patients (ITT population). The key secondary endpoint was OS in PD-L1 positive ( $vCPS \geq 10\%$ ) patients; other secondary endpoints included progression-free survival (PFS), overall response rate (ORR), duration of response (DoR), health-related quality of life and safety. Results: 512 patients (overall population) were randomized to tislelizumab (n=256) or chemotherapy (n=256), of which 108

(21%) patients were enrolled into EU/NA subgroup (n=55 tislelizumab, n=53 chemotherapy). On 1 December 2020 (data cut-off), median follow-up was 6.9 and 6.8 months in the overall population and EU/NA subgroup, respectively. Tislelizumab improved OS vs chemotherapy in the overall population (median OS 8.6 vs 6.3 months; HR 0.70, 95% CI 0.57–0.85; p=0.0001); survival benefit was consistently observed in the EU/NA subgroup (median OS 11.2 vs 6.3 months; HR 0.55; 95% CI 0.35–0.87). Treatment with tislelizumab was associated with improved ORR (20.3% [95% CI 15.6%–25.8%] vs 9.8% [95% CI 6.4%–14.1%]) and median DoR (7.1 vs 4.0 months; HR 0.42, 95% CI 0.23–0.75) vs chemotherapy in the overall population. Improvement in ORR (20.0% [95% CI 10.4%–33.0%] vs 11.3% [95% CI 4.3%–23.0%]) and median DOR (5.1 vs 2.1 months; HR 0.42, 95% CI 0.13–1.39) was also observed in the EU/NA subgroup. Fewer patients had Grade  $\geq 3$  treatment-emergent adverse events (TEAE) with tislelizumab vs chemotherapy in both the overall and EU/NA populations (46% vs 68% and 56% vs 71%, respectively). Of these, fewer Grade  $\geq 3$  AEs were treatment-related with tislelizumab vs chemotherapy (overall: 19% vs 56%; EU/NA: 13% vs 51%). AEs leading to death were similar with tislelizumab vs chemotherapy (overall: 14% vs 12%; EU/NA: 6% vs 5%). Conclusions: Second-line tislelizumab demonstrated statistically significant and clinically meaningful improvement in OS versus chemotherapy in patients with advanced or metastatic ESCC. Tislelizumab demonstrated a tolerable safety profile. Efficacy and safety results from the EU/NA subgroup were consistent with the overall population. Clinical trial identification: NCT03430843.

#### Neurology

**Zhang Y, Zhang Y, Chopp M, Pang H, Zhang ZG, Mahmood A, and Xiong Y.** Mir-17-92 cluster-enriched exosomes improve tissue and functional recovery in rats after traumatic brain injury. *J Neurotrauma* 2021; 38(14):A112-A113.

Exosomes play an important role in intercellular communication by delivering microRNAs to recipient cells. Previous studies have demonstrated that multipotent mesenchymal stromal cell (MSC)-derived exosomes improve functional recovery after experimental traumatic brain injury (TBI). This study was performed to determine whether treatment of TBI with miR-17-92 cluster-enriched exosomes (Exo-17-92) harvested from human bone marrow MSCs transfected with a miR-17-92 cluster plasmid enhances tissue and neurological recovery compared to exosomes derived from MSCs transfected with an empty plasmid vector (Exo-empty). Adult male rats were subjected to a unilateral moderate cortical contusion. Animals received a single intravenous injection of miR-17-92 cluster-enriched exosomes (100  $\mu$ g/rat, Exo-17-92) or control exosomes (100  $\mu$ g/rat, Exoempty) or Vehicle (phosphate-buffered solution) 1 day after injury. A battery of neurological functional tests were performed weekly after TBI for 5 weeks. Spatial learning and memory were measured on days 31-35 after TBI using the Morris water maze test. All animals were sacrificed 5 weeks after injury. Their brains were processed for histopathological and immunohistochemical analyses of lesion volume, cell loss, angiogenesis, neurogenesis and neuroinflammation. Compared to the vehicle, both Exo-17-92 and Exo-empty treatments significantly improved sensorimotor and cognitive function, reduced neuroinflammation and hippocampal neuronal cell loss, promoted angiogenesis and neurogenesis without altering the lesion volume. Moreover, Exo-17-92 treatment exhibited a significantly more robust therapeutic effect on improvement in functional recovery by reducing neuroinflammation and cell loss, enhancing angiogenesis and neurogenesis than did Exo-empty treatment. In conclusion, exosomes enriched with miR-17-92 cluster have a significantly better effect on improving functional recovery after TBI compared to Exo-empty, likely by reducing neuroinflammation and enhancing endogenous angiogenesis and neurogenesis. Engineering specific miRNA in exosomes may provide a novel therapeutic strategy for treatment of TBI.

## Neurosurgery

**Penning DH, Cazacu S, Jevtovic-Todorovic V, Kalkanis S, Lewis M, and Brodie C.** Neuron-glia crosstalk mediate the neurotoxic effects of ketamine via extracellular vesicles. *GLIA* 2021; 69(SUPPL 1):E302-E303.

Background: General anesthetics (GA) are associated with neurodevelopmental abnormalities including cell death, cognitive and behavioral changes. There is now powerful evidence for non-cell autonomous mechanisms in almost every pathological condition in the brain, especially relevant to glial cells, mainly astrocytes and microglia, that exhibit structural and functional contacts with neurons. These interactions were recently reported to occur via the secretion of extracellular vesicles (EVs). Here, we employed primary human neural cells to analyze ketamine effects focusing on the functions of glial cells and their polarization/differentiation state. We also explored the roles of extracellular vesicles (EVs) and different components of the BDNF pathway. Methods: Ketamine effects were analyzed on human neuronal and glial cell proliferation and apoptosis and astrocytic (A1/A2) and microglial (M1/M2) cell activation were analyzed. The impact of the neuron-glia cell interactions in the neurotoxic effects of ketamine was analyzed using transwell co-cultures. The role of the brain-derived neurotrophic factor (BDNF) pathway, was analyzed using RT-PCR, ELISA western blot and gene silencing. EVs secreted by ketamine-treated cells were isolated, characterized and analyzed for their effects in neuron-glia cell interactions. Data were analyzed using analysis of variance or a Student's t test with correction for data sets with unequal variances. Results: Ketamine induced neuronal and oligodendrocytic cell apoptosis and promoted the expression of proinflammatory astrocytes (A1) and microglia (M1) phenotypes. Astrocytes and microglia enhanced the neurotoxic effects of ketamine on neuronal cells, whereas neurons increased oligodendrocyte cell death. Ketamine modulated different components in the BDNF pathway: decreasing BDNF secretion in neurons and astrocytes while increasing the expression of p75 in neurons and oligodendrocytes. In addition, ketamine treatment increased the lncRNA BDNF-AS levels and the secretion of pro-BDNF secretion. We found an important role of EVs secreted by ketamine-treated astrocytes in neuronal cell death by delivering BDNF-AS. Conclusions: Ketamine neurotoxicity involves both autonomous and non-cell autonomous mechanisms and components of the BDNF pathway expressed by neurons and glial cells represent major regulators of ketamine effects. We demonstrated for the first time a role of EVs as important mediators of ketamine effects by the delivery of specific non-coding RNAs. These results may contribute to a better understanding of cellular and molecular mechanisms underlying ketamine neurotoxic effects in humans and to the development of potential approaches to decrease its neurodevelopmental impact.

## Neurosurgery

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neurological functional tests were performed weekly after TBI for 5 weeks. Spatial learning and memory were measured on days 31-35 after TBI using the Morris water maze test. All animals were sacrificed 5 weeks after injury. Their brains were processed for histopathological and immunohistochemical analyses of lesion volume, cell loss, angiogenesis, neurogenesis and neuroinflammation. Compared to the vehicle, both Exo-17-92 and Exo-empty treatments significantly improved sensorimotor and cognitive function, reduced neuroinflammation and hippocampal neuronal cell loss, promoted angiogenesis and neurogenesis without altering the lesion volume. Moreover, Exo-17-92 treatment exhibited a significantly more robust therapeutic effect on improvement in functional recovery by reducing neuroinflammation and cell loss, enhancing angiogenesis and neurogenesis than did Exo-empty treatment. In conclusion, exosomes enriched with miR-17-92 cluster have a significantly better effect on improving functional recovery after TBI compared to Exo-empty, likely by reducing neuroinflammation and enhancing endogenous angiogenesis and neurogenesis. Engineering specific miRNA in exosomes may provide a novel therapeutic strategy for treatment of TBI.

#### Orthopedics/Bone and Joint Center

**Franovic S, Taylor KA, Kuhlmann NA, Aboona F, Schlosser C, and Muh SJ.** PROMIS CAT Forms Demonstrate Responsiveness in Patients Following Reverse Total Arthroplasty Across Numerous Health Domains. *J Shoulder Elbow Surg* 2021; 30(7):e430.

**Aim:** The purpose of this study was to investigate the responsiveness of three PROMIS CAT domains in patients undergoing reverse shoulder arthroplasty. **Background:** To better optimize the administration and postoperative tracking of patients using PROM, the Patient-Reported Outcomes Measurement Information System (PROMIS) was established by the National Institutes of Health. PROMIS CAT domains have been since validated in multiple orthopedic interventions of the shoulder, however, no one to date has studied the responsiveness of PROMIS CAT domains in a cohort of patients undergoing reverse shoulder arthroplasty. **Methods:** Patients undergoing reverse shoulder arthroplasty by a board-certified shoulder and elbow surgeon were included in this study. PROMIS CAT Upper Extremity Physical Function ("PROMIS-UE"), Pain Interference ("PROMIS-PI"), and Depression ("PROMIS-D") scores were collected preoperatively and at five postoperative timepoints. Patient-centric demographic factors, range of motion, and clinical characteristics were also reviewed and analyzed for association with PROMIS scores. **Results:** 104 patients undergoing primary reverse shoulder arthroplasty were included in this study. The patient cohort consisted of 52 males (50.0%), an average age of 70.3 years (standard deviation, 11.2), and a BMI of 30.2 (standard deviation, 6.1). All three PROMIS domains showed significant improvement as early as 6 weeks after surgery, with values of  $32.4 \pm 6.6$ ,  $56.2 \pm 7.5$ , and  $44.6 \pm 8.6$ , for PROMIS-UE, PROMIS-PI, and PROMIS-D, respectively. Significant improvements were noted for each postoperative timepoint thereafter, with 1-year follow up values as follows:  $42.1 \pm 8.7$ ,  $52.5 \pm 8.6$ , and  $43.6 \pm 9.5$  for PROMIS-UE, PROMIS-PI, and PROMIS-D, respectively. Moderate correlations were identified with postoperative PROMIS-UE and abduction ( $r=0.439$ ,  $p<0.01$ ), as well as postoperative PROMIS-PI and PROMIS-D ( $r=0.502$ ,  $p<0.01$ ). **Conclusions:** PROMIS CAT forms demonstrate responsiveness in patients undergoing reverse shoulder arthroplasty.

#### Research Administration

**Penning DH, Cazacu S, Jevtovic-Todorovic V, Kalkanis S, Lewis M, and Brodie C.** Neuron-glia crosstalk mediate the neurotoxic effects of ketamine via extracellular vesicles. *GLIA* 2021; 69(SUPPL 1):E302-E303.

**Background:** General anesthetics (GA) are associated with neurodevelopmental abnormalities including cell death, cognitive and behavioral changes. There is now powerful evidence for non-

cell autonomous mechanisms in almost every pathological condition in the brain, especially relevant to glial cells, mainly astrocytes and microglia, that exhibit structural and functional contacts with neurons. These interactions were recently reported to occur via the secretion of extracellular vesicles (EVs). Here, we employed primary human neural cells to analyze ketamine effects focusing on the functions of glial cells and their polarization/differentiation state. We also explored the roles of extracellular vesicles (EVs) and different components of the BDNF pathway. Methods: Ketamine effects were analyzed on human neuronal and glial cell proliferation and apoptosis and astrocytic (A1/A2) and microglial (M1/M2) cell activation were analyzed. The impact of the neuron-glia cell interactions in the neurotoxic effects of ketamine was analyzed using transwell co-cultures. The role of the brain-derived neurotrophic factor (BDNF) pathway, was analyzed using RT-PCR, ELISA western blot and gene silencing. EVs secreted by ketamine-treated cells were isolated, characterized and analyzed for their effects in neuron-glia cell interactions. Data were analyzed using analysis of variance or a Student's t test with correction for data sets with unequal variances. Results: Ketamine induced neuronal and oligodendrocytic cell apoptosis and promoted the expression of proinflammatory astrocytes (A1) and microglia (M1) phenotypes. Astrocytes and microglia enhanced the neurotoxic effects of ketamine on neuronal cells, whereas neurons increased oligodendrocyte cell death. Ketamine modulated different components in the BDNF pathway: decreasing BDNF secretion in neurons and astrocytes while increasing the expression of p75 in neurons and oligodendrocytes. In addition, ketamine treatment increased the lncRNA BDNF-AS levels and the secretion of pro-BDNF secretion. We found an important role of EVs secreted by ketamine-treated astrocytes in neuronal cell death by delivering BDNF-AS. Conclusions: Ketamine neurotoxicity involves both autonomous and non-cell autonomous mechanisms and components of the BDNF pathway expressed by neurons and glial cells represent major regulators of ketamine effects. We demonstrated for the first time a role of EVs as important mediators of ketamine effects by the delivery of specific non-coding RNAs. These results may contribute to a better understanding of cellular and molecular mechanisms underlying ketamine neurotoxic effects in humans and to the development of potential approaches to decrease its neurodevelopmental impact.

### Surgery

Qasawa A, **Beltran N, Nagai S, Muszkat Y, and Jafri S.** Quality of trace mineral monitoring and replacement for patients on teduglutide for short bowel syndrome. *Transplantation* 2021; 105(7 SUPPL 1):S71.

Introduction: We evaluated serum levels of trace minerals including zinc, copper, and selenium in patients with short bowel syndrome (SBS) taking teduglutide. We worked to see if trace mineral values were being monitored and corrected. Methods: We performed a retrospective review to identify patients with SBS on teduglutide. We obtained data for two years following initiation for monitoring of serum levels for zinc, copper, and selenium. We identified if supplementation was needed and initiated with improvement. Results: Of the 148 patients evaluated for SBS, 19 were on teduglutide. Mean age was 53 years (range 28-76), 79% female, 63% Caucasian, 16% Black. 31.6% (n=19), 42.1% (n=19), and 42.1% (n=19) never had any screening of zinc, copper, and selenium respectively over the two year period. At baseline, 15.8% (n=19), 10.5% (n=19), and 10.5% (n=19) of patients had screening for zinc, copper, and selenium respectively. Of those checked no patients had a mineral deficiency at baseline. At 6 months, 31.6% (n=19), 31.6% (n=19), and 26.3% (n=19) had screening for zinc, copper, and selenium respectively. There were documented deficiencies of zinc (33.3%), copper (33.3%) and selenium (20%) in those checked at 6 months. Of those with documented deficiencies there was replacement in 62.5% of patients. Less patients were being monitored at 12 months, 18 months and 24 months respectively (Table 1). Conclusion: This study indicates that there is a lack of trace mineral monitoring in patients taking teduglutide for SBS. In those being monitored

there was a clear pattern of deficiencies being found by 6 months after initiation requiring repletion. Without adequate monitoring, it is difficult to know if patients are deficient in trace minerals and if supplementation is needed. Thorough monitoring is crucial to avoiding ongoing deficiencies.

## Books and Book Chapters

### Otolaryngology

Bokhari MR, and **Greene J**. Pleomorphic Adenoma. *StatPearls* 2021; Epub ahead of print. PMID: 28613579. [Full Text](#)

Pleomorphic adenoma, the most common salivary gland tumor, is also known as benign mixed tumors (BMT's), because of its dual origin from epithelial and myoepithelial elements. It is the commonest of all salivary gland tumors constituting up to two-thirds of all salivary gland tumors.

### Surgery

**Ahmed S**, and Sharman T. Intestinal Pseudo-Obstruction. *StatPearls* 2021; Epub ahead of print. PMID: 32809504. [Full Text](#)

Intestinal pseudo-obstruction is characterized by the dilation of bowel in the absence of an anatomical obstruction. Patients present with the signs and symptoms of bowel obstruction, including nausea, vomiting, abdominal distension, and obstipation with bowel dilation on x-ray or CT imaging. Pseudo-obstruction can be acute or chronic. Acute colonic pseudo-obstruction (ACPO), also known as Ogilvie syndrome, most commonly affects the large intestine from the cecum to the splenic flexure. The exact pathophysiology is unknown, but it has been linked to dysregulation of the autonomic nervous system. Most cases are found in patients who have undergone surgery or are critically ill. After a mechanical obstruction is ruled out, initial management includes bowel rest, nasogastric decompression, intravenous fluid resuscitation, and treatment of the underlying cause. Further treatment options include administration of Neostigmine as well as endoscopic, percutaneous, or surgical decompression. Chronic intestinal pseudo-obstruction (CIPO) is a more rare form of pseudo-obstruction, usually causing early satiety, nausea, bloating, and distension. Causes are usually infectious, metabolic, neurologic, autoimmune, or idiopathic.

### Surgery

**Bennett B**, and Akhondi H. Epiphrenic Diverticula. *StatPearls* 2021; Epub ahead of print. PMID: 32644536. [Full Text](#)

Epiphrenic diverticulum, also known as a pulsion diverticulum, is a rare type of esophageal diverticulum occurring in the distal 10 centimeters (CM) of the esophagus most commonly 4cm to 8 cm above the gastric cardia. These diverticula are made up of the mucosal and submucosal lining, herniating through a weakness in the muscularis layer of the esophagus, classifying them as false or pseudodiverticula. This anatomical weakness in the muscularis layer is where nerves and blood vessels enter to supply the distal esophagus.

### Surgery

Hope WW, and **Pfeifer C**. Laparoscopic Inguinal Hernia Repair. *StatPearls* 2021; Epub ahead of print. PMID: 28613576. [Full Text](#)

Inguinal hernia repairs are one of the most common general surgical operations performed in the world. Diagnosis of inguinal hernias is typically performed using a thorough history, and physical and is typically signified by a bulge in the groin. There are many treatment options for patients with inguinal hernias including watchful waiting, open primary repair, open tension-free repairs with the use of mesh prosthetics, and laparoscopic repairs which are typically performed with mesh prosthetics.

## HFHS Publications on COVID-19

### Cardiology/Cardiovascular Research

Bansal A, Goldstein D, Schettle S, Pepitone S, Lima B, Pham DT, **Cowger J**, Schubert A, and Pinney SP. Institutional preparedness strategies for heart failure, durable left ventricular assist device, and heart transplant patients during the Coronavirus Disease 2019 (COVID-19) pandemic. *J Thorac Cardiovasc Surg* 2021; 162(1):131-135. PMID: 32994096. [Full Text](#)

### Cardiology/Cardiovascular Research

Kadavath S, Hawwas D, Strobel A, Mohan J, Bernardo M, Kassier A, Ya'qoub L, Madan N, Ashraf S, Salehi N, **Mawri S**, Rehman KA, Siraj A, Alraies C, Saad M, and Aronow H. How the COVID-19 Pandemic Has Affected Cardiology Fellow Training. *Am J Cardiol* 2021; 151:114-117. PMID: 34052015. [Full Text](#)

### Emergency Medicine

Bunch CM, Thomas AV, Stillson JE, Gillespie L, Khan RZ, Zackariya N, Shariff F, Al-Fadhli M, Mjaess N, Miller PD, McCurdy MT, Fulkerson DH, **Miller JB**, Kwaan HC, Moore EE, Moore HB, Neal MD, Martin PL, Kricheff ML, and Walsh MM. Preventing Thrombohemorrhagic Complications of Heparinized COVID-19 Patients Using Adjunctive Thromboelastography: A Retrospective Study. *J Clin Med* 2021; 10(14). PMID: 34300263. [Full Text](#)

### Gastroenterology

Elmunzer BJ, Spitzer RL, **Dang DT**, **Piraka CR**, et al. Digestive Manifestations in Patients Hospitalized With Coronavirus Disease 2019. *Clin Gastroenterol Hepatol* 2021; 19(7):1355-1365.e1354. PMID: 33010411. [Full Text](#)

### Gastroenterology

Fernandez M, Cristina Segovia M, Dijkstra G, Herlenius G, Testro A, Sharkey L, Braun F, Rumbo C, Lacaille F, Friend P, **Jafri S**, Vilca Melendez H, Horslen S, Schiano T, Zanfi C, Solar H, Ramisch D, Mazariegos G, and Gondolesi G. The effect of the COVID-19 pandemic in intestinal rehabilitation and transplant patients, initial results of an international survey. *Transplantation* 2021; 105(7 SUPPL 1):S11-S12.

### Hematology-Oncology

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### Hospital Medicine

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