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Henry Ford Health System Publication List – May 2021

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 **144 unique citations** listed this month, with **8 articles** and **5 conference abstracts 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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Jump to:

Articles

Conference Abstracts

Articles

Administration

Fortin CN, Jiang C, **Caldwell MT**, As-Sanie S, Dalton V, and Marsh EE. Trends in Emergency Department Utilization Among Women With Leiomyomas in the United States. *Obstet Gynecol* 2021; 137(5):897-905. PMID: 33831918. Full Text

Division of Reproductive Endocrinology and Infertility and the Division of Gynecology, Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, and the Department of Emergency Medicine, Henry Ford Hospital, Detroit, Michigan.

OBJECTIVE: To describe trends in emergency department (ED) visits in the United States with a primary diagnosis of leiomyomas, subsequent admissions, and associated charges. METHODS: The Healthcare Cost and Utilization Project Nationwide Emergency Department Sample database was used to retrospectively identify all ED visits from 2006 to 2017 among women aged 18-55 years with a primary diagnosis of leiomyomas as indicated by International Classification of Diseases (ICD) diagnosis codes. Trends in ED visits and subsequent admissions were analyzed and stratified by patient and hospital characteristics. Secondary ICD codes, Current Procedural Terminology codes, and hospital charges were analyzed. A multivariate regression model was used to identify predictors of admission. RESULTS: Although the number of ED visits for leiomyomas increased from 28,732 in 2006 to 65,685 in 2017, the admission rate decreased, from 23.9% in 2006 to 11.1% in 2017. Emergency department visits for leiomyomas were highest among women who were aged 36-45 years (44.5%), in the lowest income quartile (36.1%), privately insured (38.3%), and living in the South (46.2%). Admission was more likely at nonteaching hospitals (odds ratio [OR] 1.23, 95% CI 1.08-1.39) or those located in the Northeast (OR 1.39, 95% CI 1.15-1.68). Patient characteristics associated with admission included older age (26-35 years: OR 1.42, 95% CI 1.21-1.66; 36-45 years: OR 2.01, 95% CI 1.72-2.34; 46-55 years: OR 2.60, 95% CI 2.23-3.03) and bleeding-related complaints (OR 14.92, 95% CI 14.00-15.90). Admission was least likely in uninsured patients (Medicare: OR 1.37, 95% CI 1.21-1.54; Medicaid: OR 1.26, 95% CI 1.16-1.36; private: OR 1.44, 95% CI 1.32-1.56). CONCLUSION: Although ED visits for leiomyomas are increasing, admission rates for these visits are decreasing. The substantial decline in admissions suggests many of these visits could potentially be addressed in a non-acute-care setting. However, when women with leiomyomas present with a bleeding-related complaint, the odds of admission increase 15-fold. There is an apparent disparity in likelihood of admission based on insurance type.

Allergy and Immunology

Altman MC, Flynn K, Rosasco MG, Dapas M, Kattan M, Lovinsky-Desir S, O'Connor GT, Gill MA, Gruchalla RS, Liu AH, Pongracic JA, Khurana Hershey GK, **Zoratti EM**, Teach SJ, Rastrogi D, Wood RA, Bacharier LB, LeBeau P, Gergen PJ, Togias A, Busse WW, Presnell S, Gern JE, Ober C, and Jackson DJ. Inducible expression quantitative trait locus analysis of the MUC5AC gene in asthma in urban populations of children. *J Allergy Clin Immunol* 2021; Epub ahead of print. PMID: 34019912. Full Text

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BACKGROUND: Mucus plugging can worsen asthma control, lead to reduced lung function and fatal exacerbations. MUC5AC is the secretory mucin implicated in mucus plugging, and MUC5AC gene expression has been associated with development of airway obstruction and asthma exacerbations in urban children with asthma. However, the genetic determinants of MUC5AC expression are not established. OBJECTIVE: To assess single-nucleotide polymorphisms (SNPs) that influence MUC5AC expression and relate to pulmonary functions in childhood asthma. METHODS: We used RNA-sequencing data from upper airway samples and performed cis-expression quantitative trait loci (eQTL) and allele specific expression (ASE) analyses in two cohorts of predominantly Black and Hispanic urban children, a high asthma-risk birth cohort and an exacerbation-prone asthma cohort. We further investigated inducible MUC5AC eQTLs during incipient asthma exacerbations. We tested significant eQTLs SNPs for associations with lung function measurements and investigated their functional consequences in DNA regulatory databases. RESULTS: We identified two independent groups of SNPs in the MUC5AC gene that were significantly associated with MUC5AC expression. Moreover, these SNPs showed stronger eQTL associations with MUC5AC expression during asthma exacerbations, consistent with inducible expression. SNPs in one group also showed significant association with decreased pulmonary functions. These SNPs included multiple EGR1 transcription factor binding sites suggesting a mechanism of effect. CONCLUSIONS: These findings demonstrate the applicability of organ specific RNA-sequencing data to determine genetic factors contributing to a key disease pathway. Specifically, they suggest important genetic variations that may underlie propensity to mucus plugging in asthma and could be important in targeted asthma phenotyping and disease management strategies.

Allergy and Immunology

Eapen AA, and **Kim H**. The Phenotype of the Food-Allergic Patient. *Immunol Allergy Clin North Am* 2021; 41(2):165-175. PMID: 33863477. Full Text

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Food allergy's increasing prevalence across the globe has initiated research into risk factors associated with the disease and coexistence with other allergic diseases. Longitudinal birth cohorts have identified food allergy phenotypes of patients based on genetic background, racial diversity, and environmental factors. Identifying food sensitization patterns and coexistence of other allergic diseases allows physicians to provide appropriate care for food allergy and personalized anticipatory guidance for the appearance of other allergic diseases. The authors seek to detail key findings of 4 longitudinal allergy birth cohorts that investigate food allergy and other allergic diseases to further characterize food allergy phenotypes.

Allergy and Immunology

Havstad SL, **Sitarik A**, **Kim H**, **Zoratti EM**, Ownby D, **Johnson CC**, and **Wegienka G**. Increased Risk of Asthma at Age 10 Years for Multiple-allergen Sensitized Children. *Ann Allergy Asthma Immunol* 2021; Epub ahead of print. PMID: 33971358. Full Text

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BACKGROUND: Childhood sensitization patterns have been previously found to be related to variable risk of early life allergic disease in several birth cohorts. OBJECTIVE: To determine whether these risks persist into later childhood. METHODS: In the WHEALS birth cohort, previous latent class analysis based

on sensitization to ten allergens, found four early life sensitization patterns (ELSP): "Highly sensitized", "Milk/egg dominated", "Peanut and inhalant(s)", and "Low to no sensitization" at age two years. At an age 10 study-specific visit, children were evaluated by an allergist for current asthma and atopic dermatitis (AD) through a physical exam and interviews with the child and parent/guardian. Total and specific immunoglobulin E (IgE), spirometry, and methacholine challenge were also completed. RESULTS: Compared with children sensitized to none or one allergen, children sensitized to four or more food and inhalant allergens at age two had the highest risk of current asthma (risk ratio [RR]=4.42; 95% CI 2.58-7.59; p<0.001) and bronchial hyperresponsiveness [BHR] (RR=1.77; 95% CI 1.29-2.42; p<0.001). Additionally, they had the highest levels of total IgE (geometric mean [GM]=800 IU/mL, 95% CI 416-1536) among the four groups. Risk of current atopic dermatitis did not depend on pattern of sensitization but remained increased for children with any sensitization (RR=2.23; 95% CI 1.40-3.55; p<0.001). No differences in spirometry (FEV1, FEF2575, and FEV1/FVC) were identified. CONCLUSION: The previously reported importance of a specific pattern of sensitization in early life.

Anesthesiology

Anger M, Valovska T, **Beloeil H**, Lirk P, Joshi GP, Van de Velde M, and Raeder J. PROSPECT guideline for total hip arthroplasty: a systematic review and procedure-specific postoperative pain management recommendations. *Anaesthesia* 2021; Epub ahead of print. PMID: 34015859. Full Text

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The aim of this systematic review was to develop recommendations for the management of postoperative pain after primary elective total hip arthroplasty, updating the previous procedure-specific postoperative pain management (PROSPECT) guidelines published in 2005 and updated in July 2010. Randomised controlled trials and meta-analyses published between July 2010 and December 2019 assessing postoperative pain using analgesic, anaesthetic, surgical or other interventions were identified from MEDLINE, Embase and Cochrane databases. Five hundred and twenty studies were initially identified, of which 108 randomised trials and 21 meta-analyses met the inclusion criteria. Peri-operative interventions that improved postoperative pain include: paracetamol; cyclo-oxygenase-2-selective inhibitors; non-steroidal anti-inflammatory drugs; and intravenous dexamethasone. In addition, peripheral nerve blocks (femoral nerve block; lumbar plexus block; fascia iliaca block), single-shot local infiltration analgesia, intrathecal morphine and epidural analgesia also improved pain. Limited or inconsistent evidence was found for all other approaches evaluated. Surgical and anaesthetic techniques appear to have a minor impact on postoperative pain, and thus their choice should be based on criteria other than pain. In summary, the analgesic regimen for total hip arthroplasty should include pre-operative or intra-operative paracetamol and cyclo-oxygenase-2-selective inhibitors or non-steroidal anti-inflammatory drugs, continued postoperatively with opioids used as rescue analgesics. In addition, intra-operative intravenous dexamethasone 8-10 mg is recommended. Regional analgesic techniques such as fascia iliaca block or local infiltration analgesia are recommended, especially if there are contra-indications to basic analgesics and/or in patients with high expected postoperative pain. Epidural analgesia, femoral nerve block, lumbar plexus block and gabapentinoid administration are not recommended as the adverse effects outweigh the benefits. Although intrathecal morphine 0.1 mg can be used, the PROSPECT group emphasises the risks and side-effects associated with its use and provides evidence that adequate analgesia may be achieved with basic analgesics and regional techniques without intrathecal morphine.

Anesthesiology

Patel N, **John JK**, **Pakeerappa P**, **Aiyer R**, and **Zador LN**. Slipping rib syndrome: case report of an iatrogenic result following video-assisted thoracic surgery and chest tube placement. *Pain Manag* 2021; Epub ahead of print. PMID: 33980032. Request Article

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The aim of this case report is to shed light on slipping rib syndrome (SRS), a painful and overlooked condition. A 62-year old man reported intermittent, self-resolving sharp rib pain that began after a video-assisted thoracic surgery and chest tube placement 4 years prior to presentation. The patient's pain was associated with a rigid protrusion in the right upper quadrant, and home use of acetaminophen provided no relief. After physical examination, multiple imaging and lab tests, the patient was diagnosed with SRS and was referred to physical therapy and thoracic surgery for further evaluation. SRS is an under-recognized cause of upper abdominal and lower thoracic pain that should be considered if a patient's history includes previous trauma or abdominal surgery.
Lay abstract This is a case report of slipping rib syndrome (SRS). It is a painful medical condition. A 62-year old man after a video-assisted thoracic surgery and chest tube placement had recurrent, self-resolving sharp rib pain. The pain was associated with a rigid lump in the right lower rib cage. Acetaminophen and narcotics provided no relief. After physical examination, multiple imaging and lab tests, he was diagnosed with SRS and was referred to physical therapy and thoracic surgery for further evaluation. SRS is an under-recognized cause of rib pain that should be considered if a patient's history includes previous trauma or abdominal surgery.

Behavioral Health Services/Psychiatry

Gautam M, **Patel S**, and **Sablaban I**. Intramuscular B52. *Prim Care Companion CNS Disord* 2021; 23(3). PMID: 34015196. Request Article

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Behavioral Health Services/Psychiatry

Jiang Y, Farrell AK, **Tobin ET**, Mair-Meijers HE, Wildman DE, Luca F, Slatcher RB, and Zilioli S. Socioeconomic status, financial stress, and glucocorticoid resistance among youth with asthma: Testing the moderation effects of maternal involvement and warmth. *Brain Behav Immun* 2021; Epub ahead of print. PMID: 34015429. Full Text

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OBJECTIVES: Children who grow up in more socioeconomically disadvantaged homes experience greater levels of inflammation and worse asthma symptoms than children from more advantaged families.

However, recent evidence suggests that certain family-level factors can mitigate health disparities associated with socioeconomic status (SES). In a sample of youth with asthma, we investigated the potential buffering effects of maternal involvement and warmth on SES disparities in asthma-related immune responses, assessed via glucocorticoid resistance (GR) of immune cells. METHODS: One hundred and forty-three youth (10-16 years of age) with asthma completed measures of maternal involvement and warmth, and their primary caregivers reported their levels of education, income, and financial stress. Peripheral blood mononuclear cells from youth's blood were isolated, cultured, and assayed to determine mitogen-stimulated (PMA/INO + Etho) and mitogen/hydrocortisone-stimulated (PMA/INO + Cort) levels of two Th-2 cytokines (i.e., interleukin-5, interleukin-13) and one Th-1 cytokine (i.e., interferon-γ). GR was calculated by subtracting log-transformed cytokine concentration in the PMA/INO + Etho samples from log-transformed cytokine concentration in the PMA/INO + Cort samples. RESULTS: Both maternal involvement and warmth moderated the indirect pathway from family SES to GR of Th-2 cytokines via financial stress. Specifically, we found that low family SES was associated with elevated GR of Th-2 cytokines via increased financial stress among youth reporting low levels of maternal involvement and warmth, but not among those reporting high levels of maternal involvement or warmth. CONCLUSIONS: These results highlight the protective role of maternal involvement and warmth in health-related biological processes modulated by family SES among youth with asthma.

Cardiology/Cardiovascular Research

Aurora L, **McCord J**, **Nowak R**, Giannitsis E, Christenson R, DeFilippi C, Lindahl B, Christ M, Body R, **Jacobsen G**, and Mueller C. Prognostic Utility of a Modified HEART Score When Different Troponin Cut-points Are Used. *Crit Pathw Cardiol* 2021; Epub ahead of print. PMID: 33988541. Full Text

Heart and Vascular Institute, Henry Ford Health System, Detroit, MI, USA Department of Emergency Medicine, Henry Ford Hospital, Detroit, MI, USA Depar Medizinische Klinik III, Universitätsklinikum Heidelberg, Heidelberg, Germany Department of Pathology, University of Maryland School of Medicine, Baltimore, MD, USA Department of Medicine, Inova Heart and Vascular Institute, Falls Church, VA, USA Department of Medical Sciences and Uppsala Clinical Research Center, Uppsala University, Uppsala, Sweden Department of Emergency Medicine, Cantonal Hospital Lucerne, Switzerland Manchester University NHS Foundation Trust, Manchester, United Kingdom Division of Cardiovascular Sciences, University of Manchester, Manchester, United Kingdom Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA Cardiology and Cardiovascular Research Institute Basel, University Hospital Basel, Switzerland.

BACKGROUND: Although the recommended cut-point for cardiac troponin (cTn) is the 99th percentile, many institutions use cut-points that are multiples higher than the 99th percentile for diagnosing acute myocardial infarction (AMI). Prior studies have shown that patients with a HEART score (HS) ≤ 3 and normal serial cTn values (modified HS) are at low risk for adverse events. This study aimed to evaluate the prognostic utility of the HS when various cTn cut-points are used. METHODS: This was a sub-study of TRAPID-AMI, a multicenter, international trial evaluating a rapid rule-out AMI study using high sensitivity cTnT (hs-cTnT). 1,282 patients were evaluated for AMI from 12 centers in Europe, United States of America, and Australia from 2011-2013. Blood samples of hs-cTnT were collected at presentation and 2 hours, and each patient had a HS calculated. The US Food and Drug Administration approved 99th percentile for hs-cTnT (19 ng/L) was used. RESULTS: There were 213 (17%) AMIs. Within 30 days, there were an additional 2 AMIs and 8 deaths. The adverse event rates at 30 days (death/AMI) for a HS ≤ 3 and non-elevated hs-cTnT over 2 hours using increasing hs-cTnT cut-points ranged from 0.6% to 5.1%. CONCLUSIONS: Using the recommended 99th percentile cut-point for hs-cTnT, the combination of a HS ≤ 3 with non-elevated hs-cTnT values over 2 hours identifies a low-risk cohort who can be considered for discharge from the emergency department without further testing. The prognostic utility of this strategy is greatly lessened as higher hs-cTnT cut-points are used.

Cardiology/Cardiovascular Research

Balan P, and **Eng MH**. More energy, more costs. *Catheter Cardiovasc Interv* 2021; 97(6):1235. PMID: 33974744. Full Text

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Cardiology/Cardiovascular Research
Desai ND, O'Brien SM, Cohen DJ, Carroll J, Vemulapalli S, Arnold SV, Forrest JK, Thourani VH, Kirtane AJ, **O'Neill B**, Manandhar P, Shahian DM, Badhwar V, and Bavaria JE. A Composite Metric for Benchmarking Site Performance in TAVR: Results from the STS/ACC TVT Registry. *Circulation* 2021; Epub ahead of print. PMID: 33947202. Full Text

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Background: Transcatheter aortic valve replacement (TAVR) is a transformative therapy for aortic stenosis. Despite rapid improvements in technology and techniques, serious complications remain relatively common and are not well described by single outcome measures. The purpose of this study was to determine if there is site-level variation in TAVR outcomes in the United States using a novel 30-day composite measure. Methods: We performed a retrospective cohort study using data from the STS/ACC TVT Registry to develop a novel ranked composite performance measure that incorporates mortality and serious complications. The selection and rank order of the complications for the composite was determined by their adjusted association with 1-year outcomes. Sites whose risk-adjusted outcomes were significantly more or less frequent than the national average based on a 95% probability interval were classified as performing worse or better than expected. Results: The development cohort consisted of 52,561 patients who underwent TAVR between January 1, 2015 and December 31, 2017. Based on the associations with 1-year risk-adjusted mortality and health status, we identified four periprocedural complications to include in the composite risk model in addition to mortality. Ranked empirically according to severity, these included stroke, major, life-threatening or disabling bleeding, stage III acute kidney injury, and moderate or severe peri-valvular regurgitation. Based on these ranked outcomes, we found that there was significant site-level variation in quality of care in TAVR in the United States. Overall, better than expected site performance was observed in 25/301 (8%) of sites; performance as expected was observed in 242/301 sites (80%); and worse than expected performance was observed in 34/301 (11%) of sites. Thirty-day mortality, stroke, major, life-threatening or disabling bleeding, and moderate or severe peri-valvular leak were each substantially more common in sites with worse than expected performance as compared with other sites. There was good aggregate reliability of the model. Conclusions: There are substantial variations in the quality of TAVR care received in the United States, and 11% of sites were identified as providing care below the average level of performance. Further study is necessary to determine structural, process-related, and technical factors associated with high- and low-performing sites.

Cardiology/Cardiovascular Research
Dixit P, and **Ananthasubramaniam K**. No shortcuts with left bundle branch block and myocardial perfusion imaging: Lesson learnt with dobutamine cardiac PET. *J Nucl Cardiol* 2021; Epub ahead of print. PMID: 33959844. Full Text

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Cardiology/Cardiovascular Research

Eng MH, Abbas AE, Hahn RT, **Lee J**, **Wang DD**, Eleid MF, and **O'Neill WW**. Real world outcomes using 20 mm balloon expandable SAPIEN 3/ultra valves compared to larger valves (23, 26, and 29 mm)-a propensity matched analysis. *Catheter Cardiovasc Interv* 2021; Epub ahead of print. PMID: 33984182. Full Text

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OBJECTIVE/BACKGROUND: Small balloon expandable valves have higher echocardiographic transvalvular gradients and rates of prosthesis-patient mismatch (PPM) compared to larger valves. However, the impact of these echocardiographic findings on clinical outcomes is unknown. We sought to determine the clinical outcomes of 20 mm SAPIEN 3 (S3 BEV) compared to larger S3 BEV in relation to echocardiographic hemodynamics. METHODS: Using the STS/ACC transcatheter valve registry, we performed a propensity-matched comparison of patients undergoing treatment of native aortic valve stenosis using transfemoral, balloon-expandable implantation of 20 mm and ≥ 23 mm S3 BEVs. Baseline and procedure characteristics, echocardiographic variables and survival were analyzed. Multivariable logistic regression was used to identify predictors of 1-year mortality. RESULTS: After propensity matching of the 20 mm and ≥ 23 mm SAPIEN 3 valves, 3,931 pairs with comparable baseline characteristics were identified. Small valves were associated with significantly higher echocardiographic gradients at discharge (15.7 ± 7.1 mmHg vs. 11.7 ± 5.5 mmHg, $p < 0.0001$) and severe PPM rates (21.5% vs. 9.7%, $p < 0.0001$). There was no significant difference in 1-year all-cause mortality (20 mm: 13.0% vs. ≥23 mm: 12.7%, $p = 0.72$) or other major adverse event rates and outcomes between the two cohorts. Based on a multivariable analysis, elevated discharge mean gradient (>20 mmHg), severe PPM and the use of 20 mm versus ≥23 mm were not independent predictors of 1-year mortality. CONCLUSION: SAPIEN 3 20 mm valves were associated with higher echocardiographic gradients, and severe PPM rates compared to larger valves but these factors were not associated with significant differences in 1-year all-cause mortality or rehospitalization.

Cardiology/Cardiovascular Research

Findley AS, Monziani A, Richards AL, Rhodes K, Ward MC, Kalita CA, Alazizi A, Pazokitoroudi A, Sankararaman S, Wen X, **Lanfear DE**, Pique-Regi R, Gilad Y, and Luca F. Functional dynamic genetic effects on gene regulation are specific to particular cell types and environmental conditions. *Elife* 2021; 10. PMID: 33988505. Full Text

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Genetic effects on gene expression and splicing can be modulated by cellular and environmental factors; yet interactions between genotypes, cell type and treatment have not been comprehensively studied together. We used an induced pluripotent stem cell system to study multiple cell types derived from the same individuals and exposed them to a large panel of treatments. Cellular responses involved different genes and pathways for gene expression and splicing, and were highly variable across contexts. For thousands of genes, we identified variable allelic expression across contexts and characterized different

types of gene-environment interactions, many of which are associated with complex traits. Promoter functional and evolutionary features distinguished genes with elevated allelic imbalance mean and variance. On average half of the genes with dynamic regulatory interactions were missed by large eQTL mapping studies, indicating the importance of exploring multiple treatments to reveal previously unrecognized regulatory loci that may be important for disease.

Cardiology/Cardiovascular Research
Gui H, **She R**, **Luzum J**, **Li J**, **Bryson TD**, Pinto Y, **Sabbah HN**, **Williams LK**, and **Lanfear DE**. Plasma Proteomic Profile Predicts Survival in Heart Failure with Reduced Ejection Fraction. *Circ Genom Precis Med* 2021; Epub ahead of print. PMID: 33999650. Full Text

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Background - It remains unclear whether the plasma proteome adds value to established predictors in heart failure (HF) with reduced ejection fraction (HFrEF). We sought to derive and validate a plasma proteomic risk score for survival in HFrEF patients (HFrEF-PRS). Methods - Patients meeting Framingham criteria for HF with EF<50% were enrolled (n=1017) and plasma underwent SOMAscan® profiling (4453 targets). Patients were randomly divided 2:1 into derivation and validation cohorts. The HFrEF-PRS was derived using Cox regression of all-cause mortality adjusted for clinical score and N-Terminal pro-B-Type Natriuretic Peptide (NTproBNP), then was tested in the validation cohort. Risk stratification improvement was evaluated by C-statistic, integrated discrimination index (IDI), continuous net reclassification index (NRI), and median improvement in risk score (MIRS) for 1-year and 3-year mortality. Results - Participants' mean age was 68 years, 48% identified as African American, 35% were female and 296 deaths occurred. In derivation (n=681), 128 proteins associated with mortality, 8 comprising the optimized HFrEF-PRS. In validation (n=336) the HFrEF-PRS associated with mortality (hazard ratio (HR) =2.27 [95% Confidence interval (95%CI) 1.84-2.82], p=6.3x10(-14)), Kaplan-Meier curves differed significantly between HFrEF-PRS quartiles (p=2.2x10(-6)), and it remained significant after adjustment for clinical score and NTproBNP (HR=1.37, 95%CI 1.05-1.79, p=0.021). The HFrEF-PRS improved metrics of risk stratification (C-statistic change=0.009, p=0.612; IDI=0.041, p=0.010; NRI=0.391, p=0.078; MIRS=0.039, p=0.016) and associated with cardiovascular death and HF phenotypes (e.g. 6-minute walk distance, EF change). Most HFrEF-PRS proteins had little known connection to HFrEF. Conclusions - A plasma multi-protein score improved risk stratification in HFrEF patients and identified novel candidates.

Cardiology/Cardiovascular Research
Haddad A, Bocchese M, Garber R, **O'Neill B**, Yesenosky GA, Patil P, Keane MG, Islam S, Sherrer JM, Basil A, Gangireddy C, Cooper JM, Cronin EM, and Whitman IR. Racial and ethnic differences in left atrial appendage occlusion wait time, complications, and periprocedural management. *Pacing Clin Electrophysiol* 2021; Epub ahead of print. PMID: 33959994. Full Text

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PURPOSE: Non-white patients are underrepresented in left atrial appendage occlusion (LAAO) trials, and racial disparities in LAAO periprocedural management are unknown. METHODS: We assessed sociodemographics and comorbidities of consecutive patients at our institution undergoing LAAO between 2015 and 2020, then in adjusted analyses, compared procedural wait time, procedural complications, and post-procedure oral anticoagulation (OAC) use in whites versus non-whites. RESULTS: Among 109 patients undergoing LAAO (45% white), whites had lower CHA(2) DS(2) VASc scores, on average, than non-whites (4.0 vs. 4.8, p = .006). There was no difference in median time from index event (IE) or initial outpatient cardiology encounter to LAAO procedure (whites 10.5 vs. non-whites 13.7 months, p = .9; 1.9 vs. 1.8 months, p = .6, respectively), and there was no difference in procedural complications (whites 4% vs. non-whites 5%, p = .33). After adjusting for CHA(2) DS(2) VASc score, OAC use at discharge tended to be higher in whites (OR 2.4, 95% CI [0.9-6.0], p = .07). When restricting the analysis to those with prior gastrointestinal (GI) bleed, adjusting for CHA(2) DS(2) VASc score and GI bleed severity, whites had a nearly five-fold odds of being discharged on OAC (OR 4.6, 95% CI [1-21.8], p = 0.05). The association between race and discharge OAC was not mediated through income category (total mediation effect 19% 95% CI [-.04-0.11], p = .38). CONCLUSION: Despite an increased prevalence of comorbidities amongst non-whites, wait time for LAAO and procedural complications were similar in whites versus non-whites. Among those with prior GI bleed, whites were nearly five-fold more likely to be discharged on OAC than non-whites, independent of income.

Cardiology/Cardiovascular Research

Karacsonyi J, **Alaswad K**, Choi JW, Vemmou E, Nikolakopoulos I, Poommipanit P, Rafeh NA, ElGuindy A, Ungi I, Egred M, and Brilakis ES. Laser for balloon uncrossable and undilatable chronic total occlusion interventions. *Int J Cardiol* 2021; Epub ahead of print. PMID: 34022321. Full Text

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BACKGROUND: There is limited information on use of laser in complex percutaneous coronary interventions (PCI). We examined the impact of laser on the outcomes of balloon uncrossable and balloon undilatable chronic total occlusions (CTO) PCI. METHODS: We reviewed baseline clinical and angiographic characteristics and procedural outcomes of 4845 CTO PCIs performed between 2012 and 2020 at 32 centers. RESULTS: Of the 4845 CTO lesions, 752 (15.5%) were balloon uncrossable (523 cases) or balloon undilatable (356 cases) and were included in this analysis. Mean patient age was 66.9 ± 10 years and 83% were men. Laser was used in 20.3% of the lesions. Compared with cases in which laser was not used, laser was more commonly used in longer length occlusions (33 [21, 50] vs. 25 [15, 40] mm, p = 0.0004) and in-stent restenotic lesions (41% vs. 20%, p < 0.0001). Laser use was associated with higher technical (91.5% vs. 83.1%, p = 0.010) and procedural (88.9% vs. 81.6%, p = 0.033) success rates and similar incidence of major adverse cardiac events (3.92% vs. 3.51%, p = 0.805). Laser use was associated with longer procedural (169 [109, 231] vs. 130 [87, 199], p < 0.0001) and fluoroscopy time (64 [40, 94] vs. 50 [31, 81], p = 0.003). CONCLUSIONS: In a contemporary, multicenter registry balloon uncrossable and balloon undilatable lesions represented 15.5% of all CTO PCIs. Laser was used in approximately one-fifth of these cases and was associated with high technical and procedural success and similar major complication rates.

Cardiology/Cardiovascular Research

Khan JM, Greenbaum AB, Babaliaros VC, Dvir D, Reisman M, McCabe JM, Satler L, Waksman R, **Eng MH**, Paone G, Chen MY, Bruce CG, Stine AM, Tian X, Rogers T, and Lederman RJ. BASILICA Trial: One-Year Outcomes of Transcatheter Electrosurgical Leaflet Laceration to Prevent TAVR Coronary Obstruction. *Circ Cardiovasc Interv* 2021; 14(5):e010238. PMID: 34003670. Full Text

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Cardiology/Cardiovascular Research

Kunkel KJ, Neupane S, Gupta A, **Basir MB**, and **Alaswad K**. Antegrade versus Retrograde Techniques for Chronic Total Occlusions (CTO): A Review and Comparison of Techniques and Outcomes. *Expert Rev Cardiovasc Ther* 2021; Epub ahead of print. PMID: 33945367. Request Article

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Introduction: As the field of chronic total occlusion percutaneous coronary intervention has evolved, technical approaches have evolved and been refined.Areas Covered: In this review, we discuss the major techniques utilized in modern CTO PCI including antegrade wiring, antegrade dissection re-entry, retrograde wiring, and retrograde dissection re-entry. Retrograde techniques have been extensively studied in comparison to antegrade techniques. Retrograde techniques have contributed to increases in CTO PCI success rates and are generally used in higher complexity lesions. Observational data suggests increased short term complications in procedures requiring the use of retrograde techniques however long term CTO PCI durability and patient outcomes have been shown to be similar among procedures using antegrade only versus retrograde techniques.Expert Opinion: Retrograde techniques play a vital role in the technical success of CTO PCI, particularly among more complex lesions and in patients with high burdens of comorbidities. Increases in procedural safety with equipment iteration and in the use of adjunctive imaging will play an important role in the selection of appropriate retrograde conduits and the overall success rates of CTO PCI.

Cardiology/Cardiovascular Research

Mehra MR, Cleveland JC, Jr., Uriel N, **Cowger JA**, Hall S, Horstmanshof D, Naka Y, Salerno CT, Chuang J, Williams C, and Goldstein DJ. Primary results of long-term outcomes in the MOMENTUM 3 pivotal trial and continued access protocol study phase: a study of 2200 HeartMate 3 left ventricular assist device implants. *Eur J Heart Fail* 2021; Epub ahead of print. PMID: 33932272. Full Text

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AIM: The MOMENTUM 3 pivotal trial established superiority of the HeartMate 3 (HM3) left ventricular assist device (LVAD), a fully magnetically levitated centrifugal-flow pump, over the HeartMate II axial-flow pump. We now evaluate HM3 LVAD outcomes in a single-arm prospective continuous access protocol (CAP) post-pivotal trial study. METHODS AND RESULTS: We enrolled 2200 HM3 implanted patients (515 pivotal trial and 1685 CAP patients) and compared outcomes including survival free of disabling stroke or reoperation to replace or remove a malfunctioning device (primary composite endpoint), overall survival and major adverse events at 2 years. The 2-year primary endpoint [76.7% vs. 74.8%; adjusted hazard ratio (HR) 0.87, 95% confidence interval (CI) 0.71-1.08, P = 0.21] and overall survival (81.2% vs. 79.0%) were similar among CAP and pivotal cohorts despite sicker patients (more intra-aortic balloon pump use and INTERMACS profile 1) in CAP who were more often intended for destination therapy. Survival was similar between the CAP and pivotal trial in transplant ineligible patients (79.1% vs. 76.7%; adjusted HR 0.89, 95% CI 0.68-1.16, P = 0.38). In a pooled analysis, the 2-year primary endpoint was similar between INTERMACS profiles 1-2 ('unstable' advanced heart failure), profile 3 ('stable' on inotropic therapy), and profiles 4-7 ('stable' ambulatory advanced heart failure) (75.7% vs. 77.6% vs. 72.9%, respectively). The net burden of adverse events was lower in CAP (adjusted rate ratio 0.93, 95% CI 0.88-0.98, P = 0.006), with consequent decrease in hospitalization. CONCLUSIONS: The primary results of accumulating HM3 LVAD experience suggest a lower adverse event burden and similar survival compared to the pivotal MOMENTUM 3 trial.

Cardiology/Cardiovascular Research

Napp LC, and **Basir MB**. Outcomes of mechanical circulatory support for ventricular tachycardia ablation in severe systolic heart failure. *J Interv Card Electrophysiol* 2021; Epub ahead of print. PMID: 33931793. Full Text

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Cardiology/Cardiovascular Research

O'Neill BP, Grines C, Moses JW, Ohman EM, Lansky A, Popma J, Kapur NK, Schreiber T, Mannino S, **O'Neill WW**, Medjamia AM, and Mahmud E. Outcomes of bailout percutaneous ventricular assist device versus prophylactic strategy in patients undergoing nonemergent percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2021; Epub ahead of print. PMID: 34051033. Full Text

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OBJECTIVES: To compare in-hospital outcomes of bailout support to prophylactic support with percutaneous ventricular assist devices (pVAD) for high-risk nonemergent percutaneous coronary intervention (HRPCI). BACKGROUND: Prophylactic support with pVAD for a HRPCI is used in patients felt to be at risk for hemodynamic collapse during PCI. An alternative strategy of bailout pVAD support in the event of hemodynamic collapse is also entertained. METHODS: We compared the outcomes of patients entered in the cVAD database who underwent Impella Protected PCI (ProPCI group) with patients from the cVAD and USpella databases receiving bailout Impella support for hemodynamic collapse during HRPCI (Bailout group). RESULTS: A total of 1,028 patients supported with Impella pVAD were entered into the cVAD database as of July 2019 and were included in this analysis. Of those 971 were in the ProPCI group and 57 in the Bailout group. Patients in the Bailout group were more often

female (50.9%vs. 27.2%, p = .0002) with higher median baseline left ventricular ejection fraction (LVEF) (40%vs. 30%, p < .0001) and with lower prevalence of both heart failure (42.1%vs. 56.9%, p = .0385) and left main disease (40.0%vs. 56.1%, p = .0250) compared to the ProPCI group. Unadjusted and adjusted in-hospital mortality was significantly higher in the Bailout group (49.1%vs. 4.3%, and 57.8%vs. 4.4%, p < .0001 for both). CONCLUSIONS: In our study population, the bailout group was associated with significant increased mortality compared to ProPCI group. Female gender was more frequently observed in patients requiring bailout pVAD. Further investigation is warranted in order to generalize the findings of our study.

Cardiology/Cardiovascular Research
Osman M, Balla S, Dupont A, **O'Neill WW**, and **Basir MB**. Reviving Invasive Hemodynamic Monitoring in Cardiogenic Shock. Invasive Hemodynamic Monitoring in Cardiogenic Shock. *Am J Cardiol* 2021; Epub ahead of print. PMID: 33972078. Full Text

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Cardiology/Cardiovascular Research
Pagani FD, Mehra MR, **Cowger JA**, Horstmanshof DA, Silvestry SC, Atluri P, Cleveland JC, Jr., Lindenfeld J, Roberts GJ, Bharmi R, Dalal N, Kormos RL, and Rogers JG. Clinical outcomes and healthcare expenditures in the real world with left ventricular assist devices - The CLEAR-LVAD study. *J Heart Lung Transplant* 2021; 40(5):323-333. PMID: 33744086. Full Text

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BACKGROUND: Several distinctly engineered left ventricular assist devices (LVADs) are in clinical use. However, contemporaneous real world comparisons have not been conducted, and clinical trials were not powered to evaluate differential survival outcomes across devices. OBJECTIVES: Determine real world survival outcomes and healthcare expenditures for commercially available durable LVADs. METHODS: Using a retrospective observational cohort design, Medicare claims files were linked to manufacturer device registration data to identify de-novo, durable LVAD implants performed between January 2014 and December 2018, with follow-up through December 2019. Survival outcomes were compared using a Cox proportional hazards model stratified by LVAD type and validated using propensity score matching. Healthcare resource utilization was analyzed across device types by using nonparametric bootstrap analysis methodology. Primary outcome was survival at 1-year and total Part A Medicare payments. RESULTS: A total of 4,195 de-novo LVAD implants were identified in fee-for-service Medicare beneficiaries (821 HeartMate 3; 1,840 HeartMate II; and 1,534 Other-VADs). The adjusted hazard ratio for mortality at 1-year (confirmed in a propensity score matched analysis) for the HeartMate 3 vs HeartMate II was 0.64 (95% CI; 0.52-0.79, p< 0.001) and for the HeartMate 3 vs Other-VADs was 0.51 (95% CI; 0.42-0.63, p < 0.001). The HeartMate 3 cohort experienced fewer hospitalizations per patient-

year vs Other-VADs (respectively, 2.8 vs 3.2 EPPY hospitalizations, p < 0.01) and 6.1 fewer hospital days on average (respectively, 25.2 vs 31.3 days, p < 0.01). The difference in Medicare expenditures, conditional on survival, for HeartMate 3 vs HeartMate II was -$10,722, p < 0.001 (17.4% reduction) and for HeartMate 3 vs Other-VADs was -$17,947, p < 0.001 (26.1% reduction). CONCLUSIONS: In this analysis of a large, real world, United States. administrative dataset of durable LVADs, we observed that the HeartMate 3 had superior survival, reduced healthcare resource use, and lower healthcare expenditure compared to other contemporary commercially available LVADs.

Cardiology/Cardiovascular Research
Qintar M, **Villablanca P**, **Lee J**, **Wang DD**, **Frisoli T**, **O'Neill B**, **O'Neill WW**, and **Eng MH**. Patent foramen ovale closure with vena cava thrombus: You need an arm and a neck! *Clin Case Rep* 2021; 9(5):e03884. PMID: 34026124. Full Text

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In patients with challenging femoral vein anatomy, transcatheter patent foramen ovale (PFO) closure can be safely and effectively be done through the jugular veins guided by ICE from the arm. This novel technique can potentially save resources (anesthesia and TEE) and provide an option for patients without a femoral option.

Cardiology/Cardiovascular Research
Rizik DG, Rao SV, Stone GW, Burke RF, Hermiller JB, and **O'Neill WW**. Re-instituting a live cardiology meeting without symptomatic COVID-19 transmission. *Catheter Cardiovasc Interv* 2021; Epub ahead of print. PMID: 33984174. Full Text

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Cardiology/Cardiovascular Research
Szerlip M, Spargias KS, Makkar R, Kar S, Kipperman RM, **O'Neill WW**, Ng MKC, Smith RL, Fam NP, Rinaldi MJ, Raffel OC, Walters DL, Levisay J, Montorfano M, Latib A, Carroll JD, Nickenig G, Windecker S, Marcoff L, Cohen GN, Schäfer U, Webb JG, and Lim DS. 2-Year Outcomes for Transcatheter Repair in Patients With Mitral Regurgitation From the CLASP Study. *JACC Cardiovasc Interv* 2021; Epub ahead of print. PMID: 34020928. Full Text

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OBJECTIVES: The study reports 2-year outcomes from the multicenter, prospective, single-arm CLASP study with functional mitral regurgitation (FMR) and degenerative MR (DMR) analysis. BACKGROUND: Transcatheter repair is a favorable option to treat MR. Long-term prognostic impact of the PASCAL transcatheter valve repair system in patients with clinically significant MR remains to be established. METHODS: Patients had clinically significant MR ≥3+ as evaluated by the echocardiographic core laboratory and were deemed candidates for transcatheter repair by the heart team. Assessments were performed by clinical events committee to 1 year (site-reported thereafter) and core laboratory to 2 years. RESULTS: A total of 124 patients (69% FMR, 31% DMR) were enrolled with a mean age of 75 years, 56% were male, 60% were New York Heart Association functional class III to IVa, and 100% had MR ≥3+. At 2 years, Kaplan-Meier estimates showed 80% survival (72% FMR, 94% DMR) and 84% freedom from heart failure (HF) hospitalization (78% FMR, 97% DMR), with 85% reduction in annualized HF hospitalization rate (81% FMR, 98% DMR). MR ≤1+ was achieved in 78% of patients (84% FMR, 71% DMR) and MR ≤2+ was achieved in 97% (95% FMR, 100% DMR) (all $p < 0.001$). Left ventricular end-diastolic volume decreased by 33 ml ($p < 0.001$); 93% of patients were in New York Heart Association functional class I to II ($p < 0.001$). CONCLUSIONS: The PASCAL repair system demonstrated sustained favorable outcomes at 2 years in FMR and DMR patients. Results showed high survival and freedom from HF rehospitalization rates with a significantly reduced annualized HF hospitalization rate. Durable MR reduction was achieved with evidence of left ventricular reverse remodeling and significant improvement in functional status. The CLASP IID/IIF randomized pivotal trial is ongoing.

Cardiology/Cardiovascular Research

Vemmou E, Quadros AS, Dens JA, Rafeh NA, Agostoni P, **Alaswad K**, Avran A, Bellli KC, Carlino M, Choi JW, El-Guindy A, Jaffer FA, Karmpaliotis D, Khatri JJ, Khelimskii D, Knaapen P, La Manna A, Krestyaninov O, Lamelas P, Ojeda S, Padilla L, Pan M, Piccaro de Oliveira P, Rinfret S, Spratt JC, Tanabe M, Walsh S, Nikolakopoulos I, Karacsonyi J, Rangan BV, Brilakis ES, and Azzalini L. In-Stent CTO Percutaneous Coronary Intervention: Individual Patient Data Pooled Analysis of 4 Multicenter Registries. *JACC Cardiovasc Interv* 2021; Epub ahead of print. PMID: 34052151. Full Text

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OBJECTIVES: The authors sought to examine the outcomes of percutaneous coronary intervention (PCI) for in-stent restenosis (ISR) chronic total occlusions (CTOs). BACKGROUND: The outcomes of PCI for ISR CTOs have received limited study. METHODS: The authors examined the clinical and angiographic characteristics and procedural outcomes of 11,961 CTO PCIs performed in 11,728 patients at 107 centers in Europe, North America, Latin America, and Asia between 2012 and 2020, pooling patient-level data from 4 multicenter registries. In-hospital major adverse cardiovascular events (MACE) included death, myocardial infarction, stroke, and tamponade. Long-term MACE were defined as the composite of all-cause death, myocardial infarction, and target vessel revascularization. RESULTS: ISR represented 15% of the CTOs (n = 1,755). Patients with ISR CTOs had higher prevalence of diabetes (44% vs. 38%; $p < 0.0001$) and prior coronary artery bypass graft surgery (27% vs. 24%; $p = 0.03$). Mean J-CTO (Multicenter CTO Registry in Japan) score was 2.32 ± 1.27 in the ISR group and 2.22 ± 1.27 in the de novo group ($p = 0.01$). Technical (85% vs. 85%; $p = 0.75$) and procedural (84% vs. 84%; $p = 0.82$) success was similar for ISR and de novo CTOs, as was the incidence of in-hospital MACE (1.7% vs. 2.2%; $p = 0.25$). Antegrade wiring was the most common successful strategy, in 70% of ISR and 60% of de novo CTOs, followed by retrograde crossing (16% vs. 23%) and antegrade dissection and re-entry (15% vs. 16%; $p < 0.0001$). At 12 months, patients with ISR CTOs had a higher incidence of MACE (hazard ratio: 1.31; 95% confidence intervals: 1.01 to 1.70; $p = 0.04$). CONCLUSIONS: ISR CTOs represent 15% of all CTO PCIs and can be recanalized with similar success and in-hospital MACE as de novo CTOs.

Center for Health Policy and Health Services Research

Hu J, and **Nerenz DR**. Properties of the overall hospital Star Ratings and consumer choice. *Am J Manag Care* 2021; 27(5):203-210. PMID: 34002962. Full Text

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OBJECTIVES: To examine characteristics of the CMS Overall Hospital Quality Star Ratings related to their use by consumers for choosing hospitals. STUDY DESIGN: Observational study using secondary data analyses. METHODS: Hospital Star Rating data reported in February 2019 and additional quality data from California and New York were used, with a mix of analytical approaches including descriptive statistics, correlational analysis, and Poisson regression models. RESULTS: The distribution of hospitals' Star Rating summary scores was tightly compressed, with no hospitals at or near the scores that would be obtained if a hospital were either best or worst across all quality domains. Hospitals did not consistently perform well or poorly across the range of measures and quality groups included in the Star Ratings. On average, for a given quality measure included in the Star Rating program, 12% of 1-star hospitals received top-quartile scores and 16% of 5-star hospitals received bottom-quartile scores. No significant associations were found between hospitals' overall Star Ratings and their performance on a set of condition-specific quality measures for hospitals in California and New York State. CONCLUSIONS: Hospitals' overall scores clustered in the middle of the potential distribution of scores; no hospitals were either best at everything or worst at everything. The Star Ratings did not predict hospital quality scores for separate quality measures related to specific medical conditions or health care needs. These 2 observations suggest that the Star Ratings are of limited value to consumers choosing hospitals for specific care needs.

Center for Health Policy and Health Services Research

Kalmbach DA, **Ahmedani BK**, Gelaye B, **Cheng P**, and **Drake CL**. Nocturnal cognitive hyperarousal, perinatal-focused rumination, and insomnia are associated with suicidal ideation in perinatal women with mild to moderate depression. *Sleep Med* 2021; 81:439-442. PMID: 33839373. Full Text

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OBJECTIVES: This prospective study explored associations among insomnia, nocturnal cognitive hyperarousal, and nocturnal perinatal-focused rumination with suicidal ideation (SI) in perinatal women with depression. METHODS: From late pregnancy through early postpartum, 39 depressed women completed 17 weekly surveys assessing SI, insomnia, depression, stress, and cognitive arousal. RESULTS: Women with nocturnal cognitive hyperarousal at baseline, relative to those with low cognitive arousal, were at greater risk for new onset SI (33% vs 1%). Moreover, nocturnal perinatal-focused rumination was independently associated with SI. SI-risk was highest when women reported clinical insomnia combined with nocturnal cognitive hyperarousal (OR = 5.66, p = 0.037) or perinatal-focused rumination (OR = 11.63, p = 0.018). Daytime perseverative thinking was not uniquely associated with SI. CONCLUSIONS: Nocturnal cognitive arousal predicts the development of new onset SI, and perinatal-focused rumination is also uniquely associated with SI-risk in late pregnancy and early parenting. Critically, SI-risk is highest when perinatal women endorsed insomnia and high cognitive arousal at the same time. Future research should determine whether alleviating nocturnal cognitive arousal, pregnancy- and fetal/infant-related concerns, and insomnia with psychotherapy reduces SI for women with perinatal depression.

Center for Health Policy and Health Services Research

Macki M, **Hamilton T**, **Lim S**, **Telemi E**, **Bazydlo M**, **Nerenz DR**, **Zakaria HM**, **Schultz L**, Khalil JG, Perez-Cruet MJ, Aleem IS, Park P, **Schwalb JM**, **Abdulhak MM**, and **Chang V**. Disparities in outcomes after spine surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2021;1-9. Epub ahead of print. PMID: 33962387. Full Text

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OBJECTIVE: Most studies on racial disparities in spine surgery lack data granularity to control for both comorbidities and self-assessment metrics. Analyses from large, multicenter surgical registries can provide an enhanced platform for understanding different factors that influence outcome. In this study, the authors aimed to determine the effects of race on outcomes after lumbar surgery, using patient-reported outcomes (PROs) in 3 areas: the North American Spine Society patient satisfaction index, the minimal clinically important difference (MCID) on the Oswestry Disability Index (ODI) for low-back pain, and return to work. METHODS: The Michigan Spine Surgery Improvement Collaborative was queried for all elective lumbar operations. Patient race/ethnicity was categorized as Caucasian, African American, and "other." Measures of association between race and PROs were calculated with generalized estimating equations (GEEs) to report adjusted risk ratios. RESULTS: The African American cohort consisted of a greater proportion of women with the highest comorbidity burden. Among the 7980 and 4222 patients followed up at 1 and 2 years postoperatively, respectively, African American patients experienced the lowest rates of satisfaction, MCID on ODI, and return to work. Following a GEE, African American race decreased the probability of satisfaction at both 1 and 2 years postoperatively. Race did not affect return to work or achieving MCID on the ODI. The variable of greatest association with all 3 PROs at both follow-up times was postoperative depression. CONCLUSIONS: While a complex myriad of socioeconomic factors

interplay between race and surgical success, the authors identified modifiable risk factors, specifically depression, that may improve PROs among African American patients after elective lumbar spine surgery.

Center for Individualized and Genomic Medicine Research
Findley AS, Monziani A, Richards AL, Rhodes K, Ward MC, Kalita CA, Alazizi A, Pazokitoroudi A, Sankararaman S, Wen X, **Lanfear DE**, Pique-Regi R, Gilad Y, and Luca F. Functional dynamic genetic effects on gene regulation are specific to particular cell types and environmental conditions. *Elife* 2021; 10. PMID: 33988505. Full Text

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Genetic effects on gene expression and splicing can be modulated by cellular and environmental factors; yet interactions between genotypes, cell type and treatment have not been comprehensively studied together. We used an induced pluripotent stem cell system to study multiple cell types derived from the same individuals and exposed them to a large panel of treatments. Cellular responses involved different genes and pathways for gene expression and splicing, and were highly variable across contexts. For thousands of genes, we identified variable allelic expression across contexts and characterized different types of gene-environment interactions, many of which are associated with complex traits. Promoter functional and evolutionary features distinguished genes with elevated allelic imbalance mean and variance. On average half of the genes with dynamic regulatory interactions were missed by large eQTL mapping studies, indicating the importance of exploring multiple treatments to reveal previously unrecognized regulatory loci that may be important for disease.

Center for Individualized and Genomic Medicine Research
Gui H, **She R**, **Luzum J**, **Li J**, **Bryson TD**, Pinto Y, **Sabbah HN**, **Williams LK**, and **Lanfear DE**. Plasma Proteomic Profile Predicts Survival in Heart Failure with Reduced Ejection Fraction. *Circ Genom Precis Med* 2021; Epub ahead of print. PMID: 33999650. Full Text

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Background - It remains unclear whether the plasma proteome adds value to established predictors in heart failure (HF) with reduced ejection fraction (HFrEF). We sought to derive and validate a plasma proteomic risk score for survival in HFrEF patients (HFrEF-PRS). Methods - Patients meeting Framingham criteria for HF with EF<50% were enrolled (n=1017) and plasma underwent SOMAscan® profiling (4453 targets). Patients were randomly divided 2:1 into derivation and validation cohorts. The HFrEF-PRS was derived using Cox regression of all-cause mortality adjusted for clinical score and N-Terminal pro-B-Type Natriuretic Peptide (NTproBNP), then was tested in the validation cohort. Risk stratification improvement was evaluated by C-statistic, integrated discrimination index (IDI), continuous net reclassification index (NRI), and median improvement in risk score (MIRS) for 1-year and 3-year mortality. Results - Participants' mean age was 68 years, 48% identified as African American, 35% were female and 296 deaths occurred. In derivation (n=681), 128 proteins associated with mortality, 8 comprising the optimized HFrEF-PRS. In validation (n=336) the HFrEF-PRS associated with mortality

(hazard ratio (HR) =2.27 [95% Confidence interval (95%CI) 1.84-2.82], p=6.3x10(-14)), Kaplan-Meier curves differed significantly between HFrEF-PRS quartiles (p=2.2x10(-6)), and it remained significant after adjustment for clinical score and NTproBNP (HR=1.37, 95%CI 1.05-1.79, p=0.021). The HFrEF-PRS improved metrics of risk stratification (C-statistic change=0.009, p=0.612; IDI=0.041, p=0.010; NRI=0.391, p=0.078; MIRS=0.039, p=0.016) and associated with cardiovascular death and HF phenotypes (e.g. 6-minute walk distance, EF change). Most HFrEF-PRS proteins had little known connection to HFrEF. Conclusions - A plasma multi-protein score improved risk stratification in HFrEF patients and identified novel candidates.

Dermatology

Baldwin H, Webster G, **Stein Gold L**, Callender V, Cook-Bolden FE, and Guenin E. 50 Years of Topical Retinoids for Acne: Evolution of Treatment. *Am J Clin Dermatol* 2021; 22(3):315-327. PMID: 33871811. Full Text

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Since the US Food and Drug Administration (FDA) approved tretinoin in 1971, retinoids alone or combined with other agents have become the mainstay of acne treatment. Retinoids act through binding to retinoic acid receptors, altering expression levels of hundreds of cellular proteins affecting multiple pathways involved in acne pathogenesis. Retinoids have evolved from first-generation agents, such as tretinoin, through chemical modifications resulting in a second generation (etretinate and acitretin for psoriasis), a third generation (adapalene and tazarotene) and, most recently, a fourth (trifarotene). For all topical retinoids, local irritation has been associated with poor tolerability and suboptimal adherence. Efforts to improve tolerability have utilized novel delivery systems and/or novel agents. This qualitative literature review summarizes the evolution of the four topical single-agent retinoids available for the treatment of acne in the US today and their various formulations, presenting the rationale behind their development and data from key studies.

Dermatology

Blauvelt A, Gordon KB, Lee P, Bagel J, Sofen H, Lockshin B, Soliman AM, Geng Z, Zhan T, Alperovich G, and **Stein Gold L**. Efficacy, safety, usability, and acceptability of risankizumab 150 mg formulation administered by prefilled syringe or by an autoinjector for moderate to severe plaque psoriasis. *J Dermatolog Treat* 2021;1-9. Epub ahead of print. PMID: 33947295. Full Text

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BACKGROUND: Risankizumab is approved for treatment of moderate to severe plaque psoriasis. Availability of a patient-controlled single self-injection of risankizumab may improve adherence and long-term management of psoriasis. OBJECTIVE: To investigate efficacy, safety, and usability of a new

risankizumab 150 mg/mL formulation administered as a single subcutaneous injection via prefilled syringe (PFS) or autoinjector (AI). METHODS: Efficacy, safety, usability, and acceptability of risankizumab 150 mg/mL PFS or AI were investigated in adults with moderate to severe psoriasis in two phase 3 studies. Study 1 was a multicenter, randomized, double-blinded, placebo-controlled study that investigated 150 mg/mL risankizumab PFS; study 2 was a multicenter, single-arm, open-label study that investigated 150 mg/mL risankizumab AI. RESULTS: At week 16, risankizumab 150 mg/mL demonstrated efficacy vs. placebo (Psoriasis Area and Severity Index ≥90% improvement (PASI 90), 62.9% vs. 3.8%; static Physician Global Assessment (sPGA) 0/1, 78.1% vs. 9.6%; both p< .001) in study 1; in study 2, PASI 90 and sPGA 0/1 were 66.7%, and 81.5%, respectively. All patients successfully self-administered study treatments via PFS or AI. Acceptability of self-injection was high in both studies. Efficacy and safety of risankizumab 150 mg/mL were comparable with results from previous risankizumab phase 3 studies using the 90 mg/mL formulation. CONCLUSIONS: The efficacy, safety, and usability of 150 mg/mL risankizumab delivered as a single PFS or AI injection support use of this new formulation in patients with moderate to severe plaque psoriasis. CLINICAL TRIALS: NCT03875482 and NCT0387508.

Dermatology
Narla S, Watchmaker J, **Ozog DM**, and Rohrer TE. Cosmetic Practices in the COVID-19 Era. *Advances in Cosmetic Surgery* 2021; 4(1):109-121. PMID: Not assigned. Full Text

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Dermatology
Rodrigues M, Pandya AG, **Hamzavi I**, Ezzedine K, Bekkenk MW, and Harris JE. Treatment recommendations for patients with vitiligo during COVID-19. *Australas J Dermatol* 2021; Epub ahead of print. PMID: 34028796. Full Text

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Dermatology
Tisack A, **Singh RK**, and **Kohen L**. Rosacea fulminans herpeticum: Rosacea fulminans with superimposed herpetic infection. *JAAD Case Reports* 2021; 11:106-108. PMID: 33948471. Full Text

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Dermatology
Yang QB, Li LQ, **Zhang QB**, He YL, **Mi QS**, and Zhou JG. microRNA-223 Deficiency Exacerbates Acute Inflammatory Response to Monosodium Urate Crystals by Targeting NLRP3. *J Inflamm Res* 2021; 14:1845-1858. PMID: 34007200. Full Text

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OBJECTIVE: MicroRNAs were identified as master-switch molecules limiting acute inflammatory response. This study investigated the potential role of microRNA (miR)-223 in the mechanism of gout. METHODS: Wild-type (WT) and miR-223 knock-out (KO) mice were used to evaluate the phenotypes of gout models. Inflammatory cytokines were measured in air pouch and peritoneal cavity lavage fluid. In addition to miR-223 level in gout patients, miR-223 and pro-inflammatory genes were examined in bone marrow-derived macrophages (BMDMs) from mice as well as peripheral blood mononuclear cells from healthy controls (HC) treated with monosodium urate (MSU) crystals in vitro. RESULTS: MiR-223 was up-regulated in the early phase in BMDMs from WT mice after MSU challenge and decreased rapidly, and this was not observed in miR-223 KO mice in vitro. In addition, miR-223 was required for macrophages homeostasis. In comparison with WT mice in vivo, miR-223 deficiency exacerbated swelling index of MSU-induced inflammation in foot pad and ankle joint models. MiR-223 deficiency also markedly aggravated inflammatory cells infiltration and cytokines release including interleukin (IL)-1β, IL-6 and monocyte chemotactic protein-1 (MCP-1) in the air pouch and peritonitis models. In the in vitro experiments, miR-223 deficiency promoted the inflammatory response by targeting NLR family pyrin domain containing protein 3 (NLRP3). Besides, miR-223 level was down-regulated in gout patients and in HC exposed to MSU in vitro. CONCLUSION: MiR-223 was down-regulated in gout patients and miR-223 deficiency exacerbated inflammatory response in diverse murine models, suggesting that up-regulation of miR-223 could be a potential therapeutic strategy for alleviating gouty inflammation.

Diagnostic Radiology
Jacene HA, Liu M, Cheng SC, Abbott A, Dubey S, **McCall K**, Young D, Johnston M, Van den Abbeele AD, and Overmoyer B. Imaging Androgen Receptors in Breast Cancer with (18)F-fluoro-5α-dihydrotestosterone-PET: A Pilot Study. *J Nucl Med* 2021; Epub ahead of print. PMID: 34049982. Full Text

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Most breast cancers express androgen receptors (AR). This prospective imaging sub-study explored imaging AR with (18)F-fluoro-5α-dihydrotestosterone (FDHT)-PET in patients with metastatic breast cancer (MBC) receiving selective AR modulation (SARM) therapy (GTx-024, GTx, Inc). Methods: 11 post-menopausal women with estrogen receptor positive MBC underwent FDHT-PET/CT at baseline, 6, and 12 weeks after starting SARM therapy. Abnormal tumor FDHT uptake was quantified using maximum SUV (SUVmax). AR status was determined from tumor biopsy specimens. FDHT-SUVmax percent change between scans was calculated. Best overall response was categorized as clinical benefit (CB: non-progressive disease [PD]), or PD using RECIST 1.1. Results: Median baseline FDHT-SUVmax was 4.1 (range 1.4-5.9) for AR+ tumors versus 2.3 (range 1.5-3.2) for AR- tumors (p=0.22). Quantitative AR expression and baseline FDHT uptake were weakly correlated (Pearson rho=0.39, p=0.30). Seven participants with CB at 12 weeks tended to have larger declines in FDHT uptake compared to those with PD at both 6 (median decline, range: -26.8%, -42.9 to -14.1% vs. -3.7%, -31% to +29%, respectively, p=0.11) and 12 weeks (median decline, range: -35.7%, -69.5 to -7.7% vs. -20.1%, -26.6% to +56.5%, respectively, p=0.17) after starting GTx-024. Conclusion: This hypothesis-generating data suggests that FDHT-PET/CT is worth further study as an imaging biomarker for evaluating response of MBC to SARM therapy and reiterates the feasibility of including molecular imaging in multidisciplinary therapeutic trials.

Diagnostic Radiology
Myers DT. Editorial Comment: Nodal and Deltoid Uptake on FDG and (11)C-Choline PET/CT Imaging. *AJR Am J Roentgenol* 2021; Epub ahead of print. PMID: 34037413. Full Text

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Diagnostic Radiology

Oravec D, **Drost J**, **Zauel R**, **Flynn M**, and **Yeni YN**. Assessment of Intravertebral Mechanical Strains and Cancellous Bone Texture Under Load Using a Clinically Available Digital Tomosynthesis Modality. *J Biomech Eng* 2021; Epub ahead of print. PMID: 34041529. Request Article

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Vertebral fractures are the most common osteoporotic fractures, but clinical means for assessment of vertebral bone integrity are limited in accuracy, as they typically use surrogate measures that are indirectly related to mechanics. The objective of this study was to examine the extent to which intravertebral strain distributions and changes in cancellous bone texture generated by a load of physiological magnitude can be characterized using a clinically available imaging modality. We hypothesized that digital tomosynthesis based digital volume correlation (DTS-DVC) and image texture based metrics of cancellous bone microstructure can detect development of mechanical strains under load. Isolated cadaveric T11 vertebrae and L2-L4 vertebral segments were DTS imaged in a nonloaded state and under physiological load levels. Axial strain, maximum principal strain, maximum compressive and tensile principal strains, and von Mises equivalent strain were calculated using the DVC technique. The change in textural parameters (line fraction deviation, anisotropy, and fractal parameters) under load was calculated within the cancellous centrum. The effect of load on measured strains and texture variables was tested using mixed model ANOVA, and relationships of strain and texture variables with donor age, bone density parameters, and bone size were examined using regression models. Magnitudes and heterogeneity of intravertebral strain measures correlated with applied loading and were significantly different from background noise. Image texture parameters were found to change with applied loading but these changes were not confirmed in a larger sample. DTS-DVC derived strains correlated with age more strongly than did BMD for T11.

Diagnostic Radiology

Shampain KL, Hackett CE, Towfighi S, Aslam A, Masch WR, Harris AC, Chang SD, **Khanna K**, **Mendiratta V**, Gabr AM, Owen D, and Mendiratta-Lala M. SBRT for HCC: Overview of technique and treatment response assessment. *Abdom Radiol (NY)* 2021; Epub ahead of print. PMID: 33963419. Full Text

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Stereotactic body radiation therapy (SBRT) is an emerging locoregional treatment (LRT) modality used in the management of patients with hepatocellular carcinoma (HCC). The decision to treat HCC with LRT is evaluated in a multidisciplinary setting, and the specific LRT chosen depends on the treatment intent, such as bridge-to-transplant, down-staging to transplant, definitive/curative treatment, and/or palliation, as well as underlying patient clinical factors. Accurate assessment of treatment response is necessary in order to guide clinical management in these patients. Patients who undergo LRT need continuous imaging evaluation to assess treatment response and to evaluate for recurrence. Thus, an accurate understanding of expected post-SBRT imaging findings is critical to avoid misinterpreting normal post-treatment changes as local progression or viable tumor. SBRT-treated HCC demonstrates unique imaging findings that differ from HCC treated with other forms of LRT. In particular, SBRT-treated HCC can demonstrate persistent APHE and washout on short-term follow-up imaging. This brief review summarizes current evidence for the use of SBRT for HCC, including patient population, SBRT technique

and procedure, tumor response assessment on contrast-enhanced cross-sectional imaging with expected findings, and pitfalls in treatment response evaluation.

Emergency Medicine

Aurora L, **McCord J**, **Nowak R**, Giannitsis E, Christenson R, DeFilippi C, Lindahl B, Christ M, Body R, **Jacobsen G**, and Mueller C. Prognostic Utility of a Modified HEART Score When Different Troponin Cut-points Are Used. *Crit Pathw Cardiol* 2021; Epub ahead of print. PMID: 33988541. Full Text

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BACKGROUND: Although the recommended cut-point for cardiac troponin (cTn) is the 99th percentile, many institutions use cut-points that are multiples higher than the 99th percentile for diagnosing acute myocardial infarction (AMI). Prior studies have shown that patients with a HEART score (HS) ≤ 3 and normal serial cTn values (modified HS) are at low risk for adverse events. This study aimed to evaluate the prognostic utility of the HS when various cTn cut-points are used. METHODS: This was a sub-study of TRAPID-AMI, a multicenter, international trial evaluating a rapid rule-out AMI study using high sensitivity cTnT (hs-cTnT). 1,282 patients were evaluated for AMI from 12 centers in Europe, United States of America, and Australia from 2011-2013. Blood samples of hs-cTnT were collected at presentation and 2 hours, and each patient had a HS calculated. The US Food and Drug Administration approved 99th percentile for hs-cTnT (19 ng/L) was used. RESULTS: There were 213 (17%) AMIs. Within 30 days, there were an additional 2 AMIs and 8 deaths. The adverse event rates at 30 days (death/AMI) for a HS ≤ 3 and non-elevated hs-cTnT over 2 hours using increasing hs-cTnT cut-points ranged from 0.6% to 5.1%. CONCLUSIONS: Using the recommended 99th percentile cut-point for hs-cTnT, the combination of a HS ≤ 3 with non-elevated hs-cTnT values over 2 hours identifies a low-risk cohort who can be considered for discharge from the emergency department without further testing. The prognostic utility of this strategy is greatly lessened as higher hs-cTnT cut-points are used.

Emergency Medicine

Fadel RA, **Ross J**, **Asmar T**, **Sridasyam K**, **Demertzis Z**, **Ahluwalia G**, **Roumayah T**, **Scott M**, **Ibrahim H**, **Hammoudeh R**, **Gandhi N**, Flynn M, **Haftka-George A**, **Heidemann D**, Sims S, Levy P, and **Miller J**. Visual Analytics Dashboard Promises to Improve Hypertension Guideline Implementation. *Am J Hypertens* 2021; Epub ahead of print. PMID: 34043744. Full Text

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BACKGROUND: Primary care management of hypertension under new guidelines incorporates assessment of cardiovascular disease risk and commonly requires review of electronic health record (EHR) data. Visual analytics can streamline the review of complex data and may lessen the burden clinicians face using the EHR. This study sought to assess the utility of a visual analytics dashboard in addition to EHR in managing hypertension in a primary care setting. METHODS: Primary care physicians within an urban, academic internal medicine clinic were tasked with performing two simulated patient

encounters for HTN management: the first using standard EHR, and the second using EHR paired with a visual dashboard. The dashboard included graphical blood pressure trends with guideline-directed targets, calculated ASCVD risk score, and relevant medications. Guideline-appropriate antihypertensive prescribing, correct target blood pressure goal, and total encounter time were assessed. RESULTS: We evaluated 70 case simulations. Use of the dashboard with the EHR compared to use of the EHR alone was associated with greater adherence to prescribing guidelines (95% vs. 62%, p<0.001) and more correct identification of BP target (95% vs. 57%, p<0.01). Total encounter time fell an average of 121 seconds (95% CI 69 - 157 seconds, p<0.001) in encounters that used the dashboard combined with the EHR. CONCLUSIONS: The integration of a hypertension-specific visual analytics dashboard with EHR demonstrates the potential to reduce time and improve hypertension guideline implementation. Further widespread testing in clinical practice is warranted.

Emergency Medicine

Jayaprakash N, **Pflaum-Carlson J**, **Gardner-Gray J**, **Hurst G**, **Kinni H**, Coba V, and **Deledda J**. This Health Care Problem Needs a Collaborative Closing of the Gap. *Ann Emerg Med* 2021; 77(5):553-555. PMID: 33902834. Full Text

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Emergency Medicine

Rosenthal ES, Elm JJ, Ingles J, Rogers AJ, Terndrup TE, Holsti M, Thomas DG, Babcock L, Okada PJ, Lipsky RH, **Miller JB**, Hickey RW, Barra ME, Bleck TP, Cloyd JC, Silbergleit R, Lowenstein DH, Coles LD, Kapur J, Shinnar S, and Chamberlain JM. Early Neurologic Recovery, Practice Pattern Variation, and the Risk of Endotracheal Intubation Following Established Status Epilepticus. *Neurology* 2021; 96(19):e2372-e2386. PMID: 34032604. Full Text

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OBJECTIVE: To quantify the association between early neurologic recovery, practice pattern variation, and endotracheal intubation during established status epilepticus, we performed a secondary analysis within the cohort of patients enrolled in the Established Status Epilepticus Treatment Trial (ESETT). METHODS: We evaluated factors associated with the endpoint of endotracheal intubation occurring within 120 minutes of ESETT study drug initiation. We defined a blocked, stepwise multivariate regression, examining 4 phases during status epilepticus management: (1) baseline characteristics, (2) acute treatment, (3) 20-minute neurologic recovery, and (4) 60-minute recovery, including seizure cessation and improving responsiveness. RESULTS: Of 478 patients, 117 (24.5%) were intubated within 120 minutes. Among high-enrolling sites, intubation rates ranged from 4% to 32% at pediatric sites and 19% to 39% at adult sites. Baseline characteristics, including seizure precipitant, benzodiazepine dosing, and admission vital signs, provided limited discrimination for predicting intubation (area under the curve [AUC] 0.63). However, treatment at sites with an intubation rate in the highest (vs lowest) quartile strongly predicted endotracheal intubation independently of other treatment variables (adjusted odds ratio [aOR] 8.12, 95% confidence interval [CI] 3.08-21.4, model AUC 0.70). Site-specific variation was the factor most strongly associated with endotracheal intubation after adjustment for 20-minute (aOR 23.4, 95% CI 6.99-78.3, model AUC 0.88) and 60-minute (aOR 14.7, 95% CI 3.20-67.5, model AUC 0.98) neurologic recovery. CONCLUSIONS: Endotracheal intubation after established status epilepticus is strongly associated with site-specific practice pattern variation, independently of baseline characteristics, and early neurologic recovery and should not alone serve as a clinical trial endpoint in established status epilepticus. TRIAL REGISTRATION INFORMATION: ClinicalTrials.gov Identifier: NCT01960075.

Endocrinology and Metabolism

Bergenstal RM, Johnson ML, Aroda VR, Brazg RL, Dreon DM, Frias JP, **Kruger DF**, Molitch ME, Mullen DM, Peyrot M, Richter S, Rosenstock J, Serusclat P, Vance C, Weinstock RS, and Levy BL. Comparing Patch vs Pen Bolus Insulin Delivery in Type 2 Diabetes Using Continuous Glucose Monitoring Metrics and Profiles. *J Diabetes Sci Technol* 2021; Epub ahead of print. PMID: 34008442. Full Text

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OBJECTIVE: CeQur Simplicity™ (CeQur, Marlborough, MA) is a 3-day insulin delivery patch designed to meet mealtime insulin requirements. A recently reported 48-week, randomized, multicenter, interventional trial compared efficacy, safety and self-reported outcomes in 278 adults with type 2 diabetes (T2D) on basal insulin therapy who initiated and managed mealtime insulin therapy with a patch pump versus insulin pen. We assessed changes in key glycemic metrics among a subset of patients who wore a continuous glucose monitoring (CGM) device. METHODS: Study participants (patch, n = 49; pen, n = 48) wore a CGM device in masked setting during the baseline period and prior to week 24. Glycemic control was assessed using international consensus guidelines for percentage of Time In Range (%TIR: >70% at 70-180 mg/dL), Time Below Range (%TBR: <4% at <70 mg/dL; <1% at <54 mg/dL), and Time Above Range (%TAR: <25% at >180 mg/dL; <5% at >250 mg/dL). RESULTS: Both the patch and pen groups achieved recommended targets in %TIR (74.1% ± 18.7%, 75.2 ± 16.1%, respectively) and marked reductions in %TAR >180 mg/dL (21.1% ± 19.9%, 19.7% ± 17.5%, respectively) but with increased %TBR <70 mg/dL (4.7% ± 5.2%, 5.1 ± 5.8, respectively), all P < .0001. No significant between-group differences in glycemic improvements or adverse events were observed. CONCLUSIONS: CGM confirmed that the patch or pen can be used to safely initiate and optimize basal-bolus therapy using a simple insulin adjustment algorithm with SMBG. Preference data suggest that use of the patch vs pen may enhance treatment adherence.

Endocrinology and Metabolism

Shah M, Appuswamy AV, **Rao SD**, and Dhaliwal R. Treatment of bone fragility in patients with diabetes: antiresorptive versus anabolic? *Curr Opin Endocrinol Diabetes Obes* 2021; Epub ahead of print. PMID: 34010225. Full Text

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PURPOSE OF REVIEW: The pathogenesis of bone fragility in diabetes has not been fully characterized. The antifracture efficacy of available therapies remains unproven in patients with diabetes. We aim to collate current evidence of the treatment of diabetic bone fragility, and to provide a rationale for considering optimal therapeutic option in patients with diabetes. RECENT FINDINGS: The antifracture efficacy of antiresorptive and anabolic therapies is well established in patients without diabetes. Studies in patients with osteoporosis have shown that anabolic therapies lead to faster and larger benefits to bone mineral density and offer greater protection against fracture than antiresorptive therapies. Available data suggest that antiresorptive and anabolic therapies have similar effect on bone density and fracture risk reduction in patients with and without diabetes. However, the evidence in diabetes is limited to observational studies and post hoc analyses of osteoporosis studies. SUMMARY: There are no specific guidelines for the treatment of bone fragility in patients with diabetes. We offer a rationale for use of anabolic therapies in diabetes which is a low bone formation state, in contrast to postmenopausal osteoporosis that is characterized by increased bone turnover. Prospective studies evaluating the effect of available therapies on bone quality and fracture outcomes in patients with diabetes are needed.

Gastroenterology

Forns X, Feld JJ, Dylla DE, Pol S, Chayama K, Hou J, Heo J, Lampertico P, Brown A, Bondin M, Tatsch F, Burroughs M, Marcinak J, Zhang Z, Emmett A, **Gordon SC**, and Jacobson IM. Safety of Patients with Hepatitis C Virus Treated with Glecaprevir/Pibrentasvir from Clinical Trials and Real-World Cohorts. *Adv Ther* 2021; Epub ahead of print. PMID: 34021887. Full Text

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INTRODUCTION: More than 70 million people are estimated to be infected with hepatitis C virus (HCV) globally. If left untreated, HCV infection can lead to complications such as extensive liver fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). Evolution of treatments has resulted in highly effective and well-tolerated all-oral direct-acting antivirals. The pangenotypic regimen of glecaprevir/pibrentasvir is approved for treating HCV for patients without cirrhosis or with compensated cirrhosis (CC). Guidelines have evolved to simplify treatment to enable non-specialists to manage and treat HCV-infected patients. Simultaneously, such treatment algorithms provide guidance on the pretreatment identification of small subsets of patients who may require specialist treatment and long-term follow-up for advanced liver disease, including those at risk of developing HCC. This study describes the safety profile of glecaprevir/pibrentasvir in patients identified using previously described noninvasive laboratory measures who may be eligible for treatment by non-liver specialists. METHODS: This post hoc analysis of glecaprevir/pibrentasvir in patients, identified by noninvasive laboratory measures, intended to exclude patients with advanced liver disease and severe renal impairment, who can be managed within non-liver specialist settings. Patients were included from clinical trials and real-world studies of glecaprevir/pibrentasvir for HCV treatment. Baseline demographics, clinical characteristics, and safety assessments, including adverse events and laboratory abnormalities, were summarized. RESULTS: Data across these large-scale studies confirm that glecaprevir/pibrentasvir is well tolerated across different patient populations, with fewer than 0.1% of patients experiencing a serious adverse event related to treatment drugs, and few patients developing HCC during or after treatment. CONCLUSION: The safety profile of glecaprevir/pibrentasvir enhances the confidence of non-liver specialists to treat the majority of HCV-infected patients, and provides an opportunity to expand the treater pool, potentially increasing diagnosis and treatment rates for HCV, contributing to elimination of HCV.

Gastroenterology

Modi K, Segovia M, Mavis A, Schiano T, Patel Y, Boike J, Sudan D, **Nagai S**, and **Jafri SM**. Efficacy and Safety of Mammalian Target of Rapamycin Inhibitors Following Intestinal and Multivisceral Transplantation. *Clin Transplant* 2021;e14324. Epub ahead of print. PMID: 34046945. Full Text

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This is a descriptive study reviewing the outcomes of mammalian target of rapamycin inhibitors (mTORs) in intestinal (IT) and multivisceral transplantation (MVT). This study included 22 patients, 20 adults, and 2 children, and an overall mean age of 46 years old at the time of transplantation. Twelve patients (54.5%) received IT, and the remainder (45.5%) MVT. The mean time between transplantation and mTORs initiation was 24 months. The indication was worsening renal function in 13 patients (59%), with

9/13(69.2%) noted to have an increase in glomerular filtration rate of at least 10 mL/min/1.73m2. The indication for 4 patients (18.2%) was history of neuroendocrine tumor. After mTOR initiation, 50% of patients were reduced or weaned off tacrolimus and 13.7% off prednisone. mTORs were discontinued in 11/22 patients. Six patients (54.5%) stopped due to side effects, two (18.1%) for surgery, and one (9%) for acute cellular rejection. Side effects were edema (33.3%), headaches (33.3%), diarrhea (16.7%), and oral ulcers (16.7%). Average duration of mTORs prior to discontinuation due to side effects was 7 months. mTORs may function in their own niche of patients due to the potential renal safety profile, but use is most limited by tolerance to side effects.

Gastroenterology

Shampain KL, Hackett CE, Towfighi S, Aslam A, Masch WR, Harris AC, Chang SD, **Khanna K**, **Mendiratta V**, Gabr AM, Owen D, and Mendiratta-Lala M. SBRT for HCC: Overview of technique and treatment response assessment. *Abdom Radiol (NY)* 2021; Epub ahead of print. PMID: 33963419. Full Text

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Stereotactic body radiation therapy (SBRT) is an emerging locoregional treatment (LRT) modality used in the management of patients with hepatocellular carcinoma (HCC). The decision to treat HCC with LRT is evaluated in a multidisciplinary setting, and the specific LRT chosen depends on the treatment intent, such as bridge-to-transplant, down-staging to transplant, definitive/curative treatment, and/or palliation, as well as underlying patient clinical factors. Accurate assessment of treatment response is necessary in order to guide clinical management in these patients. Patients who undergo LRT need continuous imaging evaluation to assess treatment response and to evaluate for recurrence. Thus, an accurate understanding of expected post-SBRT imaging findings is critical to avoid misinterpreting normal post-treatment changes as local progression or viable tumor. SBRT-treated HCC demonstrates unique imaging findings that differ from HCC treated with other forms of LRT. In particular, SBRT-treated HCC can demonstrate persistent APHE and washout on short-term follow-up imaging. This brief review summarizes current evidence for the use of SBRT for HCC, including patient population, SBRT technique and procedure, tumor response assessment on contrast-enhanced cross-sectional imaging with expected findings, and pitfalls in treatment response evaluation.

Gastroenterology

Shinn B, Boortalary T, Raijman I, Nieto J, Khara HS, Kumar SV, Confer B, Diehl DL, El Halabi M, Ichkhanian Y, Runge T, Kumbhari V, Khashab M, Tyberg A, Shahid H, Sarkar A, Gaidhane M, Bareket R, Kahaleh M, **Piraka C**, **Zuchelli T**, Law R, Sondhi A, Kedia P, Robbins J, Calogero C, Bakhit M, Chiang A, Schlachterman A, Kowalski T, and Loren D. Maximizing success in single-session EUS-directed transgastric ERCP: a retrospective cohort study to identify predictive factors of stent migration. *Gastrointest Endosc* 2021; Epub ahead of print. PMID: 33957105. Full Text

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BACKGROUND AND AIMS: EUS-directed transgastric ERCP (the EDGE procedure) is a simplified method of performing ERCP in Roux-en-Y gastric bypass patients. [1] The EDGE procedure involves placement of a lumen-apposing metal stent (LAMS) into the excluded stomach to serve as a conduit for passage of the duodenoscope for pancreatobiliary intervention. Originally a multistep process, urgent indications for ERCP have led to the development of single-session EDGE (SS-EDGE) with LAMS placement and ERCP performed in the same session. [2-3] The goal of this study was to identify predictive factors of intraprocedural LAMS migration in SS-EDGE. METHODS: We conducted a multicenter retrospective review that included 9 tertiary medical centers across the United States. Data were collected and analyzed from 128 SS-EDGE procedures. The primary outcome was intraprocedural LAMS migration. Secondary outcomes included other procedural adverse events such as bleeding and perforation. RESULTS: In total, 11 LAMS migrations were observed in 128 procedures (8.6%). Univariate analysis of clinically relevant variables was performed, as was a binary logistic regression analysis of stent diameter and stent dilation. This revealed that use of a smaller (15 mm) diameter LAMS was an independent predictor of intraprocedural stent migration (OR, 5.36; 95% CI,1.29-22.24; p=0.021). Adverse events included 3 patients who required surgery and 2 who experienced intraprocedural bleeding. CONCLUSIONS: Use of larger-diameter LAMS is a predictive factor for a nonmigrated stent and improved procedural success in SS-EDGE. Although larger patient cohorts are needed to adequately assess, performance of LAMS dilation and fixation may also decrease risk of intraprocedural LAMS migration and improve procedural success.

Gastroenterology

Siddiqui MA, **Suresh S**, **Simmer S**, **Abu-Ghanimeh M**, **Karrick M**, **Nimri F**, **Musleh M**, **Mediratta V**, **Al-Shammari M**, **Russell S**, **Jou J**, **Dang D**, **Salgia R**, and **Zuchelli T**. Increased Morbidity and Mortality in COVID-19 Patients with Liver Injury. *Dig Dis Sci* 2021;1-7. Epub ahead of print. PMID: 33945064. Full Text

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BACKGROUND: There is a high prevalence of liver injury (LI) in patients with coronavirus disease 2019 (COVID-19); however, few large-scale studies assessing risk factors and clinical outcomes in these patients have been done. AIMS: To evaluate the risk factors and clinical outcomes associated with LI in a large inpatient cohort of COVID-19 patients. METHODS: Adult patients with COVID-19 between March 1 and April 30, 2020, were included. LI was defined as peak levels of alanine aminotransferase/aspartate aminotransferase that were 3 times the ULN or peak levels in alkaline phosphatase/total bilirubin that were 2 times the ULN. Mild elevation in liver enzymes (MEL) was defined as abnormal peak liver enzyme levels lower than the threshold for LI. Patients with MEL and LI were compared to a control group comprising patients with normal liver enzymes throughout hospitalization. RESULTS: Of 1935 hospitalized COVID-19 patients, 1031 (53.2%) had MEL and 396 (20.5%) had LI. Compared to control patients, MEL and LI groups contained proportionately more men. Patients in the MEL cohort were older compared to control, and African-Americans were more highly represented in the LI group. Patients with LI had an increased risk of mortality (relative risk [RR] 4.26), intensive care unit admission (RR, 5.52), intubation (RR, 11.01), 30-day readmission (RR, 1.81), length of hospitalization, and intensive care unit stay (10.49 and 10.06 days, respectively) compared to control. CONCLUSION: Our study showed that patients with COVID-19 who presented with LI had a significantly increased risk of mortality and poor clinical outcomes.

Gastroenterology

Wright AP, Patel AH, Farida JP, **Suresh S**, Rizk RS, and Prabhu A. Simulation Training Improves Trainee Technical Skill and Procedural Attitudes in Endoscopic Gastrostomy Tube Placement. *Simul Healthc* 2021; Epub ahead of print. PMID: 33993139. Full Text

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INTRODUCTION: Percutaneous endoscopic gastrostomy (PEG) tube placement remains a core competency of gastroenterology fellowship, although this procedure is performed infrequently. Some training programs lack sufficient procedural volume for trainees to develop confidence and competence in this procedure. We aimed to determine the impact of a simulation-based educational intervention on trainee technical skill and procedural attitudes in simulated PEG tube placement. METHODS: Gastroenterology fellows were invited to participate in the study. Baseline procedural attitudes toward PEG tube placement (self-confidence, perceived skill level, perceived level of required supervision) were assessed before simulation training using a Likert scale. Baseline technical skills were assessed by video recording-simulated PEG tube placement on a PEG tube simulator with scoring using a procedural checklist. Fellows next underwent individualized simulation training and repeated simulated PEG tube placement until greater than 90% of checklist items were achieved. Procedural attitudes were reassessed directly after the simulation. Technical skill and procedural attitudes were then reassessed 6 to 12 weeks later (delayed posttraining). RESULTS: Twelve fellows completed the study. Simulation training led to significant improvement in technical skill at delayed reassessment (52.9 ± 14.3% vs. 78.0 ± 8.9% correct, P = 0.0002). Simulation training also led to significant immediate improvements in self-confidence (2.1 ± 0.7 vs. 3.1 ± 0.3, P = 0.001), perceived skill level (2.2 ± 1.0 vs. 4 ± 1.1, P < 0.001), and perceived level of required supervision (2.2 ± 0.9 vs. 3.2 ± 0.6, P = 0.003). CONCLUSIONS: Simulation training led to sustained improvements in gastroenterology fellows' technical skill and procedural attitudes in PEG tube placement. Incorporation of simulation curricula in gastroenterology fellowships for this infrequently performed procedure should be considered.

Hematology-Oncology

Garon EB, Aerts J, Kim JS, Muehlenbein CE, Peterson P, Rizzo MT, and **Gadgeel SM**. Safety of pemetrexed plus platinum in combination with pembrolizumab for metastatic nonsquamous non-small cell lung cancer: A post hoc analysis of KEYNOTE-189. *Lung Cancer* 2021; 155:53-60. PMID: 33730652. Full Text

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OBJECTIVES: This post hoc analysis assessed the safety of pemetrexed and platinum in combination with pembrolizumab, including time-to-onset and time-to-resolution of all-cause any-grade and grade ≥3 adverse events (AEs) and renal AEs. MATERIALS AND METHODS: Patient-level data from KEYNOTE-189 were analyzed in the all-subjects-as-treated population (pembrolizumab arm, n = 405; placebo arm, n = 202), and among patients who received ≥5 cycles of pemetrexed (pemetrexed/pembrolizumab/platinum arm, n = 310; pemetrexed/placebo/platinum arm, n = 135). All-cause AEs were selected based on ≥2 % incidence from previously reported KEYNOTE-189 data and included neutropenia, febrile neutropenia, anemia, thrombocytopenia, asthenia, fatigue, dyspnea, diarrhea, nausea, vomiting, pneumonitis, and renal events. Descriptive statistics summarized all-cause AEs. Medians and interquartile ranges were used to examine time-to-onset and time-to-resolution. The

data cutoff was November 8, 2017. RESULTS: In both treatment arms, most non-hematologic (nausea, vomiting, diarrhea, and asthenia), and hematologic (febrile neutropenia, thrombocytopenia, and neutropenia) grade ≥3 AEs with ≥2 % incidence had a median time-to-onset within the first 4 cycles, and a median time-to-resolution of within 2 weeks from onset. A small number of AEs had longer median time-to-onset (pneumonitis and fatigue) and median time-to-resolution (pneumonitis, fatigue, acute kidney injury, and anemia). Among patients who received ≥5 cycles of pemetrexed, the incidence of any-grade renal toxicity in the pemetrexed/pembrolizumab/platinum arm was 2.3 % in Cycles 1-4, 4.8 % in Cycles 5-8, 2.6 % in Cycles 9-12, and 2.5 % in Cycles ≥13; and, in the pemetrexed/placebo/platinum arm, 0.7 % in Cycles 1-4, 1.5 % in Cycles 5-8, 1.3 % in Cycles 9-12, and 2.0 % in Cycles ≥13. CONCLUSION: Pemetrexed/pembrolizumab/platinum has manageable toxicity with longer duration of treatment. While the incidence of renal toxicity was slightly higher in the pembrolizumab combination as compared to pemetrexed, the incidence did not increase in later treatment cycles. These results support the safe use of the KEYNOTE-189 regimen in clinical practice. CLINICAL TRIAL REGISTRATION NUMBER: NCT02578680 (clinicaltrials.gov).

Hematology-Oncology

Hwang C, Izano MA, Thompson MA, **Gadgeel SM**, Weese JL, **Mikkelsen T**, Schrag A, Teka M, Walters S, Wolf FM, Hirsch J, Rivera DR, Kluetz PG, Singh H, and Brown TD. Rapid real-world data analysis of patients with cancer, with and without COVID-19, across distinct health systems. *Cancer Rep (Hoboken)* 2021;e1388. Epub ahead of print. PMID: 34014037. Full Text

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BACKGROUND: The understanding of the impact of COVID-19 in patients with cancer is evolving, with need for rapid analysis. AIMS: This study aims to compare the clinical and demographic characteristics of patients with cancer (with and without COVID-19) and characterize the clinical outcomes of patients with COVID-19 and cancer. METHODS AND RESULTS: Real-world data (RWD) from two health systems were used to identify 146 702 adults diagnosed with cancer between 2015 and 2020; 1267 COVID-19 cases were identified between February 1 and July 30, 2020. Demographic, clinical, and socioeconomic characteristics were extracted. Incidence of all-cause mortality, hospitalizations, and invasive respiratory support was assessed between February 1 and August 14, 2020. Among patients with cancer, patients with COVID-19 were more likely to be Non-Hispanic black (NHB), have active cancer, have comorbidities, and/or live in zip codes with median household income <$30 000. Patients with COVID-19 living in lower-income areas and NHB patients were at greatest risk for hospitalization from pneumonia, fluid and electrolyte disorders, cough, respiratory failure, and acute renal failure and were more likely to receive hydroxychloroquine. All-cause mortality, hospital admission, and invasive respiratory support were more frequent among patients with cancer and COVID-19. Male sex, increasing age, living in zip codes with median household income <$30 000, history of pulmonary circulation disorders, and recent treatment with immune checkpoint inhibitors or chemotherapy were associated with greater odds of all-cause mortality in multivariable logistic regression models. CONCLUSION: RWD can be rapidly leveraged to understand urgent healthcare challenges. Patients with cancer are more vulnerable to COVID-19 effects, especially in the setting of active cancer and comorbidities, with additional risk observed in NHB patients and those living in zip codes with median household income <$30 000.

Hematology-Oncology

Kemp SB, Carpenter ES, Steele NG, Donahue KL, Nwosu ZC, Pacheco A, Velez-Delgado A, Menjivar RE, Lima F, The S, Espinoza CE, Brown K, Long D, Lyssiotis CA, Rao A, Zhang Y, Pasca di Magliano M, and **Crawford HC**. Apolipoprotein E promotes immune suppression in pancreatic cancer through NF-kB-mediated production of CXCL1. *Cancer Res* 2021; Epub ahead of print. PMID: 34049975. Full Text

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Pancreatic ductal adenocarcinoma (PDA) is a lethal malignancy with few effective therapeutic options. PDA is characterized by an extensive fibroinflammatory stroma that includes abundant infiltrating immune cells. Tumor-associated macrophages (TAM) are prevalent within the stroma and are key drivers of immunosuppression. TAMs in human and murine PDA are characterized by elevated expression of apolipoprotein E (ApoE), an apolipoprotein that mediates cholesterol metabolism and has known roles in cardiovascular and Alzheimer's disease but no known role in PDA. We report here that ApoE is also elevated in peripheral blood monocytes in PDA patients, and plasma ApoE protein levels stratify patient survival. Orthotopic implantation of mouse PDA cells into syngeneic wild-type or in ApoE-/- mice showed reduced tumor growth in ApoE-/- mice. Histological and mass cytometric (CyTOF) analysis of these tumors showed an increase in CD8+ T cells in tumors in ApoE-/- mice. Mechanistically, ApoE induced pancreatic tumor cell expression of Cxcl1 and Cxcl5, known immunosuppressive factors, through LDL receptor and NF-kB signaling. Taken together, this study reveals a novel immunosuppressive role of ApoE in the PDA microenvironment.

Hematology-Oncology

Tan B, Khattak A, Felip E, Kelly K, Rich P, **Wang D**, Helwig C, Dussault I, Ojalvo LS, and Isambert N. Bintrafusp Alfa, a Bifunctional Fusion Protein Targeting TGF-β and PD-L1, in Patients with Esophageal Adenocarcinoma: Results from a Phase 1 Cohort. *Target Oncol* 2021; Epub ahead of print. PMID: 34009501. Full Text

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BACKGROUND: Esophageal adenocarcinoma patients have limited treatment options. TGF-β can be upregulated in esophageal adenocarcinoma, and blocking this pathway may enhance clinical response to PD-(L)1 inhibitors. Bintrafusp alfa is a first-in-class bifunctional fusion protein composed of the extracellular domain of the TGF-βRII receptor (a TGF-β "trap") fused to a human IgG1 mAb blocking PD-L1. OBJECTIVE: The objective of this study was to investigate the efficacy and safety of bintrafusp alfa in patients with advanced, post-platinum esophageal adenocarcinoma, unselected for PD-L1 expression. PATIENTS AND METHODS: In this phase 1 study, patients with post-platinum, PD-L1-unselected esophageal adenocarcinoma received bintrafusp alfa 1200 mg every 2 weeks until disease progression, unacceptable toxicity, or withdrawal. The primary endpoint was confirmed best overall response per RECIST 1.1 by independent review committee (IRC). RESULTS: By the database cutoff of 24 August 2018, 30 patients (80.0% had two or more prior anticancer regimens) received bintrafusp alfa for a median of 6.1 weeks. The confirmed objective response rate (ORR) per IRC was 20.0% (95% CI 7.7-

38.6); responses lasted 1.3-8.3 months. Most responses (83.3%) occurred in tumors with an immune-excluded phenotype. Investigator-assessed confirmed ORR was 13.3% (95% CI 3.8-30.7). Nineteen patients (63.3%) had treatment-related adverse events: seven patients (23.3%) had grade 3 events; no grade 4 events or treatment-related deaths occurred. CONCLUSIONS: Bintrafusp alfa showed signs of clinical efficacy with a manageable safety profile in patients with heavily pretreated, advanced esophageal adenocarcinoma. CLINICAL TRIALS REGISTRATION: NCT02517398.

Infectious Diseases

Heldman MR, Kates OS, Safa K, Kotton CN, Georgia SJ, Steinbrink JM, Alexander BD, Hemmersbach-Miller M, Blumberg EA, Crespo MM, Multani A, Lewis AV, Beaird OE, Haydel B, La Hoz RM, Moni L, Condor Y, Flores S, Munoz CG, Guitierrez J, Diaz EI, Diaz D, Vianna R, Guerra G, Loebe M, Rakita RM, Malinis M, Azar MM, Hemmige V, McCort ME, **Chaudhry ZS**, Singh P, Hughes K, Velioglu A, Yabu JM, Morillis JA, Mehta SA, Tanna SD, Ison MG, Tomic R, Derenge AC, van Duin D, Maximin A, Gilbert C, Goldman JD, Sehgal S, Weisshaar D, Girgis RE, Nelson J, Lease ED, Fisher CE, and Limaye AP. Covid-19 in hospitalized lung and non-lung solid organ transplant recipients: a comparative analysis from a multicenter study. *Am J Transplant* 2021; Epub ahead of print. PMID: 34008917. Full Text

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Lung transplant recipients (LTR) with Covid-19 may have higher mortality than non-lung solid organ transplant recipients (SOTR), but direct comparisons are limited. Risk factors for mortality specifically in LTR have not been explored. We performed a multicenter cohort study of adult SOTR with Covid-19 to compare mortality by 28-days between hospitalized LTR and non-lung SOTR. Multivariable logistic regression models were used to assess comorbidity-adjusted mortality among LTR vs. non-lung SOTR and to determine risk factors for death in LTR. Of 1,616 SOTR with Covid-19, 1,051 (65%) were hospitalized including 117/159 (74%) LTR and 934/1457 (64%) non-lung SOTR (p=0.02). Mortality was higher among LTR compared to non-lung SOTR (24% vs. 16%, respectively, p=0.035) and lung transplant was independently associated with death after adjusting for age and comorbidities (aOR 1.7, 95% CI 1.0-2.6, p=0.05). Among LTR, independent risk factors for mortality included single lung transplant (aOR 2.8, 95% CI 1.0-7.7, p=0.04) and chronic lung allograft dysfunction (aOR 3.6, 95% CI 1.0-12.4, p=0.05), but not age >65 years, heart failure, or obesity. Among SOTR hospitalized for Covid-19, LTR had higher mortality than non-lung SOTR. In LTR, single lung transplant and chronic allograft dysfunction were independently associated with mortality.

Infectious Diseases

Maksimowicz-McKinnon K, **Zhou J**, **Hudy J**, **Hegab S**, and **McKinnon JE**. Subclinical CMV viremia is associated with increased nosocomial infections and prolonged hospitalization in patients with systemic autoimmune diseases. *J Clin Virol* 2021; 140:104849. PMID: 34023574. Full Text

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OBJECTIVE: Subclinical cytomegalovirus (CMV) viremia has been associated with other infections, prolonged hospitalization, and mortality in select immunosuppressed populations. We examined the incidence and outcomes of subclinical CMV viremia in hospitalized patients with systemic autoimmune diseases (AD) [systemic lupus erythematosus (SLE) or anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV)] using a highly sensitive CMV assay. METHODS: Prospectively collected samples were obtained from AD hospitalized patients at study entry with a second sample collected 1 week later or at hospital discharge. Controls included age- and gender- matched inpatients without AD and outpatients with AD. All samples were tested in batch using the Abbott RealTime CMV for investigational use assay (RT assay), with a LLOD (LLOQ) at 21 IU/mL (32 IU/mL). RESULTS: Twenty-three inpatients (10 SLE, 8 AAV, 5 controls), and 31 outpatient controls were recruited. Subclinical CMV viremia was found in 61% (11/18) of inpatient AD subjects, 3% (1/31) of outpatient AD subjects, and in none of the five inpatient controls ($p < 0.001$). CMV viremia was associated with increased median length of ICU stay (13 vs. 4 days, $p = 0.033$), hospital stay (17 vs. 9 days, $p = 0.014$) and increased nosocomial infections (7 vs. 1, $p = 0.007$). CMV viremia was not associated with overall severity of illness nor with disease-specific activity or damage. CONCLUSION: Over one-half of hospitalized AD patients in our cohort had detectable CMV viremia, which was associated with increased length of hospital stay and nosocomial infections. These data suggest that further study of the immunomodulatory effects of subclinical CMV viremia in AD is warranted.

Infectious Diseases

Shallal A, **Tibbetts R**, **Alangaden G**, and **Williams J**. Pulmonary nodules in a lung transplant recipient. *Am J Transplant* 2021; 21(5):1975-1977. PMID: 33939276. Full Text

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Internal Medicine
Basal Y, Oommen J, Faraj U, **Acho R**, and **Aravapally A**. Facklamia hominis in hidradenitis suppurativa. *JAAD Case Reports* 2021; 11:20-22. PMID: 33898677. Full Text

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Internal Medicine
Brisson RJ, Quinn TJ, and Deraniyagala RL. The role of chemotherapy in the management of olfactory neuroblastoma: A 40-year surveillance, epidemiology, and end results registry study. *Health Sci Rep* 2021; 4(2):e257. PMID: 33969231. Full Text

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BACKGROUND: In this retrospective surveillance, epidemiology, and end results (SEER) registry analysis, we investigated the role of chemotherapy (CT) in the treatment of olfactory neuroblastoma (ON), an exceedingly rare sino-nasal tumor typically treated with surgery and/or radiation therapy (RT). METHODS: We analyzed all patients in the SEER registry diagnosed with a single primary malignancy of ON, a primary tumor site within the nasal cavity or surrounding sinuses, sufficient staging information to derive Kadish staging, and >0 days of survival, ensuring follow-up data. Receipt of CT in the SEER registry was documented as either Yes or No/Unknown. RESULTS: Six hundred and thirty-six patients were identified. One hundred and ninety-five patients received CT as part of their treatment for ON. Following propensity score matching and inverse probability of treatment weighting, there was inferior overall survival (OS) (HR 1.7, 95% CI: 1.3-2.2, P = .001) and cancer-specific survival (CSS) (HR 1.8, 95% CI: 1.3-2.4, P < .001) for patients who received CT compared to those who were not treated with CT or had unknown CT status. On subgroup analysis, the only patient population that derived benefit from CT were patients who did not receive surgery and were treated with CT and/or RT (HR 0.3, 95% CI: 0.14-0.61, P < .001). CONCLUSIONS: Based on this retrospective SEER registry analysis, the use of CT in the management of ON is associated with decreased OS. Our analysis suggests that patients who are considered nonsurgical candidates may benefit from the addition of CT.

Internal Medicine
Fadel RA, **Ross J**, **Asmar T**, **Sridasyam K**, **Demertzis Z**, **Ahluwalia G**, **Roumayah T**, **Scott M**, **Ibrahim H**, **Hammoudeh R**, **Gandhi N**, Flynn M, **Haftka-George A**, **Heidemann D**, Sims S, Levy P, and **Miller J**. Visual Analytics Dashboard Promises to Improve Hypertension Guideline Implementation. *Am J Hypertens* 2021; Epub ahead of print. PMID: 34043744. Full Text

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BACKGROUND: Primary care management of hypertension under new guidelines incorporates assessment of cardiovascular disease risk and commonly requires review of electronic health record (EHR) data. Visual analytics can streamline the review of complex data and may lessen the burden clinicians face using the EHR. This study sought to assess the utility of a visual analytics dashboard in addition to EHR in managing hypertension in a primary care setting. METHODS: Primary care physicians

within an urban, academic internal medicine clinic were tasked with performing two simulated patient encounters for HTN management: the first using standard EHR, and the second using EHR paired with a visual dashboard. The dashboard included graphical blood pressure trends with guideline-directed targets, calculated ASCVD risk score, and relevant medications. Guideline-appropriate antihypertensive prescribing, correct target blood pressure goal, and total encounter time were assessed. RESULTS: We evaluated 70 case simulations. Use of the dashboard with the EHR compared to use of the EHR alone was associated with greater adherence to prescribing guidelines (95% vs. 62%, p<0.001) and more correct identification of BP target (95% vs. 57%, p<0.01). Total encounter time fell an average of 121 seconds (95% CI 69 - 157 seconds, p<0.001) in encounters that used the dashboard combined with the EHR. CONCLUSIONS: The integration of a hypertension-specific visual analytics dashboard with EHR demonstrates the potential to reduce time and improve hypertension guideline implementation. Further widespread testing in clinical practice is warranted.

Internal Medicine
Heidemann DL, Adhami A, **Nair A**, **Haftka-George A**, **Zaidan M**, **Seshadri V**, **Tang A**, and **Willens DE**. Using a Frontline Staff Intervention to Improve Cervical Cancer Screening in a Large Academic Internal Medicine Clinic. *J Gen Intern Med* 2021; Epub ahead of print. PMID: 33987788. Full Text

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BACKGROUND: Cervical cancer is the third most common malignancy affecting women. Screening with Papanicolaou (Pap) tests effectively identifies precancerous lesions and early-stage cervical cancer. While the nationwide rate of cervical cancer screening (CCS) is 84%, our urban general internal medicine (GIM) clinic population had a CCS rate of 70% in 2016. OBJECTIVE: To improve our clinic's CCS rate to match or exceed the national average within 18 months by identifying barriers and testing solutions. DESIGN: A quality improvement project led by a multidisciplinary group of healthcare providers. PARTICIPANTS: Our GIM clinic includes 16 attending physicians, 116 resident physicians, and 20 medical assistants (MAs) with an insured and underserved patient population. INTERVENTION: Phase 1 lasted 9 months and implemented CCS patient outreach, patient financial incentives, and clinic staff education. Phase 2 lasted 9 months and involved a workflow change in which MAs identified candidates for CCS during patient check-in. Feedback spanned the entire study period. MAIN MEASURES: Our primary outcome was the number of Pap tests completed per month during the 2 study phases. Our secondary outcome was the clinic population's CCS rate for all eligible clinic patients. KEY RESULTS: After interventions, the average number of monthly Pap tests increased from 35 to 56 in phase 1 and to 75 in phase 2. Of 385 patients contacted in phase 1, 283 scheduled a Pap test and 115 (41%) completed it. Compared to baseline, both interventions improved cervical cancer screening (phase 1 relative risk, 1.86; 95% CI, 1.64-2.10; P < 0.001; phase 2 relative risk, 2.70; 95% CI, 2.40-3.02; P < 0.001). Our clinic's CCS rate improved from 70% to 75% after the 18-month intervention. CONCLUSIONS: The rate of CCS increased by 5% after a systematic 2-phase organizational intervention that empowered MAs to remind, identify, and prepare candidates during check-in for CCS.

Internal Medicine
Modi K, Segovia M, Mavis A, Schiano T, Patel Y, Boike J, Sudan D, **Nagai S**, and **Jafri SM**. Efficacy and Safety of Mammalian Target of Rapamycin Inhibitors Following Intestinal and Multivisceral Transplantation. *Clin Transplant* 2021;e14324. Epub ahead of print. PMID: 34046945. Full Text

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This is a descriptive study reviewing the outcomes of mammalian target of rapamycin inhibitors (mTORs) in intestinal (IT) and multivisceral transplantation (MVT). This study included 22 patients, 20 adults, and 2 children, and an overall mean age of 46 years old at the time of transplantation. Twelve patients (54.5%) received IT, and the remainder (45.5%) MVT. The mean time between transplantation and mTORs initiation was 24 months. The indication was worsening renal function in 13 patients (59%), with 9/13(69.2%) noted to have an increase in glomerular filtration rate of at least 10 mL/min/1.73m2. The indication for 4 patients (18.2%) was history of neuroendocrine tumor. After mTOR initiation, 50% of patients were reduced or weaned off tacrolimus and 13.7% off prednisone. mTORs were discontinued in 11/22 patients. Six patients (54.5%) stopped due to side effects, two (18.1%) for surgery, and one (9%) for acute cellular rejection. Side effects were edema (33.3%), headaches (33.3%), diarrhea (16.7%), and oral ulcers (16.7%). Average duration of mTORs prior to discontinuation due to side effects was 7 months. mTORs may function in their own niche of patients due to the potential renal safety profile, but use is most limited by tolerance to side effects.

Internal Medicine

Nadkarni A, **Devgun J**, Jamal SM, Bardales D, Mease J, Matto F, Okabe T, Daoud EG, and Afzal MR. Subcutaneous cardiac rhythm monitors: state of the art review. *Expert Rev Med Devices* 2021; Epub ahead of print. PMID: 34057872. Request Article

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INTRODUCTION: Subcutaneous cardiac rhythm monitors (SCRMs) provide continuous ambulatory electrocardiographic monitoring for surveillance of known and identification of infrequent arrhythmias. SCRMs have proven to be helpful for the evaluation of unexplained symptoms and correlation with intermittent cardiac arrhythmias. Successful functioning of SCRM is dependent on accurate detection and successful transmission of the data to the device clinic. As the use of SCRM is steadily increasing, the amount of data that requires timely adjudication requires substantial resources. Newer algorithms for accurate detection and modified workflow systems have been proposed by physicians and the manufacturers to circumvent the issue of data deluge. AREAS COVERED: This paper provides an overview of the various aspects of ambulatory rhythm monitoring with SCRMs including indications, implantation techniques, programming strategies, troubleshooting for issue of false positive and intermittent connectivity and strategies to circumvent data deluge. EXPERT COMMENTARY: : SCRM is an invaluable technology for prolonged rhythm monitoring. The clinical benefits from SCRM hinge on accurate arrhythmia detection, reliable transmission of the data and timely adjudication for possible intervention. Further improvement in SCRM technology is needed to minimize false positive detection, improve connectivity to the central web-based server and devise strategies to minimize data deluge.

Internal Medicine

Siddiqui MA, **Suresh S**, **Simmer S**, **Abu-Ghanimeh M**, **Karrick M**, **Nimri F**, **Musleh M**, **Mediratta V**, **Al-Shammari M**, **Russell S**, **Jou J**, **Dang D**, **Salgia R**, and **Zuchelli T**. Increased Morbidity and Mortality in COVID-19 Patients with Liver Injury. *Dig Dis Sci* 2021;1-7. Epub ahead of print. PMID: 33945064. Full Text

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BACKGROUND: There is a high prevalence of liver injury (LI) in patients with coronavirus disease 2019 (COVID-19); however, few large-scale studies assessing risk factors and clinical outcomes in these patients have been done. AIMS: To evaluate the risk factors and clinical outcomes associated with LI in a large inpatient cohort of COVID-19 patients. METHODS: Adult patients with COVID-19 between March 1 and April 30, 2020, were included. LI was defined as peak levels of alanine aminotransferase/aspartate aminotransferase that were 3 times the ULN or peak levels in alkaline phosphatase/total bilirubin that were 2 times the ULN. Mild elevation in liver enzymes (MEL) was defined as abnormal peak liver enzyme levels lower than the threshold for LI. Patients with MEL and LI were compared to a control group comprising patients with normal liver enzymes throughout hospitalization. RESULTS: Of 1935 hospitalized COVID-19 patients, 1031 (53.2%) had MEL and 396 (20.5%) had LI. Compared to control patients, MEL and LI groups contained proportionately more men. Patients in the MEL cohort were older compared to control, and African-Americans were more highly represented in the LI group. Patients with LI had an increased risk of mortality (relative risk [RR] 4.26), intensive care unit admission (RR, 5.52), intubation (RR, 11.01), 30-day readmission (RR, 1.81), length of hospitalization, and intensive care unit stay (10.49 and 10.06 days, respectively) compared to control. CONCLUSION: Our study showed that patients with COVID-19 who presented with LI had a significantly increased risk of mortality and poor clinical outcomes.

Nephrology

Beers KH, Sperati CJ, Weisman DS, Abdel-Kader K, **Soman S**, Plantinga L, Choi MJ, Jaar BG, and Greer RC. Improving Primary Care Delivery for Patients Receiving Maintenance Hemodialysis. *Am J Kidney Dis* 2021; Epub ahead of print. PMID: 33992728. Full Text

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The beneficial impact of primary care, focused on all aspects of a patients' health (rather than a disease-specific focus) is well established. Recognized benefits include greater receipt of preventive care and counseling, lower utilization of emergency care and hospitalization for ambulatory care sensitive conditions, and decreased early mortality. While the importance of primary care and care coordination at the primary care-specialty interface is well recognized, the role of primary care within traditional and emerging care models for patients receiving maintenance in-center hemodialysis remains ill-defined. In this perspective article, we will describe: 1) the role of primary care for patients receiving maintenance hemodialysis and the current evidence regarding the receipt of primary care among those patients; 2) the key challenges to delivery of primary care for these complex patients, including suboptimal care coordination between nephrology and primary care providers (PCPs), the intensity of dialysis care, and the limited capacity of nephrologists and PCPs to meet the broad health needs of hemodialysis patients; 3) the potential strategies for improving the delivery of primary care for patients receiving hemodialysis; and 4) future research needs to improve primary care delivery for this high-risk population.

Nephrology

Nagai S, **Suzuki Y**, **Kitajima T**, **Ivanics T**, **Shimada S**, **Kuno Y**, **Shamaa MT**, **Yeddula S**, **Samaniego M**, **Collins K**, **Rizzari M**, **Yoshida A**, and **Abouljoud M**. Paradigm change in liver transplant practice after the implementation of the liver-kidney allocation policy. *Liver Transpl* 2021; Epub ahead of print. PMID: 34043869. Full Text

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The OPTN/UNOS policy regarding kidney allocation for liver transplant (LT) patients was implemented in August 2017. This study aimed to evaluate the effects of the simultaneous liver-kidney transplant policy on outcomes in LT alone (LTA) patients with kidney dysfunction. We analyzed adult primary LTA patients with kidney dysfunction at listing (estimated glomerular filtration rate [eGFR] less than 30mL/min or dialysis requirement) between January 2015 and March 2019 using the OPTN/UNOS registry. Waitlist practice and kidney transplant (KT) listing after LTA were compared between pre- and post-policy groups. 3,821 LTA listings with eGFR<30mL/min were included. The daily number of listings on dialysis was significantly higher in Era2 (post-policy group) than Era1 (pre-policy group) (1.21/day vs. 0.95/day, P<0.001). Of these LTA listings, 90-day LT waitlist mortality, LTA probability, and one-year post-LTA survival were similar between eras. LTA recipients in Era2 had a higher probability for KT listing post-LTA than those in Era1 (6.2% vs. 3.9%, odds ratio=3.30, P<0.001), especially those on dialysis (8.4% vs. 2.0%, odds ratio=4.38, P<0.001). Under the safety-net rule, there was a higher KT probability after LTA (26.7% and 53% at 6 months in Eras 1 and 2, respectively, P=0.017). Conclusion: After the implementation of the policy, the number of LTA listings among patients on dialysis significantly increased. While their post-transplant survival was not changed, KT listing after LTA increased. The safety-net rule led to high KT probability and low waitlist mortality rate in patients who were listed for KT after LTA. These results suggest that the policy successfully achieved the goals, which did not compromise LTA waitlist or post-transplant outcomes in patients with kidney dysfunction, and provided KT opportunities if they developed kidney failure after LTA.

Neurology

Hwang C, Izano MA, Thompson MA, **Gadgeel SM**, Weese JL, **Mikkelsen T**, Schrag A, Teka M, Walters S, Wolf FM, Hirsch J, Rivera DR, Kluetz PG, Singh H, and Brown TD. Rapid real-world data analysis of patients with cancer, with and without COVID-19, across distinct health systems. *Cancer Rep (Hoboken)* 2021;e1388. Epub ahead of print. PMID: 34014037. Full Text

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BACKGROUND: The understanding of the impact of COVID-19 in patients with cancer is evolving, with need for rapid analysis. AIMS: This study aims to compare the clinical and demographic characteristics of patients with cancer (with and without COVID-19) and characterize the clinical outcomes of patients with COVID-19 and cancer. METHODS AND RESULTS: Real-world data (RWD) from two health systems were used to identify 146 702 adults diagnosed with cancer between 2015 and 2020; 1267 COVID-19 cases were identified between February 1 and July 30, 2020. Demographic, clinical, and socioeconomic characteristics were extracted. Incidence of all-cause mortality, hospitalizations, and invasive respiratory support was assessed between February 1 and August 14, 2020. Among patients with cancer, patients with COVID-19 were more likely to be Non-Hispanic black (NHB), have active cancer, have comorbidities, and/or live in zip codes with median household income <$30 000. Patients with COVID-19 living in lower-income areas and NHB patients were at greatest risk for hospitalization from pneumonia, fluid and electrolyte disorders, cough, respiratory failure, and acute renal failure and were more likely to receive hydroxychloroquine. All-cause mortality, hospital admission, and invasive respiratory support were more frequent among patients with cancer and COVID-19. Male sex, increasing age, living in zip codes with median household income <$30 000, history of pulmonary circulation disorders, and recent treatment with immune checkpoint inhibitors or chemotherapy were associated with greater odds of all-cause mortality in

multivariable logistic regression models. CONCLUSION: RWD can be rapidly leveraged to understand urgent healthcare challenges. Patients with cancer are more vulnerable to COVID-19 effects, especially in the setting of active cancer and comorbidities, with additional risk observed in NHB patients and those living in zip codes with median household income <$30 000.

Neurology
Liu Z, **Xin H**, and **Chopp M**. Axonal remodeling of the corticospinal tract during neurological recovery after stroke. *Neural Regen Res* 2021; 16(5):939-943. PMID: 33229733. Full Text

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Stroke remains the leading cause of long-term disability. Hemiparesis is one of the most common post-stroke motor deficits and is largely attributed to loss or disruption of the motor signals from the affected motor cortex. As the only direct descending motor pathway, the corticospinal tract (CST) is the primary pathway to innervate spinal motor neurons, and thus, forms the neuroanatomical basis to control the peripheral muscles for voluntary movements. Here, we review evidence from both experimental animals and stroke patients, regarding CST axonal damage, functional contribution of CST axonal integrity and remodeling to neurological recovery, and therapeutic approaches aimed to enhance CST axonal remodeling after stroke. The new insights gleaned from preclinical and clinical studies may encourage the development of more rational therapeutics with a strategy targeted to promote axonal rewiring for corticospinal innervation, which will significantly impact the current clinical needs of subacute and chronic stroke treatment.

Neurology
Martinez-Nunez AE, Fynke JE, and **Miller DJ**. Under pressure: pressure-dependent pontine compression by a dolichoectasia basilar artery, a case report. *Neuroradiol J* 2021; Epub ahead of print. PMID: 34028323. Full Text

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Basilar artery dolichoectasia can lead to ischemic stroke through thrombosis of small perforating vessels of the brainstem. Here we report the case of a patient with transient paramedian pontine syndrome in the setting of a hypertensive crisis, finding a dolichoectasia basilar artery compressing on the ventral surface of the pons. The outcome was near-complete resolution of deficits after blood pressure control. We propose increased basilar artery pulse pressure as a novel mechanism of transient compression of the brainstem by a dolichoectasia artery.

Neurology
Schwedt TJ, Sahai-Srivastava S, Murinova N, Birlea M, Ahmed Z, Digre K, Lopez K, Mullally W, Blaya MT, Pippitt K, Cutrer FM, DeLange J, Schecht H, Rizzoli P, Lane J, **Wald J**, Cortez MM, Martin VT, Spare NM, Hentz JG, Robert T, and Dodick DW. Determinants of pain interference and headache impact in patients who have chronic migraine with medication overuse: Results from the MOTS trial. *Cephalalgia* 2021; Epub ahead of print. PMID: 33938249. Full Text

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Brigham and Women's Hospital, Department of Neurology, Boston, MA, USA.
Memorial Healthcare, Department of Neurology, Hollywood, FL, USA.

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Mayo Clinic, Department of Neurology, Rochester, MN, USA.
Northern Arizona Healthcare, Department of Neurology, Flagstaff, AZ, USA.
The Toledo Clinic, Department of Neurology, Toledo, OH, USA.
Blue Sky Neurology, Department of Neurology, Denver, CO, USA.
Henry Ford Allegiance, Department of Neurology, Jackson, MI, USA.
University of Cincinnati, Department of Internal Medicine, Cincinnati, OH, USA.
Thomas Jefferson University, Department of Neurology, Philadelphia, PA, USA.
Patient advocate and educator, Washington, WV, USA.

OBJECTIVE: "Pain interference" and "headache impact" refer to negative consequences that pain and headache have on one's life. This study investigated determinants of these negative impacts in a large patient cohort who have chronic migraine with medication overuse. METHODS: Six hundred and eleven adults were enrolled from 34 headache, neurology, and primary care clinics. Negative consequences of chronic migraine with medication overuse were determined using the Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference 6b questionnaire and the Headache Impact Test 6. Relationships between PROMIS-6b and Headache Impact Test 6 scores with demographics, headache characteristics, medication use, anxiety symptoms, and depression symptoms were assessed with linear regression. Elastic Net regression was used to develop a multiple regression model. RESULTS: PROMIS-6b T-Scores averaged 65.2 (SD 5.4) and Headache Impact Test 6 scores averaged 65.0 (SD 5.3), indicating severe negative consequences of chronic migraine with medication overuse. Chronic migraine with medication overuse interfered with enjoyment of life, concentration, daily activities, doing tasks away from home, and socializing. Depression symptom severity had the strongest relationship with pain interference and headache impact. Moderate-to-severe headache frequency, headache intensity, and anxiety symptoms were also associated with pain interference and headache impact. CONCLUSIONS: Chronic migraine with medication overuse is associated with substantial negative consequences, the extent of which is most strongly related to depression symptoms.

Neurology

Zhang Y, **Zhang Y**, **Chopp M**, **Pang H**, **Zhang ZG**, **Mahmood A**, and **Xiong Y**. MiR-17-92 Cluster-Enriched Exosomes Derived from Human Bone Marrow Mesenchymal Stromal Cells Improve Tissue and Functional Recovery in Rats after Traumatic Brain Injury. *J Neurotrauma* 2021; 38(11):1535-1550. PMID: 33787364. Full Text

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Exosomes play an important role in intercellular communication by delivering microribonucleic acids (miRNAs) to recipient cells. Previous studies have demonstrated that multi-potent mesenchymal stromal cell (MSC)-derived exosomes improve functional recovery after experimental traumatic brain injury (TBI). This study was performed to determine efficacy of miR-17-92 cluster-enriched exosomes (Exo-17-92) harvested from human bone marrow MSCs transfected with a miR-17-92 cluster plasmid in enhancing tissue and neurological recovery compared with exosomes derived from MSCs transfected with an empty plasmid vector (Exo-empty) for treatment of TBI. Adult male rats underwent a unilateral moderate cortical contusion. Animals received a single intravenous injection of miR-17-92 cluster-enriched exosomes (100 μg/rat, approximately 3.75x10(11) particles, Exo-17-92) or control exosomes (100 μg/rat, Exo-empty) or Vehicle (phosphate-buffered solution) one day after injury. A battery of neurological functional tests was performed weekly after TBI for five weeks. Spatial learning and memory were measured on days 31-35 after TBI using the Morris water maze test. All animals were sacrificed five weeks after injury. Their brains were processed for histopathological and immunohistochemical analyses of lesion volume, cell loss, angiogenesis, neurogenesis, and neuroinflammation. Compared with 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. Exosomes enriched with miR-17-92 cluster have a significantly better effect on improving functional recovery after TBI compared with Exo-empty, likely by reducing neuroinflammation and enhancing endogenous angiogenesis and neurogenesis. Engineering specific miRNA in exosomes may provide a novel therapeutic strategy for management of unilateral moderate cortical contusion TBI.

Neurology

Zheng Z, **Chopp M**, and **Chen J**. Multifaceted roles of pericytes-interorgan interactions. *Neural Regen Res* 2021; 16(5):982-983. PMID: 33229743. Full Text

Department of Neurology, Henry Ford Hospital, Detroit, MI, USA.
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Neurosurgery

Khalifeh JM, **Massie LW**, Dibble CF, Dorward IG, **Macki M**, Khandpur U, **Alshohatee K**, Jain D, **Chang V**, and Ray WZ. Decompression of Lumbar Central Spinal Canal Stenosis Following Minimally Invasive Transforaminal Lumbar Interbody Fusion. *Clin Spine Surg* 2021; Epub ahead of print. PMID: 33979102. Full Text

Department of Neurosurgery, The Johns Hopkins Hospital, Baltimore, MD Department of Neurological Surgery, Washington University School of Medicine, St. Louis, MO Department of Neurological Surgery, Henry Ford Health System, Detroit, MI Department of Orthopaedic Surgery, Washington University School of Medicine, St. Louis, MO.

STUDY DESIGN: This was a retrospective clinical series. OBJECTIVE: The objective of this study was to evaluate radiologic changes in central spinal canal dimensions following minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF) with placement of a static or an expandable interbody device. SUMMARY OF BACKGROUND DATA: MIS-TLIF is used to treat lumbar degenerative diseases and low-grade spondylolisthesis. MIS-TLIF enables direct and indirect decompression of lumbar spinal stenosis, with patients experiencing relief from radiculopathy and neurogenic claudication. However, the effects of MIS-TLIF on the central spinal canal are not well-characterized. MATERIALS AND METHODS: We identified patients who underwent MIS-TLIF for degenerative lumbar spondylolisthesis and concurrent moderate to severe spinal stenosis. We selected patients who had both preoperative and postoperative magnetic resonance imaging (MRI) and upright lateral radiographs of the lumbar spine. Measurements on axial T2-weighted MRI scans include anteroposterior and transverse dimensions of the dural sac and osseous spinal canal. Measurements on radiographs include disk height, neural foraminal height, segmental lordosis, and spondylolisthesis. We made pairwise comparisons between each of the central canal dimensions and lumbar sagittal segmental radiologic outcome measures relative to their corresponding preoperative values. Correlation coefficients were used to quantify the association between changes in lumbar sagittal segmental parameters relative to changes in radiologic outcomes of central canal dimensions. Statistical analysis was performed for "all patients" and further stratified by interbody device subgroups (static and expandable). RESULTS: Fifty-one patients (age 60.4 y, 68.6% female) who underwent MIS-TLIF at 55 levels (65.5% at L4-L5) were included in the analysis. Expandable interbody devices were used in 45/55 (81.8%) levels. Mean duration from surgery to postoperative MRI scan was 16.5 months (SD 11.9). MIS-TLIF was associated with significant improvements in dural sac dimensions (anteroposterior +0.31 cm, transverse +0.38 cm) and osseous spinal canal dimensions (anteroposterior +0.16 cm, transverse +0.32 cm). Sagittal lumbar segmental parameters of disk height (+0.56 cm), neural foraminal height (+0.35 cm), segmental lordosis (+4.26 degrees), and spondylolisthesis (-7.5%) were also improved following MIS-TLIF. We did not find meaningful associations between the changes in central canal dimensions relative to the corresponding changes in any of the sagittal lumbar segmental parameters. Stratified analysis by interbody device type (static and expandable) revealed similar within-group changes as in the overall cohort and minimal between-group differences. CONCLUSIONS: MIS-TLIF is associated with radiologic decompression of neural foraminal and central spinal canal stenosis. The mechanism for neural foraminal and central canal decompression is likely driven by a combination of direct and indirect corrective techniques.

Neurosurgery

Macki M, **Hamilton T**, **Lim S**, **Telemi E**, **Bazydlo M**, **Nerenz DR**, **Zakaria HM**, **Schultz L**, Khalil JG, Perez-Cruet MJ, Aleem IS, Park P, **Schwalb JM**, **Abdulhak MM**, and **Chang V**. Disparities in outcomes after spine surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2021;1-9. Epub ahead of print. PMID: 33962387. Full Text

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OBJECTIVE: Most studies on racial disparities in spine surgery lack data granularity to control for both comorbidities and self-assessment metrics. Analyses from large, multicenter surgical registries can provide an enhanced platform for understanding different factors that influence outcome. In this study, the authors aimed to determine the effects of race on outcomes after lumbar surgery, using patient-reported outcomes (PROs) in 3 areas: the North American Spine Society patient satisfaction index, the minimal clinically important difference (MCID) on the Oswestry Disability Index (ODI) for low-back pain, and return to work. METHODS: The Michigan Spine Surgery Improvement Collaborative was queried for all elective lumbar operations. Patient race/ethnicity was categorized as Caucasian, African American, and "other." Measures of association between race and PROs were calculated with generalized estimating equations (GEEs) to report adjusted risk ratios. RESULTS: The African American cohort consisted of a greater proportion of women with the highest comorbidity burden. Among the 7980 and 4222 patients followed up at 1 and 2 years postoperatively, respectively, African American patients experienced the lowest rates of satisfaction, MCID on ODI, and return to work. Following a GEE, African American race decreased the probability of satisfaction at both 1 and 2 years postoperatively. Race did not affect return to work or achieving MCID on the ODI. The variable of greatest association with all 3 PROs at both follow-up times was postoperative depression. CONCLUSIONS: While a complex myriad of socioeconomic factors interplay between race and surgical success, the authors identified modifiable risk factors, specifically depression, that may improve PROs among African American patients after elective lumbar spine surgery.

Neurosurgery

Miller WK, Becker KN, Caras AJ, **Mansour TR**, Mays MT, Rashid M, and **Schwalb J**. Magnetic resonance-guided focused ultrasound treatment for essential tremor shows sustained efficacy: a meta-analysis. *Neurosurg Rev* 2021; Epub ahead of print. PMID: 33978922. Full Text

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Although magnetic resonance-guided focused ultrasound (MRgFUS) is a viable treatment option for essential tremor, some studies note a diminished treatment benefit over time. A PubMed search was performed adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies were included if hand tremor scores (HTS), total Clinical Rating Scale for Tremor (CRST) scores, or Quality of Life in Essential Tremor Questionnaire (QUEST) scores at regular intervals following MRgFUS treatment for essential tremor were documented. Data analyses included a random effects model of meta-analysis and mixed-effects model of meta-regression. Twenty-one articles reporting HTS for 395 patients were included. Mean pre-operative HTS was 19.2 ± 5.0. Mean HTS at 3 months post-treatment was 7.4 ± 5.0 (61.5% improvement, $p < 0.001$). Treatment effect was mildly decreased at 36 months at 9.1 ± 5.4 (8.8% reduction). Meta-regression of time since treatment as a modifier of HTS revealed a downward trend in effect size, though this was not statistically significant ($p = 0.208$). Only 4 studies included follow-up ≥ 24 months. Thirteen included articles reported total CRST scores with

standardized follow-up for 250 patients. Mean pre-operative total CRST score decreased by 46.2% at 3 months post-treatment ($p < 0.001$). Additionally, mean QUEST scores at 3 months post-treatment significantly improved compared to baseline ($p < 0.001$). HTS is significantly improved from baseline ≥ 24 months post-treatment and possibly ≥ 48 months post-treatment. There is a current paucity of long-term CRST and QUEST score reporting in the literature.

Neurosurgery

Zhang Y, **Zhang Y**, **Chopp M**, **Pang H**, **Zhang ZG**, **Mahmood A**, and **Xiong Y**. MiR-17-92 Cluster-Enriched Exosomes Derived from Human Bone Marrow Mesenchymal Stromal Cells Improve Tissue and Functional Recovery in Rats after Traumatic Brain Injury. *J Neurotrauma* 2021; 38(11):1535-1550. PMID: 33787364. Full Text

Department of Neurosurgery and Henry Ford Hospital, Detroit, Michigan, USA.
Department of Neurology, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Physics, Oakland University, Rochester, Michigan, USA.

Exosomes play an important role in intercellular communication by delivering microribonucleic acids (miRNAs) to recipient cells. Previous studies have demonstrated that multi-potent mesenchymal stromal cell (MSC)-derived exosomes improve functional recovery after experimental traumatic brain injury (TBI). This study was performed to determine efficacy of miR-17-92 cluster-enriched exosomes (Exo-17-92) harvested from human bone marrow MSCs transfected with a miR-17-92 cluster plasmid in enhancing tissue and neurological recovery compared with exosomes derived from MSCs transfected with an empty plasmid vector (Exo-empty) for treatment of TBI. Adult male rats underwent a unilateral moderate cortical contusion. Animals received a single intravenous injection of miR-17-92 cluster-enriched exosomes (100 µg/rat, approximately 3.75x10(11) particles, Exo-17-92) or control exosomes (100 µg/rat, Exo-empty) or Vehicle (phosphate-buffered solution) one day after injury. A battery of neurological functional tests was performed weekly after TBI for five weeks. Spatial learning and memory were measured on days 31-35 after TBI using the Morris water maze test. All animals were sacrificed five weeks after injury. Their brains were processed for histopathological and immunohistochemical analyses of lesion volume, cell loss, angiogenesis, neurogenesis, and neuroinflammation. Compared with 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. Exosomes enriched with miR-17-92 cluster have a significantly better effect on improving functional recovery after TBI compared with Exo-empty, likely by reducing neuroinflammation and enhancing endogenous angiogenesis and neurogenesis. Engineering specific miRNA in exosomes may provide a novel therapeutic strategy for management of unilateral moderate cortical contusion TBI.

Neurosurgery

Zhu Y, Gujar AD, Wong CH, Tjong H, Ngan CY, Gong L, Chen YA, Kim H, Liu J, Li M, Mil-Homens A, Maurya R, Kuhlberg C, Sun F, Yi E, **deCarvalho AC**, Ruan Y, Verhaak RGW, and Wei CL. Oncogenic extrachromosomal DNA functions as mobile enhancers to globally amplify chromosomal transcription. *Cancer Cell* 2021; 39(5):694-707.e697. PMID: 33836152. Request Article

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Extrachromosomal, circular DNA (ecDNA) is emerging as a prevalent yet less characterized oncogenic alteration in cancer genomes. We leverage ChIA-PET and ChIA-Drop chromatin interaction assays to characterize genome-wide ecDNA-mediated chromatin contacts that impact transcriptional programs in

cancers. ecDNAs in glioblastoma patient-derived neurosphere and prostate cancer cell cultures are marked by widespread intra-ecDNA and genome-wide chromosomal interactions. ecDNA-chromatin contact foci are characterized by broad and high-level H3K27ac signals converging predominantly on chromosomal genes of increased expression levels. Prostate cancer cells harboring synthetic ecDNA circles composed of characterized enhancers result in the genome-wide activation of chromosomal gene transcription. Deciphering the chromosomal targets of ecDNAs at single-molecule resolution reveals an association with actively expressed oncogenes spatially clustered within ecDNA-directed interaction networks. Our results suggest that ecDNA can function as mobile transcriptional enhancers to promote tumor progression and manifest a potential synthetic aneuploidy mechanism of transcription control in cancer.

Nursing

Mianecki TB, and **Peterson EL**. The Relationship Between Central Line-Associated Bloodstream Infections and Extended Intravenous Solution Hang Times. *J Infus Nurs* 2021; 44(3):157-161. PMID: 33935250. Full Text

Department of Nursing, Henry Ford Hospital, Detroit, Michigan (Dr Mianecki); Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan (Dr Peterson).
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Edward L. Peterson, PhD, is a biostatistical consultant at Henry Ford Health System. As a biostatistician with 36 years' experience, he has been supported on 35 grants and coauthored more than 250 manuscripts.

Central line-associated bloodstream infections (CLABSIs) can result in increased morbidity and mortality and billions of dollars of costs per year to institutions and patients. Fluctuating availability of manufacturers' supplies of intravenous (IV) solutions have created issues for health systems in which policy and procedures have been examined regarding extended hang time for IV solutions. This article examined the relationship between extended hang times of nonadditive IV solutions and incidence of CLABSIs in intensive and general practice inpatient units in a quaternary care setting. The incidence of CLABSIs with extended hang times of up to 96 hours, of nonadditive IV solutions, has demonstrated that significant changes in CLABSIs were not evident.

Obstetrics, Gynecology and Women's Health Services

Kalmbach DA, O'Brien LM, **Pitts DS**, **Sagong C**, **Arnett LK**, **Harb NC**, **Cheng P**, and **Drake CL**. Mother-to-Infant Bonding is Associated with Maternal Insomnia, Snoring, Cognitive Arousal, and Infant Sleep Problems and Colic. *Behav Sleep Med* 2021;1-17. Epub ahead of print. PMID: 34047659. Request Article

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Objective: Emerging evidence links maternal and infant sleep problems to impairments in the mother-to-infant bond, but the independence and directionality of these associations remain unclear. The present study characterized concurrent and prospective effects of maternal sleep disturbances and poor infant sleep on the mother-infant relationship. As common sequalae of problematic sleep, nocturnal cognitive hyperarousal and daytime sleepiness were investigated as facilitating mechanisms.Participants: Sixty-seven pregnant women enrolled in a prospective study on maternal sleep.Methods: Sociodemographic information and clinical symptoms were measured prenatally then weekly across the first two postpartum months. Women reported insomnia symptoms, sleep duration, snoring, daytime sleepiness, nocturnal

cognitive arousal (broadly focused and perinatal-specific), perseverative thinking, depression, infant colic, infant sleep quality, and mother-infant relationship quality. Mixed effects models were conducted to test hypotheses.Results: Prenatal snoring and weak maternal-fetal attachment augured poorer postpartum bonding. Poor infant sleep was associated with increased odds for maternal insomnia and short sleep. Impairments in the mother-to-infant bond were linked to maternal insomnia, nocturnal perinatal-focused rumination, daytime sleepiness, depression, and poor infant sleep. Postnatal insomnia predicted future decreases in mother-infant relationship quality, and nocturnal cognitive hyperarousal partially mediated this association.Conclusions: Both maternal and infant sleep problems were associated with poorer mother-to-infant bonding, independent of the effects of maternal depression and infant colic. Perseverative thinking at night, particularly on infant-related concerns, was linked to impaired bonding, rejection and anger, and infant-focused anxiety. Improving maternal and infant sleep, and reducing maternal cognitive arousal, may improve the maternal-to-infant bond.

Obstetrics, Gynecology and Women's Health Services

Vilkins AL, and As-Sanie S. Opioid prescribing in gynecologic surgery - more work to be done. *J Minim Invasive Gynecol* 2021; Epub ahead of print. PMID: 34029746. Full Text

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Ophthalmology and Eye Care Services

Legocki AT, Moshiri Y, Zepeda EM, Gillette TB, Shariff A, **Grant LE**, Ding L, Lee AY, Lee CS, Tarczy-Hornoch K, and Cabrera MT. Dome-shaped macula in premature infants visualized by handheld spectral-domain optical coherence tomography. *J aapos* 2021; Epub ahead of print. PMID: 34044111. Full Text

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PURPOSE: To describe dome-shaped macula and associated clinical findings in premature infants. METHODS: This prospective, observational cohort study included a consecutive sample of premature infants screened for retinopathy of prematurity (ROP) with 9-month follow-up. Handheld spectral domain optical coherence tomography (SD-OCT) was performed at the time of ROP screening. Images were assessed for dome-shaped macula, cystoid macular edema, epiretinal membrane, vitreous bands, and punctate hyperreflective vitreous opacities. Dome height measurements were performed in a subset of images. Teller visual acuity and cycloplegic refraction were performed at an adjusted age of 8-10 months. RESULTS: Of 37 infants (74 eyes; 49% male; mean gestational age 27.8 ± 3.2 weeks; mean birth weight 949 ± 284 g), 24/37 (65%) demonstrated dome-shaped macula in at least one eye (13 both eyes, 5 right eye only, and 6 left eye only). Of the 74 eyes, 26 (35%) could be reliably measured, with a mean dome height of 139.0 ± 72.3 μm (range, 54-369 μm). Presence of dome-shaped macula was associated with a diagnosis of ROP (P = 0.02; OR, 3.03; 95% CI, 1.18-7.82) and pre-plus or plus disease (P = 0.02; OR, 4.20; 95% CI, 1.05-16.78). Infants with dome-shaped macula had lower birth weight compared with those without (877 vs 1081 g; P = 0.04). No associations with other demographics, OCT findings, and 9-month refractive outcomes were found. CONCLUSIONS: Dome-shaped macula was frequently identified by handheld SD-OCT in premature infants, especially those with lower birth weight and severe ROP. The long-term clinical significance of this finding is unknown.

Ophthalmology and Eye Care Services

Woodward MA, Maganti N, Niziol LM, **Amin S**, **Hou A**, and Singh K. Development and Validation of a Natural Language Processing Algorithm to Extract Descriptors of Microbial Keratitis From the Electronic Health Record. *Cornea* 2021; Epub ahead of print. PMID: 34029244. Full Text

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PURPOSE: The purpose of this article was to develop and validate a natural language processing (NLP) algorithm to extract qualitative descriptors of microbial keratitis (MK) from electronic health records. METHODS: In this retrospective cohort study, patients with MK diagnoses from 2 academic centers were identified using electronic health records. An NLP algorithm was created to extract MK centrality, depth, and thinning. A random sample of patient with MK encounters were used to train the algorithm (400 encounters of 100 patients) and compared with expert chart review. The algorithm was evaluated in internal (n = 100) and external validation data sets (n = 59) in comparison with masked chart review. Outcomes were sensitivity and specificity of the NLP algorithm to extract qualitative MK features as compared with masked chart review performed by an ophthalmologist. RESULTS: Across data sets, gold-standard chart review found centrality was documented in 64.0% to 79.3% of charts, depth in 15.0% to 20.3%, and thinning in 25.4% to 31.3%. Compared with chart review, the NLP algorithm had a sensitivity of 80.3%, 50.0%, and 66.7% for identifying central MK, 85.4%, 66.7%, and 100% for deep MK, and 100.0%, 95.2%, and 100% for thin MK, in the training, internal, and external validation samples, respectively. Specificity was 41.1%, 38.6%, and 46.2% for centrality, 100%, 83.3%, and 71.4% for depth, and 93.3%, 100%, and was not applicable (n = 0) to the external data for thinning, in the samples, respectively. CONCLUSIONS: MK features are not documented consistently showing a lack of standardization in recording MK examination elements. NLP shows promise but will be limited if the available clinical data are missing from the chart.

Orthopedics/Bone and Joint Center

Abbas MJ, **Jildeh TR**, **Buckley P**, Mehran N, and **Okoroha KR**. Anterior Cruciate Reconstruction with Quadriceps Autograft using QuadLink Anterior Cruciate Ligament FiberTag TightRope Implant. *Arthroscopy Techniques* 2021; 10(5):e1389-e1394. PMID: Not assigned. Full Text

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Quadriceps tendon autografts have been shown to be a reliable option for anterior cruciate ligament (ACL) reconstruction. The graft allows for optimal functional outcomes while reducing donor site morbidity. Although quadriceps graft fixation can be achieved using a variety of techniques, there is a lack of consensus on the optimal technique. Additionally, femoral fixation techniques have variance in durability and reproducibility. The purpose of this Technical Note and video is to provide our preferred method of quadriceps tendon autograft preparation and fixation using the Quad Link ACL FiberTag TightRope Implant in a single-bundle ACL reconstruction.

Orthopedics/Bone and Joint Center

Darrith B, **Khalil LS**, **Franovic S**, **Bazydlo M**, **Weir RM**, **Banka TR**, and **Davis JJ**. Preoperative Patient-Reported Outcomes Measurement Information System Global Health Scores Predict Patients Achieving the Minimal Clinically Important Difference in the Early Postoperative Time Period After Total Knee Arthroplasty. *J Am Acad Orthop Surg* 2021; Epub ahead of print. PMID: 34061813. Full Text

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INTRODUCTION: The patient-specific factors influencing postoperative improvement after total knee arthroplasty (TKA) are important considerations for the surgeon and patient. The primary purpose of this study was to determine which patient demographic factors influence the postoperative Patient-Reported

Outcomes Measurement Information System (PROMIS) Global Health (GH) scores. In addition, we aimed to compare the prognostic utility of preoperative PROMIS-GH scores and the Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS-JR) in predicting postoperative improvement. METHODS: This retrospective cohort study of a consecutive series of patients who underwent primary, unilateral TKA analyzed prospectively collected KOOS-JR and PROMIS-GH surveys. PROMIS-GH includes physical health (PH) and mental health scores. Patient demographic and presurgical characteristics were evaluated for prognostic capability in predicting postoperative improvement in the PROMIS scores and achievement of the minimal clinically important difference (MCID). Receiver operating characteristic curves were used to understand the prognostic thresholds of the preoperative PROMIS score and KOOS-JR for predicting MCID achievement. RESULTS: A total of 872 patients were included. Although unadjusted analyses showed associations between patient demographic factors and PROMIS-PH scores, multivariable regression analysis for predictors of MCID achievement demonstrated that PROMIS-PH was the only significant preoperative variable. Receiver operating characteristic analysis revealed that the area under the curve of PROMIS-PH (0.70; 95% CI, 0.67 to 0.74) was less than that of the KOOS-JR (0.77; 95% CI, 0.73 to 0.81; P = 0.032). Sensitivity and specificity for achieving the MCID were maximized for preoperative PROMIS-PH scores of ≤ 38 (59% and 70%) and for preoperative KOOS-JR ≤ 51 (71% and 69%). CONCLUSIONS: Preoperative KOOS-JR and PROMIS-PH scores predict clinically meaningful improvement after TKA. The KOOS-JR has greater prognostic utility in the early postoperative period. LEVEL OF EVIDENCE: Level III, Prognostic Study.

Orthopedics/Bone and Joint Center

Franovic S, **Pietroski A**, **Kuhlmann N**, **Bazzi T**, **Zhou Y**, and **Muh S**. Rockwood Grade-III Acromioclavicular Joint Separation: A Cost-Effectiveness Analysis of Treatment Options. *JB JS Open Access* 2021; 6(2). PMID: 34056509. Full Text

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BACKGROUND: The treatment of Rockwood Grade-III acromioclavicular (AC) joint separation has been widely disputed since the introduction of the classification system. The present literature does not reach consensus on whether operative or nonoperative management is more advantageous, nor does it effectively distinguish between operative measures. We hypothesized that nonoperative treatment of Rockwood Grade-III AC joint separation would be more cost-effective when compared with surgical options. METHODS: We created a decision-tree model outlining the treatment of Rockwood Grade-III separations using nonoperative management or hook-plate, suture-button, or allograft fixation. After nonoperative intervention, the possible outcomes predicted by the model were uneventful healing, delayed operative management, a second round of sling use and physical therapy, or no reduction and no action; and after operative intervention, the possible outcomes were uneventful healing, loss of reduction and revision, and depending on the implant, loss of reduction and no action, or removal of the implant. A systematic review was conducted, and probabilities of each model state were averaged. A cost-effectiveness analysis was conducted both through rollback analysis yielding net monetary benefit and through incremental cost-effectiveness ratios (ICERs). Thresholds of $50,000/quality-adjusted life-year (QALY) and $100,000/QALY were used for ICER analysis. Furthermore, a sensitivity analysis was utilized to determine whether differential probabilities could impact the model. RESULTS: Forty-five papers were selected from a potential 768 papers identified through our literature review. Nonoperative treatment was used as our reference case and showed dominance over all 3 of the operative measures at both the $50,000 and $100,000 ICER thresholds. Nonoperative treatment also showed the greatest net monetary benefit. Nonoperative management yielded the lowest total cost ($6,060) and greatest utility (0.95 QALY). Sensitivity analysis showed that allograft fixation became the favored technique at a willingness-to-pay threshold of $50,000 if the rate of failure of nonoperative treatment rose to 14.6%. Similarly, at the $100,000 threshold, allograft became dominant if the probability of failure of nonoperative treatment rose to 22.8%. CONCLUSIONS: The cost-effectiveness of nonoperative treatment is fueled by its notably lower costs and overall high rates of success in Grade-III separations. It is important to note that, in our analysis, the societal cost (measured in lost productivity) of nonoperative treatment neared that of surgical treatment, but the cost from the health-care system perspective was minimal. Physicians should bear in mind the sensitivity of these conclusions and should consider cost-effectiveness analyses

in their decision-making guidelines. LEVEL OF EVIDENCE: Economic and Decision Analysis Level IV. See Instructions for Authors for a complete description of levels of evidence.

Orthopedics/Bone and Joint Center
Hessburg LT, **Ziedas AC**, **Cross AG**, **Elhage K**, **Yedulla N**, **Koolmees D**, **Muh SJ**, **Moutzouros V**, and **Makhni EC**. Patients with Preoperative Clinical Depression Symptomology Experience Significant Improvements in Postoperative Pain, Function, and Depressive Symptoms Following Rotator Cuff Repair. *Arthroscopy* 2021; Epub ahead of print. PMID: 34052382. Full Text

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PURPOSE: To determine the impact of clinical depression on outcomes following rotator cuff repair (RCR), as measured by Patient-Reported Outcomes Measurement Information System (PROMIS) Computer Adaptive Test (CAT) health domains. METHODS: RCR patients were given PROMIS CAT assessments for physical function (PROMIS UE), pain interference (PROMIS PI), and depression (PROMIS D) during pre- and postoperative clinic visits. PROMIS D scores ≥ 55 correlate with mild clinical depression; thus, patients with PROMIS D scores ≥ 55 were placed in the "clinical depression" (CD) group, while patients with scores <55 were placed in the "no clinical depression" (NCD) group. Categorical variables were compared at preoperative and postoperative (6m and ≥1y) timepoints using chi-squared tests. Continuous variables were compared using student's t-tests. RESULTS: Of the 340 RCR patients included in this study, 65 (19.1%) were found to have mild clinical depression preoperatively, with that number being reduced to 23 (6.8%) at 6m and 19 (5.6%) at ≥1y postoperatively. Compared with preoperative PROMIS scores, CD patients had significant postoperative improvements at 6m and ≥1y in mean PROMIS UE (26.7 vs 35.5 vs 38.9; p<.001) and PROMIS PI (67.6 vs 56.7 vs 56.4; p<.001). NCD patients had similar postoperative improvements at 6m and ≥1y in mean PROMIS UE (30.8 vs 38.6 vs 46.9; p<.001) and PROMIS PI (61.7 vs 53.0 vs 47.6; p<.001). The improvement in PROMIS scores was similar for the CD and NCD groups in both PROMIS UE (12.2 vs 16.1, respectively) and PROMIS PI (-11.2 vs -14.1, respectively). CONCLUSION: Despite starting with worse PROMIS UE and PROMIS PI scores, patients undergoing RCR with symptoms of CD experienced significant improvement in function, pain, and depressive symptoms. Preoperative depression should not be a contraindication to arthroscopic RCR in patients who are otherwise appropriate operative candidates.

Orthopedics/Bone and Joint Center
Jildeh TR, **Meta F**, Young J, Page B, and **Okoroha KR**. Concussion in National Football League Athletes Is Not Associated With Increased Risk of Acute, Noncontact Lower Extremity Musculoskeletal Injury. *Orthop J Sports Med* 2021; 9(5):23259671211003491. PMID: 34017880. Full Text

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BACKGROUND: Impaired neuromuscular function after concussion has recently been linked to increased risk of lower extremity injuries in athletes. PURPOSE: To determine if National Football League (NFL) athletes have an increased risk of sustaining an acute, noncontact lower extremity injury in the 90-day period after return to play (RTP) and whether on-field performance differs pre- and postconcussion. STUDY DESIGN: Cohort study, Level of evidence, 3. METHODS: NFL concussions in offensive players from the 2012-2013 to the 2016-2017 seasons were studied. Age, position, injury location/type, RTP, and athlete factors were noted. A 90-day RTP postconcussive period was analyzed for lower extremity injuries. Concussion and injury data were obtained from publicly available sources. Nonconcussed, offensive skill position NFL athletes from the same period were used as a control cohort, with the 2014 season as the reference season. Power rating performance metrics were calculated for ±1, ±2, and ±3 seasons pre- and postconcussion. Conditional logistic regression was used to determine associations between concussion and lower extremity injury as well as the relationship of concussions to on-field performance. RESULTS: In total, 116 concussions were recorded in 108 NFL athletes during the study

period. There was no statistically significant difference in the incidence of an acute, noncontact lower extremity injury between concussed and control athletes (8.5% vs 12.8%; P = .143), which correlates with an odds ratio of 0.573 (95% CI, 0.270-1.217). Days (66.4 ± 81.9 days vs 45.1 ± 69.2 days; P = .423) and games missed (3.67 ± 3.0 vs 2.9 ± 2.7 games; P = .470) were similar in concussed athletes and control athletes after a lower extremity injury. No significant changes in power ratings were noted in concussed athletes in the acute period (±1 season to injury) when comparing pre- and postconcussion. CONCLUSION: Concussed, NFL offensive athletes did not demonstrate increased odds of acute, noncontact, lower extremity injury in a 90-day RTP period when compared with nonconcussed controls. Immediate on-field performance of skill position players did not appear to be affected by concussion.

Orthopedics/Bone and Joint Center

Oravec D, **Drost J**, **Zauel R**, **Flynn M**, and **Yeni YN**. Assessment of Intravertebral Mechanical Strains and Cancellous Bone Texture Under Load Using a Clinically Available Digital Tomosynthesis Modality. *J Biomech Eng* 2021; Epub ahead of print. PMID: 34041529. Request Article

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Vertebral fractures are the most common osteoporotic fractures, but clinical means for assessment of vertebral bone integrity are limited in accuracy, as they typically use surrogate measures that are indirectly related to mechanics. The objective of this study was to examine the extent to which intravertebral strain distributions and changes in cancellous bone texture generated by a load of physiological magnitude can be characterized using a clinically available imaging modality. We hypothesized that digital tomosynthesis based digital volume correlation (DTS-DVC) and image texture based metrics of cancellous bone microstructure can detect development of mechanical strains under load. Isolated cadaveric T11 vertebrae and L2-L4 vertebral segments were DTS imaged in a nonloaded state and under physiological load levels. Axial strain, maximum principal strain, maximum compressive and tensile principal strains, and von Mises equivalent strain were calculated using the DVC technique. The change in textural parameters (line fraction deviation, anisotropy, and fractal parameters) under load was calculated within the cancellous centrum. The effect of load on measured strains and texture variables was tested using mixed model ANOVA, and relationships of strain and texture variables with donor age, bone density parameters, and bone size were examined using regression models. Magnitudes and heterogeneity of intravertebral strain measures correlated with applied loading and were significantly different from background noise. Image texture parameters were found to change with applied loading but these changes were not confirmed in a larger sample. DTS-DVC derived strains correlated with age more strongly than did BMD for T11.

Orthopedics/Bone and Joint Center

Ziedas AC, **Abed V**, **Swantek AJ**, **Rahman TM**, **Cross A**, **Thomashow K**, and **Makhni EC**. PROMIS Physical Function Instruments Compare Favorably to Legacy Patient Reported Outcome Measures in Upper and Lower Extremity Orthopedic Patients: A Systematic Review of the Literature. *Arthroscopy* 2021; Epub ahead of print. PMID: 34052370. Full Text

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PURPOSE: The purpose of this systematic review is to compare Patient-Reported Outcomes Measurement Information System (PROMIS) Physical Function (PF) with traditional ("legacy") patient reported outcome measures (PROMs) in regard to correlations, ease of use, and quality criteria for upper (UE) and lower extremity (LE) orthopedic conditions. METHODS: A systematic search of the PubMed/MEDLINE database was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to identify published articles that referenced the various PROMIS PF measures. Two authors independently reviewed selected studies. The search returned 857 studies, 85 of which were selected for independent review by two authors. Of these, 54

were selected for inclusion. Mixed linear models were performed to assess for differences between legacy PROMs and PROMIS measures. RESULTS: The combined sample size of all included studies yielded 6,074 UE and 9,366 LE patients. Overall, PROMIS PF measures demonstrated strong correlations with legacy PROMs among UE (weighted Pearson correlation, 0.624, standard error [SE] = 0.042; weighted Spearman correlation, 0.566, SE = 0.042) and LE patients (weighted Pearson correlation, 0.645, SE = 0.062; weighted Spearman correlation, 0.631, SE = 0.041). PROMIS PF questionnaires completed by UE patients had fewer questions than legacy PROMs (5.9 vs 17.7, P = 0.0093) and were completed in less time (90.5 vs 223.8 seconds, P = 0.084). PROMIS PF questionnaires completed by LE patients had fewer questions than legacy PROMs (4.81 vs 15.33, P < 0.001) and were completed in less time (63.6 vs 203.2 seconds, P = 0.0063). The differences for the reliability measures were not significant. CONCLUSIONS: PROMIS PF scores correlate strongly with commonly used legacy PROMs in orthopedics, particularly in UE and LE patients. PROMIS PF forms can be administered efficiently and to a broad patient population while remaining highly reliable. Therefore, they can be justified for standardized use among orthopedic patients with UE and LE conditions, improving the ability to aggregate and compare outcomes in orthopedic research.

Otolaryngology – Head and Neck Surgery

Kappagantu A, **Yaremchuk K**, and **Tam S**. Head and Neck Injuries and Electronic Scooter Use in the United States. *Laryngoscope* 2021; Epub ahead of print. PMID: 34002874. Full Text

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OBJECTIVE: To quantify electric scooter injuries encountered in United States emergency departments, focusing on the head and neck, to understand the safety impact of these scooters to improve safe usage. STUDY DESIGN: Retrospective cross-sectional study from January 2009 to December 2019 of patients presenting to United States emergency departments with electric scooter injuries collected from a national database. About 2,823 cases of injuries were related to electric scooter use from January 2009 to December 2019. Stratified weighted counts and incidence rates were estimated for injury characteristics. Piecewise linear regression quantified the yearly change in incidence of injuries before and after introduction of rideshare programs. RESULTS: The estimated national total of electric scooter cases from 2009 to 2019 was 103,943 (95% CI: 79,650-128,237). Incidence grew in 2019 to 8.63 cases per 100,000 person-years from 4.46 in 2018 to 2.42 in 2017. Head and neck injuries represented 28.5% of total injuries (weighted estimate = 29,610). The most common age group of head and neck injuries before 2018 was ≤17 years, but injuries in 18- to 44-year-olds grew significantly to become the most injured group in 2018 to 2019 (P < .001). From 2009 to 2017, incidence of head and neck injuries fell by 0.02 cases per 100,000 person-years, but cases grew by 1.22 cases per 100,000 person-years post-2017 (P < .001). CONCLUSION: Injuries following the launch of rideshare electric scooter programs increased significantly, especially in patients 18 to 44 years of age. Head and neck injuries represent many of these injuries. User safety education must be addressed to prevent injury as programs become more pervasive in the United States. LEVEL OF EVIDENCE: Level 2 Laryngoscope, 2021.

Otolaryngology – Head and Neck Surgery

Scharpf J, Liu JC, Sinclair C, **Singer M**, Liddy W, Orloff L, Steward D, Bonilla Velez J, and Randolph GW. Critical Review and Consensus Statement for Neural Monitoring in Otolaryngologic Head, Neck, and Endocrine Surgery. *Otolaryngol Head Neck Surg* 2021; Epub ahead of print. PMID: 34000898. Full Text

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BACKGROUND: Enhancing patient outcomes in an array of surgical procedures in the head and neck requires the maintenance of complex regional functions through the protection of cranial nerve integrity. This review and consensus statement cover the scope of cranial nerve monitoring of all cranial nerves that are of practical importance in head, neck, and endocrine surgery except for cranial nerves VII and VIII within the temporal bone. Complete and applied understanding of neurophysiologic principles facilitates the surgeon's ability to monitor the at-risk nerve. METHODS: The American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) identified the need for a consensus statement on cranial nerve monitoring. An AAO-HNS task force was created through soliciting experts on the subject. Relevant domains were identified, including residency education, neurophysiology, application, and various techniques for monitoring pertinent cranial nerves. A document was generated to incorporate and consolidate these domains. The panel used a modified Delphi method for consensus generation. RESULTS: Consensus was achieved in the domains of education needs and anesthesia considerations, as well as setup, troubleshooting, and documentation. Specific cranial nerve monitoring was evaluated and reached consensus for all cranial nerves in statement 4 with the exception of the spinal accessory nerve. Although the spinal accessory nerve's value can never be marginalized, the task force did not feel that the existing literature was as robust to support a recommendation of routine monitoring of this nerve. In contrast, there is robust supporting literature cited and consensus for routine monitoring in certain procedures, such as thyroid surgery, to optimize patient outcomes. CONCLUSIONS: The AAO-HNS Cranial Nerve Monitoring Task Force has provided a state-of-the-art review in neural monitoring in otolaryngologic head, neck, and endocrine surgery. The evidence-based review was complemented by consensus statements utilizing a modified Delphi method to prioritize key statements to enhance patient outcomes in an array of surgical procedures in the head and neck. A precise definition of what actually constitutes intraoperative nerve monitoring and its benefits have been provided.

Pathology and Laboratory Medicine

Alhamar M, Jabbar A, Deebajah M, **Diaz M**, Alanee S, **Hassan O**, Williamson SR, **Schultz D**, and **Gupta N**. Prognostic significance of histomorphologic features of lymph node metastases in prostate cancer patients treated with radical prostatectomy: A single center study. *Urol Oncol* 2021; Epub ahead of print. PMID: 33985876. Full Text

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OBJECTIVE: We assessed the prognostic value of histomorphologic features of lymph node (LN) metastases in patients with prostate cancer treated with radical prostatectomy MATERIALS AND METHODS: We evaluated the effect of the features of LN metastasis on the risk of biochemical recurrence (BCR) in 280 LN-positive patients who underwent radical prostatectomy between 2006 to 2018. LN specific parameters recorded included number of metastatic LNs, size of the largest metastatic focus, Gleason Grade (GG) of the metastatic focus, and extranodal extension (ENE). RESULTS: A solitary positive LN was found in 166/280 (59%), 95/280 (34%) patients had 2-4 positive LNs, and 19/280 (7%) had 5 or more positive LNs. The size of the largest metastatic focus > 2 mm (macrometastasis) in 154/261 (59%). GG of the metastatic focus was as follows: GG 1-2: 29/224 (13%); GG 3: 27/224 (12%); and GG 4-5: 168/224 (75%). ENE was identified in 99/244 (41%). We found the number of LNs positive (2-4 vs. 1 Hazard ratio (HR) = 1.60; 95% CI: 1.02 to 2.5; P = 0.04) and GG of the metastatic focus (GG 4&5 vs. 1-3 HR = 1.90; 95% CI: 1.14-3.2; P= 0.014) to be independent predictors of the risk of BCR after surgery on multivariate analysis. CONCLUSIONS: Our study showed the number of LNs positive and GG of the LN metastatic focus to be significant independent predictors of BCR after radical prostatectomy.

We recommend reporting histomorphologic parameters of LN metastasis as they may help in defining BCR risk categorization.

Pathology and Laboratory Medicine

Anderson J, **Putnam E**, **Liu W**, and Menon MP. Discovery of G6PD deficiency in a patient with DUSP22-rearranged ALK-negative anaplastic large cell lymphoma in leukemic phase. *Int J Lab Hematol* 2021; Epub ahead of print. PMID: 34019742. Full Text

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Pathology and Laboratory Medicine

Chang JC, Offin M, Falcon C, Brown D, Houck-Loomis BR, Meng F, Rudneva VA, Won HH, Amir S, **Montecalvo J**, Desmeules P, Kadota K, Adusumilli PS, Rusch VW, Teed S, Sabari JK, Benayed R, Nafa K, Borsu L, Li BT, Schram AM, Arcila ME, Travis WD, Ladanyi M, Drilon A, and Rekhtman N. Comprehensive Molecular and Clinicopathologic Analysis of 200 Pulmonary Invasive Mucinous Adenocarcinomas Identifies Distinct Characteristics of Molecular Subtypes. *Clin Cancer Res* 2021; Epub ahead of print. PMID: 33947695. Full Text

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PURPOSE: Invasive mucinous adenocarcinoma (IMA) is a unique subtype of lung adenocarcinoma, characterized genomically by frequent KRAS mutations or specific gene fusions, most commonly involving NRG1. Comprehensive analysis of a large series of IMAs using broad DNA- and RNA-sequencing methods is still lacking, and it remains unclear whether molecular subtypes of IMA differ clinicopathologically. EXPERIMENTAL DESIGN: A total of 200 IMAs were analyzed by 410-gene DNA next-generation sequencing (MSK-IMPACT; n = 136) or hotspot 8-oncogene genotyping (n = 64). Driver-negative cases were further analyzed by 62-gene RNA sequencing (MSK-Fusion) and those lacking fusions were further tested by whole-exome sequencing and whole-transcriptome sequencing (WTS). RESULTS: Combined MSK-IMPACT and MSK-Fusion testing identified mutually exclusive driver alterations in 96% of IMAs, including KRAS mutations (76%), NRG1 fusions (7%), ERBB2 alterations (6%), and other less common events. In addition, WTS identified a novel NRG2 fusion (F11R-NRG2). Overall, targetable gene fusions were identified in 51% of KRAS wild-type IMAs, leading to durable responses to targeted therapy in some patients. Compared with KRAS-mutant IMAs, NRG1-rearranged tumors exhibited several more aggressive characteristics, including worse recurrence-free survival ($P < 0.0001$). CONCLUSIONS: This is the largest molecular study of IMAs to date, where we demonstrate the presence of a major oncogenic driver in nearly all cases. This study is the first to document more aggressive characteristics of NRG1-rearranged IMAs, ERBB2 as the third most common alteration, and a novel NRG2 fusion in these tumors. Comprehensive molecular testing of KRAS wild-type IMAs that includes fusion testing is essential, given the high prevalence of alterations with established and investigational targeted therapies in this subset.

Pathology and Laboratory Medicine

Fucinari J, **Elshaikh MA**, Ruterbusch JJ, **Khalil R**, Dyson G, **Shultz D**, Ali-Fehmi R, and Cote ML. The impact of race, comorbid conditions and obesity on survival endpoints in women with high grade endometrial carcinoma. *Gynecol Oncol* 2021; Epub ahead of print. PMID: 33985795. Full Text

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OBJECTIVE: To estimate overall survival, disease-specific survival, and progression-free survival among high grade endometrial carcinoma cases and to determine factors impacting survival for non-Hispanic white and non-Hispanic black women. METHODS: We identified high grade endometrial carcinoma cases among non-Hispanic white and non-Hispanic black women from ongoing institutional studies, and determined eligibility through medical record and pathologic review. We estimated effects of demographic and clinical variables on survival outcomes using Kaplan Meier methods and Cox proportional hazards modelling. RESULTS: Non-Hispanic Black women with BMI <25.0 had poorest overall survival compared to non-Hispanic white women with BMI <25.0 (HR 3.03; 95% CI [1.35, 6.81]), followed by non-Hispanic black women with BMI 25.0+ (HR 2.43; 95% CI [1.28, 4.60]). A similar pattern emerged for disease-specific survival. Non-Hispanic black women also had poorer progression-free survival than non-Hispanic white women (HR 1.40; 95% CI [1.01, 1.93]). Other significant factors impacting survival outcomes included receipt of National Cancer Center Network (NCCN) guideline-concordant treatment (GCT), earlier stage at diagnosis, and fewer comorbid conditions. CONCLUSIONS: BMI and race interact and modify the association with high grade endometrial carcinoma survival. Other potentially modifiable factors, such as reducing comorbidities and increasing access to GCT will potentially improve survival after diagnosis of high grade endometrial carcinomas. A better understanding of the molecular drivers of these high grade carcinomas may lead to targeted therapies that reduce morbidity and mortality associated with these aggressive tumors.

Pathology and Laboratory Medicine

Rodgers S, Datta L, **Perry KD**, and **Stone CH**. Rhabdomyosarcoma with epithelioid morphology: A challenging cytologic diagnosis in a pleural effusion. *Diagn Cytopathol* 2021; Epub ahead of print. PMID: 34004052. Full Text

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Rhabdomyosarcomas (RMS) are rare malignant skeletal muscle tumors that present more commonly in pediatric populations. The WHO currently classifies RMS into four types, embryonal, alveolar, pleomorphic, and spindle cell/sclerosing variants. Epithelioid rhabdomyosarcoma (EpiRMS) is another rare, recently described subtype of RMS presenting in older patients with a male predominance and has a rapidly progressive clinical course with frequent metastases. EpiRMS closely mimics poorly differentiated carcinoma or melanoma, demonstrating discohesive large epithelioid cells with abundant eosinophilic cytoplasm, frequent glassy cytoplasmic inclusions, large vesicular nuclei, and prominent nucleoli. We present a case of metastatic rhabdomyosarcoma with features reminiscent of EpiRMS presenting as a pleural effusion, closely followed by an inguinal lymph node biopsy. The malignant cells in the pleural fluid were diffusely positive for desmin, negative for MyoD1, myogenin, S100 and SOX10, and retained INI-1 expression. Subsequent lymph node biopsy demonstrated identical malignant epithelioid cells that were positive for desmin, myoD1 and myogenin, and a cytological diagnosis of "metastatic rhabdomyosarcoma, favor epithelioid rhabdomyosarcoma" was given considering the concurrent lymph node biopsy morphology and immunoprofile. A diagnosis of rhabdomyosarcoma, though rare and

challenging, should not be overlooked when considering malignant cells with an epithelioid morphology in cytology specimens.

Pathology and Laboratory Medicine
Shallal A, **Tibbetts R**, **Alangaden G**, and **Williams J**. Pulmonary nodules in a lung transplant recipient. *Am J Transplant* 2021; 21(5):1975-1977. PMID: 33939276. Full Text

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Pathology and Laboratory Medicine
Straughen JK, **Sitarik AR**, **Johnson CC**, **Wegienka G**, **Ownby DR**, **Johnson-Hooper TM**, **Allo G**, **Levin AM**, and **Cassidy-Bushrow AE**. Prenatal IgE as a Risk Factor for the Development of Childhood Neurodevelopmental Disorders. *Front Pediatr* 2021; 9:601092. PMID: 34055677. Full Text

Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI, United States.
Division of Allergy and Clinical Immunology, Department of Pediatrics, Medical College of Georgia at Augusta University, Augusta, GA, United States.
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Department of Pathology, Henry Ford Hospital, Detroit, MI, United States.

Background: Few studies have examined if maternal allergic disease is associated with an offspring's neurodevelopment. We hypothesized that Th-2 biased maternal immune function assessed as total serum immunoglobulin (Ig) E is associated with attention deficit hyperactivity disorder (ADHD). Methods: Data are from the Wayne County Health, Environment, Allergy, and Asthma Longitudinal Study (WHEALS), a racially and socioeconomically diverse birth cohort in metropolitan Detroit, Michigan. Maternal total IgE was measured prenatally and at 1-month postpartum. Child total IgE was assessed at birth, 6 months, and 2 years of age. ADHD diagnosis was based on the parental report at the 10-12-year study visits or medical chart abstraction. Total IgE was log(2) transformed. Poisson regression models with robust error variance were used to calculate the risk ratios (RR). Inverse probability weighting was used to correct for potential bias due to a loss to follow-up and non-response. Results: Of the 636 maternal-child pairs in the analysis, 513 children were neurotypical and 123 had ADHD. Maternal prenatal total IgE was significantly associated with ADHD even after adjustment for potential confounders (RR = 1.08, 95% CI 1.03-1.13). Maternal and child IgE measures were positively and significantly correlated, but child total IgE was not associated with ADHD at any time point. Conclusions: Maternal prenatal IgE may influence neurodevelopment, but additional studies are needed to confirm and expand these findings.

Pathology and Laboratory Medicine
Uzuni A, **Wlosinski L**, and **Lopez-Plaza I**. Updated Evaluation of RhD Status Among Women of Child-Bearing Age in Detroit, Michigan. *Am J Clin Pathol* 2021; Epub ahead of print. PMID: 34050357. Full Text

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OBJECTIVES: The Rh blood group system is one of the most important and immunogenic blood group systems after the ABO blood group system and, like other blood group antigens, it follows ethnic and racial trends. However, when it comes to D variants-partial D and weak D-most of the cohorts studied in the literature have been of European descent. This study aimed to discover the variant D trends in Detroit, Michigan, with an emphasis on Black communities. METHODS: From 2016 to 2018, there were 102 patients (women of childbearing potential: < 50 years) at Henry Ford Hospital that had serologic D discrepant testing. These patients were sent out for molecular RHD determination. RESULTS: In total, 12.7% of patients were characterized as RhD positive and 87.3% of patients were characterized as RhD variants (nominated as RhD negative at our institution). CONCLUSIONS: Our predominantly Black cohort sheds light on the diversity of the RhD antigen. The majority of Blacks were classified as RhD variants

(RhD negative nomination at our institution). Therefore, molecular testing for this patient population with serologic RhD discrepancies is paramount to properly manage their obstetric care.

Pediatrics

Straughen JK, **Sitarik AR**, **Johnson CC**, **Wegienka G**, **Ownby DR**, **Johnson-Hooper TM**, **Allo G**, **Levin AM**, and **Cassidy-Bushrow AE**. Prenatal IgE as a Risk Factor for the Development of Childhood Neurodevelopmental Disorders. *Front Pediatr* 2021; 9:601092. PMID: 34055677. Full Text

Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI, United States.
Division of Allergy and Clinical Immunology, Department of Pediatrics, Medical College of Georgia at Augusta University, Augusta, GA, United States.
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Department of Pathology, Henry Ford Hospital, Detroit, MI, United States.

Background: Few studies have examined if maternal allergic disease is associated with an offspring's neurodevelopment. We hypothesized that Th-2 biased maternal immune function assessed as total serum immunoglobulin (Ig) E is associated with attention deficit hyperactivity disorder (ADHD). Methods: Data are from the Wayne County Health, Environment, Allergy, and Asthma Longitudinal Study (WHEALS), a racially and socioeconomically diverse birth cohort in metropolitan Detroit, Michigan. Maternal total IgE was measured prenatally and at 1-month postpartum. Child total IgE was assessed at birth, 6 months, and 2 years of age. ADHD diagnosis was based on the parental report at the 10-12-year study visits or medical chart abstraction. Total IgE was log(2) transformed. Poisson regression models with robust error variance were used to calculate the risk ratios (RR). Inverse probability weighting was used to correct for potential bias due to a loss to follow-up and non-response. Results: Of the 636 maternal-child pairs in the analysis, 513 children were neurotypical and 123 had ADHD. Maternal prenatal total IgE was significantly associated with ADHD even after adjustment for potential confounders (RR = 1.08, 95% CI 1.03-1.13). Maternal and child IgE measures were positively and significantly correlated, but child total IgE was not associated with ADHD at any time point. Conclusions: Maternal prenatal IgE may influence neurodevelopment, but additional studies are needed to confirm and expand these findings.

Pharmacy

Kalus JS, Dagam JK, Hoying M, Erdman D, Mieure KD, Melroy MJ, Beehrle-Hobbs D, and Silvester JA. Enhancing pharmacy residency training program quality and efficiency through alignment of pharmacy residency programs within a multihospital health system. *Am J Health Syst Pharm* 2021; Epub ahead of print. PMID: 33999157. Full Text

Department of Pharmacy, Henry Ford Hospital, Detroit, MI, USA.
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Cleveland Clinic Akron General Medical Center, Akron, OH, USA.
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Pharmacy

Kwiatkowski S, **Mulugeta S**, **Davis S**, **Kenney R**, **Kalus J**, Walton L, and **Patel N**. Optimizing preoperative antibiotics in patients with β-lactam allergies: A role for pharmacy. *Am J Health Syst Pharm* 2021; Epub ahead of print. PMID: 34037708. Full Text

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PURPOSE: Patients with a reported β-lactam allergy (BLA) are often given alternative perioperative antibiotic prophylaxis, increasing risk of surgical site infections (SSIs), acute kidney injury (AKI), and Clostridioides difficile infection (CDI). The purpose of this study was to implement and evaluate a pharmacist-led BLA clarification interview service in the preoperative setting. METHODS: A pharmacist performed BLA clarification telephone interviews before elective procedures from November 2018 to March 2019. On the basis of allergy history and a decision algorithm, first-line preoperative antibiotics, alternative antibiotics, or allergy testing referral was recommended. The pharmacist intervention (PI) group was compared to a standard of care (SOC) group who underwent surgery from November 2017 to March 2018. RESULTS: Eighty-seven patients were included, with 50 (57%) and 37 (43%) in the SOC and PI groups, respectively. The most common surgeries included orthopedic surgery in 41 patients (47%) and neurosurgery in 17 patients (20%). In the PI group, all BLA labels were updated after interview. Twenty-three patients were referred for allergy testing, 12 of the 23 (52%) completed BLA testing, and penicillin allergies were removed for 9 of the 12 patients. Overall, 28 of the 37 (76%) pharmacy antibiotic recommendations were accepted. Cefazolin use significantly increased from 28% to 65% after the intervention (P = 0.001). SSI occurred in 5 (10%) patients in the SOC group and no patients in the PI group (P = 0.051). All of these SSIs were associated with alternative antibiotics. Incidence of AKI and CDI was similar between the groups. No allergic reactions occurred in either group. CONCLUSION: Implementation of a pharmacy-driven BLA reconciliation significantly increased β-lactam preoperative use without negative safety outcomes.

Public Health Sciences

Aurora L, **McCord J**, **Nowak R**, Giannitsis E, Christenson R, DeFilippi C, Lindahl B, Christ M, Body R, **Jacobsen G**, and Mueller C. Prognostic Utility of a Modified HEART Score When Different Troponin Cut-points Are Used. *Crit Pathw Cardiol* 2021; Epub ahead of print. PMID: 33988541. Full Text

Heart and Vascular Institute, Henry Ford Health System, Detroit, MI, USA Department of Emergency Medicine, Henry Ford Hospital, Detroit, MI, USA Depar Medizinische Klinik III, Universitätsklinikum Heidelberg, Heidelberg, Germany Department of Pathology, University of Maryland School of Medicine, Baltimore, MD, USA Department of Medicine, Inova Heart and Vascular Institute, Falls Church, VA, USA Department of Medical Sciences and Uppsala Clinical Research Center, Uppsala University, Uppsala, Sweden Department of Emergency Medicine, Cantonal Hospital Lucerne, Switzerland Manchester University NHS Foundation Trust, Manchester, United Kingdom Division of Cardiovascular Sciences, University of Manchester, Manchester, United Kingdom Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA Cardiology and Cardiovascular Research Institute Basel, University Hospital Basel, Switzerland.

BACKGROUND: Although the recommended cut-point for cardiac troponin (cTn) is the 99th percentile, many institutions use cut-points that are multiples higher than the 99th percentile for diagnosing acute myocardial infarction (AMI). Prior studies have shown that patients with a HEART score (HS) ≤ 3 and normal serial cTn values (modified HS) are at low risk for adverse events. This study aimed to evaluate the prognostic utility of the HS when various cTn cut-points are used. METHODS: This was a sub-study of TRAPID-AMI, a multicenter, international trial evaluating a rapid rule-out AMI study using high sensitivity cTnT (hs-cTnT). 1,282 patients were evaluated for AMI from 12 centers in Europe, United States of America, and Australia from 2011-2013. Blood samples of hs-cTnT were collected at presentation and 2 hours, and each patient had a HS calculated. The US Food and Drug Administration approved 99th percentile for hs-cTnT (19 ng/L) was used. RESULTS: There were 213 (17%) AMIs. Within 30 days, there were an additional 2 AMIs and 8 deaths. The adverse event rates at 30 days (death/AMI) for a HS ≤ 3 and non-elevated hs-cTnT over 2 hours using increasing hs-cTnT cut-points ranged from 0.6% to 5.1%. CONCLUSIONS: Using the recommended 99th percentile cut-point for hs-cTnT, the combination of a HS ≤ 3 with non-elevated hs-cTnT values over 2 hours identifies a low-risk cohort who can be considered for

discharge from the emergency department without further testing. The prognostic utility of this strategy is greatly lessened as higher hs-cTnT cut-points are used.

Public Health Sciences

Chudy-Onwugaje K, Huang WY, Su LJ, Purdue MP, **Johnson CC**, Wang L, Katki HA, Barry KH, and Berndt SI. Aspirin, ibuprofen, and reduced risk of advanced colorectal adenoma incidence and recurrence and colorectal cancer in the PLCO Cancer Screening Trial. *Cancer* 2021; Epub ahead of print. PMID: 33974712. Full Text

Division of Gastroenterology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania.
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Program in Oncology, University of Maryland Marlene and Stewart Greenbaum Comprehensive Cancer Center, Baltimore, Maryland.

BACKGROUND: Studying the differential impact of aspirin and other nonsteroidal anti-inflammatory drugs across the stages of colorectal neoplasia from early adenoma to cancer is critical for understanding the benefits of these widely used drugs. METHODS: With 13 years of follow-up, the authors prospectively evaluated the association between aspirin and ibuprofen use and incident distal adenoma (1221 cases), recurrent adenoma (862 cases), and incident colorectal cancer (CRC; 2826 cases) among men and women in the population-based Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. With multivariable-adjusted models, odds ratio (ORs) and 95% confidence intervals (CIs) for adenoma incidence and recurrence and hazard ratios (HRs) and 95% CIs for incident CRC were determined. RESULTS: The authors observed a significantly reduced risk of incident adenoma with ibuprofen use (≥30 vs <4 pills per month: OR, 0.76 [95% CI, 0.60-0.95]; P(trend) = .04), particularly advanced adenoma (OR, 0.48 [95% CI, 0.28-0.83]; P(trend) = .005). Among those with a previous adenoma detected through screening, aspirin use was associated with a decreased risk of advanced recurrent adenoma (≥30 vs <4 pills per month: OR, 0.56 [95% CI, 0.36-0.87]; P(trend) = 0.006). Both aspirin (HR, 0.88 [95% CI, 0.81-0.96]; P(trend) <.0001) and ibuprofen use (HR, 0.81 [95% CI, 0.70-0.93); P(trend) = 0.003) ≥30 versus <4 pills per month were significantly associated with reduced CRC risk. CONCLUSIONS: In this large prospective study with long-term follow-up, a beneficial role for not only aspirin, but also ibuprofen, in preventing advanced adenoma and curbing progression to recurrence and cancer among older adults was observed.

Public Health Sciences

Gui H, **She R**, **Luzum J**, **Li J**, **Bryson TD**, Pinto Y, **Sabbah HN**, **Williams LK**, and **Lanfear DE**. Plasma Proteomic Profile Predicts Survival in Heart Failure with Reduced Ejection Fraction. *Circ Genom Precis Med* 2021; Epub ahead of print. PMID: 33999650. Full Text

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Background - It remains unclear whether the plasma proteome adds value to established predictors in heart failure (HF) with reduced ejection fraction (HFrEF). We sought to derive and validate a plasma proteomic risk score for survival in HFrEF patients (HFrEF-PRS). Methods - Patients meeting Framingham criteria for HF with EF<50% were enrolled (n=1017) and plasma underwent SOMAscan® profiling (4453 targets). Patients were randomly divided 2:1 into derivation and validation cohorts. The HFrEF-PRS was derived using Cox regression of all-cause mortality adjusted for clinical score and N-Terminal pro-B-Type Natriuretic Peptide (NTproBNP), then was tested in the validation cohort. Risk stratification improvement was evaluated by C-statistic, integrated discrimination index (IDI), continuous net reclassification index (NRI), and median improvement in risk score (MIRS) for 1-year and 3-year mortality. Results - Participants' mean age was 68 years, 48% identified as African American, 35% were female and 296 deaths occurred. In derivation (n=681), 128 proteins associated with mortality, 8 comprising the optimized HFrEF-PRS. In validation (n=336) the HFrEF-PRS associated with mortality (hazard ratio (HR) =2.27 [95% Confidence interval (95%CI) 1.84-2.82], p=6.3x10(-14)), Kaplan-Meier curves differed significantly between HFrEF-PRS quartiles (p=2.2x10(-6)), and it remained significant after adjustment for clinical score and NTproBNP (HR=1.37, 95%CI 1.05-1.79, p=0.021). The HFrEF-PRS improved metrics of risk stratification (C-statistic change=0.009, p=0.612; IDI=0.041, p=0.010; NRI=0.391, p=0.078; MIRS=0.039, p=0.016) and associated with cardiovascular death and HF phenotypes (e.g. 6-minute walk distance, EF change). Most HFrEF-PRS proteins had little known connection to HFrEF. Conclusions - A plasma multi-protein score improved risk stratification in HFrEF patients and identified novel candidates.

Public Health Sciences

Havstad SL, **Sitarik A**, **Kim H**, **Zoratti EM**, Ownby D, **Johnson CC**, and **Wegienka G**. Increased Risk of Asthma at Age 10 Years for Multiple-allergen Sensitized Children. *Ann Allergy Asthma Immunol* 2021; Epub ahead of print. PMID: 33971358. Full Text

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BACKGROUND: Childhood sensitization patterns have been previously found to be related to variable risk of early life allergic disease in several birth cohorts. OBJECTIVE: To determine whether these risks persist into later childhood. METHODS: In the WHEALS birth cohort, previous latent class analysis based on sensitization to ten allergens, found four early life sensitization patterns (ELSP): "Highly sensitized", "Milk/egg dominated", "Peanut and inhalant(s)", and "Low to no sensitization" at age two years. At an age 10 study-specific visit, children were evaluated by an allergist for current asthma and atopic dermatitis (AD) through a physical exam and interviews with the child and parent/guardian. Total and specific immunoglobulin E (IgE), spirometry, and methacholine challenge were also completed. RESULTS: Compared with children sensitized to none or one allergen, children sensitized to four or more food and inhalant allergens at age two had the highest risk of current asthma (risk ratio [RR]=4.42; 95% CI 2.58-7.59; p<0.001) and bronchial hyperresponsiveness [BHR] (RR=1.77; 95% CI 1.29-2.42; p<0.001). Additionally, they had the highest levels of total IgE (geometric mean [GM]=800 IU/mL, 95% CI 416-1536) among the four groups. Risk of current atopic dermatitis did not depend on pattern of sensitization but remained increased for children with any sensitization (RR=2.23; 95% CI 1.40-3.55; p<0.001). No differences in spirometry (FEV1, FEF2575, and FEV1/FVC) were identified. CONCLUSION: The previously reported importance of a specific pattern of sensitization in early life.

Public Health Sciences

Heidemann DL, Adhami A, **Nair A**, **Haftka-George A**, **Zaidan M**, **Seshadri V**, **Tang A**, and **Willens DE**. Using a Frontline Staff Intervention to Improve Cervical Cancer Screening in a Large Academic Internal Medicine Clinic. *J Gen Intern Med* 2021; Epub ahead of print. PMID: 33987788. Full Text

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BACKGROUND: Cervical cancer is the third most common malignancy affecting women. Screening with Papanicolaou (Pap) tests effectively identifies precancerous lesions and early-stage cervical cancer. While the nationwide rate of cervical cancer screening (CCS) is 84%, our urban general internal medicine (GIM) clinic population had a CCS rate of 70% in 2016. OBJECTIVE: To improve our clinic's CCS rate to match or exceed the national average within 18 months by identifying barriers and testing solutions. DESIGN: A quality improvement project led by a multidisciplinary group of healthcare providers. PARTICIPANTS: Our GIM clinic includes 16 attending physicians, 116 resident physicians, and 20 medical assistants (MAs) with an insured and underserved patient population. INTERVENTION: Phase 1 lasted 9 months and implemented CCS patient outreach, patient financial incentives, and clinic staff education. Phase 2 lasted 9 months and involved a workflow change in which MAs identified candidates for CCS during patient check-in. Feedback spanned the entire study period. MAIN MEASURES: Our primary outcome was the number of Pap tests completed per month during the 2 study phases. Our secondary outcome was the clinic population's CCS rate for all eligible clinic patients. KEY RESULTS: After interventions, the average number of monthly Pap tests increased from 35 to 56 in phase 1 and to 75 in phase 2. Of 385 patients contacted in phase 1, 283 scheduled a Pap test and 115 (41%) completed it. Compared to baseline, both interventions improved cervical cancer screening (phase 1 relative risk, 1.86; 95% CI, 1.64-2.10; P < 0.001; phase 2 relative risk, 2.70; 95% CI, 2.40-3.02; P < 0.001). Our clinic's CCS rate improved from 70% to 75% after the 18-month intervention. CONCLUSIONS: The rate of CCS increased by 5% after a systematic 2-phase organizational intervention that empowered MAs to remind, identify, and prepare candidates during check-in for CCS.

Public Health Sciences

Johnson CC, Chandran A, **Havstad S**, Li X, McEvoy CT, **Ownby DR**, Litonjua AA, Karagas MR, Camargo CA, Jr., Gern JE, Gilliland F, and Togias A. US Childhood Asthma Incidence Rate Patterns From the ECHO Consortium to Identify High-Risk Groups for Primary Prevention. *JAMA Pediatr* 2021; e210667. Epub ahead of print. PMID: 33999100. Full Text

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IMPORTANCE: Asthma is the leading chronic illness in US children, but most descriptive epidemiological data are focused on prevalence. OBJECTIVE: To evaluate childhood asthma incidence rates across the nation by core demographic strata and parental history of asthma. DESIGN, SETTING, AND PARTICIPANTS: For this cohort study, a distributed meta-analysis was conducted within the Environmental Influences on Child Health Outcomes (ECHO) consortium for data collected from May 1, 1980, through March 31, 2018. Birth cohort data of children from 34 gestational weeks of age or older to 18 years of age from 31 cohorts in the ECHO consortium were included. Data were analyzed from June 14, 2018, to February 18, 2020. EXPOSURES: Caregiver report of physician-diagnosed asthma with age of diagnosis. MAIN OUTCOME AND MEASURES: Asthma incidence survival tables generated by each cohort were combined for each year of age using the Kaplan-Meier method. Age-specific incidence rates for each stratum and asthma incidence rate ratios by parental family history (FH), sex, and race/ethnicity

were calculated. RESULTS: Of the 11 404 children (mean [SD] age, 10.0 [0.7] years; 5836 boys [51%]; 5909 White children [53%]) included in the primary analysis, 7326 children (64%) had no FH of asthma, 4078 (36%) had an FH of asthma, and 2494 (23%) were non-Hispanic Black children. Children with an FH had a nearly 2-fold higher incidence rate through the fourth year of life (incidence rate ratio [IRR], 1.94; 95% CI, 1.76-2.16) after which the rates converged with the non-FH group. Regardless of FH, asthma incidence rates among non-Hispanic Black children were markedly higher than those of non-Hispanic White children during the preschool years (IRR, 1.58; 95% CI, 1.31-1.86) with no FH at age 4 years and became lower than that of White children after age 9 to 10 years (IRR, 0.67; 95% CI, 0.50-0.89) with no FH. The rates for boys declined with age, whereas rates among girls were relatively steady across all ages, particularly among those without an FH of asthma. CONCLUSIONS AND RELEVANCE: Analysis of these diverse birth cohorts suggests that asthma FH, as well as race/ethnicity and sex, were all associated with childhood asthma incidence rates. Black children had much higher incidences rates but only during the preschool years, irrespective of FH. To prevent asthma among children with an FH of asthma or among Black infants, results suggest that interventions should be developed to target early life.

Public Health Sciences

Macki M, **Hamilton T**, **Lim S**, **Telemi E**, **Bazydlo M**, **Nerenz DR**, **Zakaria HM**, **Schultz L**, Khalil JG, Perez-Cruet MJ, Aleem IS, Park P, **Schwalb JM**, **Abdulhak MM**, and **Chang V**. Disparities in outcomes after spine surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2021;1-9. Epub ahead of print. PMID: 33962387. Full Text

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OBJECTIVE: Most studies on racial disparities in spine surgery lack data granularity to control for both comorbidities and self-assessment metrics. Analyses from large, multicenter surgical registries can provide an enhanced platform for understanding different factors that influence outcome. In this study, the authors aimed to determine the effects of race on outcomes after lumbar surgery, using patient-reported outcomes (PROs) in 3 areas: the North American Spine Society patient satisfaction index, the minimal clinically important difference (MCID) on the Oswestry Disability Index (ODI) for low-back pain, and return to work. METHODS: The Michigan Spine Surgery Improvement Collaborative was queried for all elective lumbar operations. Patient race/ethnicity was categorized as Caucasian, African American, and "other." Measures of association between race and PROs were calculated with generalized estimating equations (GEEs) to report adjusted risk ratios. RESULTS: The African American cohort consisted of a greater proportion of women with the highest comorbidity burden. Among the 7980 and 4222 patients followed up at 1 and 2 years postoperatively, respectively, African American patients experienced the lowest rates of satisfaction, MCID on ODI, and return to work. Following a GEE, African American race decreased the probability of satisfaction at both 1 and 2 years postoperatively. Race did not affect return to work or achieving MCID on the ODI. The variable of greatest association with all 3 PROs at both follow-up times was postoperative depression. CONCLUSIONS: While a complex myriad of socioeconomic factors interplay between race and surgical success, the authors identified modifiable risk factors, specifically depression, that may improve PROs among African American patients after elective lumbar spine surgery.

Public Health Sciences

Mianecki TB, and **Peterson EL**. The Relationship Between Central Line-Associated Bloodstream Infections and Extended Intravenous Solution Hang Times. *J Infus Nurs* 2021; 44(3):157-161. PMID: 33935250. Full Text

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Central line-associated bloodstream infections (CLABSIs) can result in increased morbidity and mortality and billions of dollars of costs per year to institutions and patients. Fluctuating availability of manufacturers' supplies of intravenous (IV) solutions have created issues for health systems in which policy and procedures have been examined regarding extended hang time for IV solutions. This article examined the relationship between extended hang times of nonadditive IV solutions and incidence of CLABSIs in intensive and general practice inpatient units in a quaternary care setting. The incidence of CLABSIs with extended hang times of up to 96 hours, of nonadditive IV solutions, has demonstrated that significant changes in CLABSIs were not evident.

Public Health Sciences
Romano ME, Buckley JP, Elliott AJ, **Johnson CC**, and Paneth N. SPR Perspectives: scientific opportunities in the Environmental influences on Child Health Outcomes Program. *Pediatr Res* 2021;1-7. Epub ahead of print. PMID: 34035428. Full Text

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Drawing upon extant data from existing pediatric cohorts and new follow-up of a diverse set of pediatric cohorts from across the United States, the Environmental influences on Child Health Outcomes (ECHO) Program creates the opportunity for novel and innovative investigations of many previously inaccessible scientific questions in the area of child health. We describe how the large sample size, diversity of participants, emphasis on team science, and infrastructure for improving research methodology make the ECHO Program a major research resource for improving our understanding of early life determinants of childhood health and well-being. Pediatric researchers leverage the unique features of the ECHO Program to address research questions with the potential to yield far-reaching and long-term impacts on child health. IMPACT: The ECHO Program unites pediatric cohorts from across the United States, allowing for investigations of compelling research questions that were previously infeasible due to limited sample sizes or lack of participant diversity. The focus of the ECHO Program on team science, solution-oriented research, and methodological innovation propels novel scientific investigations that are responsive to the needs of a wide range of stakeholders. Features of the ECHO program's infrastructure poise its investigators to rapidly launch research endeavors that are responsive to time-sensitive and critical needs within the realm of pediatric research.

Public Health Sciences
Straughen JK, **Sitarik AR**, **Johnson CC**, **Wegienka G**, **Ownby DR**, **Johnson-Hooper TM**, **Allo G**, **Levin AM**, and **Cassidy-Bushrow AE**. Prenatal IgE as a Risk Factor for the Development of Childhood Neurodevelopmental Disorders. *Front Pediatr* 2021; 9:601092. PMID: 34055677. Full Text

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Background: Few studies have examined if maternal allergic disease is associated with an offspring's neurodevelopment. We hypothesized that Th-2 biased maternal immune function assessed as total serum immunoglobulin (Ig) E is associated with attention deficit hyperactivity disorder (ADHD). Methods: Data are from the Wayne County Health, Environment, Allergy, and Asthma Longitudinal Study (WHEALS), a racially and socioeconomically diverse birth cohort in metropolitan Detroit, Michigan. Maternal total IgE was measured prenatally and at 1-month postpartum. Child total IgE was assessed at birth, 6 months, and 2 years of age. ADHD diagnosis was based on the parental report at the 10-12-year study visits or medical chart abstraction. Total IgE was log(2) transformed. Poisson regression models with robust error variance were used to calculate the risk ratios (RR). Inverse probability weighting was used to correct for potential bias due to a loss to follow-up and non-response. Results: Of the 636 maternal-child pairs in the analysis, 513 children were neurotypical and 123 had ADHD. Maternal prenatal total IgE was significantly associated with ADHD even after adjustment for potential confounders (RR = 1.08, 95% CI 1.03-1.13). Maternal and child IgE measures were positively and significantly correlated, but child total IgE was not associated with ADHD at any time point. Conclusions: Maternal prenatal IgE may influence neurodevelopment, but additional studies are needed to confirm and expand these findings.

Pulmonary and Critical Care Medicine

Chaudhuri R, Rubin A, Sumino K, Lapa ESJR, Niven R, Siddiqui S, Klooster K, McEvoy C, Shah PL, **Simoff M**, Khatri S, Barbers R, Mark Grubb G, McMullen EA, Olson JL, and Laviolette M. Safety and effectiveness of bronchial thermoplasty after 10 years in patients with persistent asthma (BT10+): a follow-up of three randomised controlled trials. *Lancet Respir Med* 2021; 9(5):457-466. PMID: 33524320. Full Text

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Boston Scientific Corporation, Marlborough, MA, USA.
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BACKGROUND: Bronchial thermoplasty is an endoscopic treatment for uncontrolled asthma. Previous randomised clinical trials have shown that bronchial thermoplasty reduces severe exacerbations in people

with asthma. However, the long-term efficacy and safety of bronchial thermoplasty beyond 5 years is unknown. The BT10+ study aimed to investigate the efficacy and safety of bronchial thermoplasty after 10 or more years of follow-up. METHODS: BT10+ was an international, multicentre, follow-up study of participants who were previously enrolled in the AIR, RISA, and AIR2 trials and who had 10 or more years of follow-up since bronchial thermoplasty treatment. Data on patient demographics, quality of life, lung function, CT scans (AIR2 participants only), severe exacerbations, and health-care use during the previous year were collected at the BT10+ 10-year outcomes study visit. The primary effectiveness endpoint was durability of the thermoplasty treatment effect, determined by comparing the proportion of participants who had severe exacerbations during the first and fifth years after bronchial thermoplasty treatment with the proportion of participants who had severe exacerbations during the 12-month period before the BT10+ visit. The primary safety endpoint was the absence of clinically significant post-treatment respiratory image changes after bronchial thermoplasty, defined as bronchiectasis or bronchial stenosis as confirmed by pulmonary volumetric high-resolution CT scan at the BT10+ visit (AIR2 participants only). All analyses were done on an intention-to-treat basis. The trial is registered with ClinicalTrials.gov, NCT03243292. The last patient was enrolled on Dec 11, 2018. The last patient completed follow-up on Jan 10, 2019. FINDINGS: The BT10+ study enrolled 192 (45%) of the 429 participants who were enrolled in the AIR, RISA, and AIR2 trials. The BT10+ participants comprised 136 who received bronchial thermoplasty (52% of the 260 participants who received bronchial thermoplasty in the original trials), and 56 sham or control participants (33% of 169 from the original trials). 18 (32%) sham or control participants received bronchial thermoplasty after the previous trials concluded. The participants included in BT10+ were followed for 10·8-15·6 years (median 12·1 years) post-treatment. Baseline characteristics were similar between participants enrolled in BT10+ and those not enrolled. Participants treated with bronchial thermoplasty had similar proportions of severe exacerbations at the BT10+ visit (34 [25%] of 136 participants) compared with 1 year (33 [24%] of 135 participants; difference 0·6%, 95% CI -9·7 to 10·8) and 5 years (28 [22%] of 130 participants; difference 3·5%, -6·7% to 13·6) after treatment. Quality of life measurements and spirometry were similar between year 1, year 5, and the BT10+ visit. At the BT10+ study visit, pulmonary high-resolution CT scans from AIR2 participants treated with bronchial thermoplasty showed that 13 (13%) of 97 participants had bronchiectasis. When compared with baseline high-resolution CT scans, six (7%) of 89 participants treated with bronchial thermoplasty who did not have bronchiectasis at baseline had developed bronchiectasis after treatment (5 classified as mild, 1 classified as moderate). Participants treated with bronchial thermoplasty after the original study and participants in the sham or control group also had reductions in severe exacerbations at the BT10+ visit compared with baseline. INTERPRETATION: Our findings suggest that efficacy of bronchial thermoplasty is sustained for 10 years or more, with an acceptable safety profile. Therefore, bronchial thermoplasty is a long-acting therapeutic option for patients with asthma that remains uncontrolled despite optimised medical treatment. FUNDING: Boston Scientific.

Pulmonary and Critical Care Medicine

Hariri LP, Roden AC, Chung JH, Danoff SK, Gomez Manjarres DC, Hartwig M, Kheir F, King C, Kreider M, Lynch DA, Mooney J, Muniappan A, Myers JL, Paoletti L, Raj R, Safdar Z, Suliman S, **Thavarajah K**, Lederer DJ, Rudell FL, Bianchi P, Shea BS, and Ley B. The Role of Surgical Lung Biopsy in the Diagnosis of Fibrotic Interstitial Lung Disease: Perspective from the Pulmonary Fibrosis Foundation. *Ann Am Thorac Soc* 2021; Epub ahead of print. PMID: 34004127. Full Text

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Diagnosis of interstitial lung disease (ILD) requires a multidisciplinary diagnosis (MDD) approach that includes clinicians, radiologists, and pathologists. Surgical lung biopsy (SLB) is currently the recommended standard in obtaining pathological specimens for patients with ILD requiring a tissue diagnosis. The increased diagnostic confidence and accuracy provided by microscopic pathology assessment of SLB specimens must be balanced with the associated risks in ILD patients. This document was developed by the Surgical Lung Biopsy Working Group of the Pulmonary Fibrosis Foundation, composed of a multidisciplinary group of ILD physicians including pulmonologists, radiologists, pathologists, and thoracic surgeons. In this document, we present an up-to-date literature review of the indications, contraindications, risks, and alternatives to SLB in the diagnosis of fibrotic ILD, outline an integrated approach to the decision-making around SLB in the diagnosis of fibrotic ILD, and provide practical information to maximize the yield and safety of SLB.

Pulmonary and Critical Care Medicine

Jayaprakash N, **Pflaum-Carlson J**, **Gardner-Gray J**, **Hurst G**, **Kinni H**, Coba V, and **Deledda J**. This Health Care Problem Needs a Collaborative Closing of the Gap. *Ann Emerg Med* 2021; 77(5):553-555. PMID: 33902834. Full Text

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Pulmonary and Critical Care Medicine

Maksimowicz-McKinnon K, **Zhou J**, **Hudy J**, **Hegab S**, and **McKinnon JE**. Subclinical CMV viremia is associated with increased nosocomial infections and prolonged hospitalization in patients with systemic autoimmune diseases. *J Clin Virol* 2021; 140:104849. PMID: 34023574. Full Text

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OBJECTIVE: Subclinical cytomegalovirus (CMV) viremia has been associated with other infections, prolonged hospitalization, and mortality in select immunosuppressed populations. We examined the incidence and outcomes of subclinical CMV viremia in hospitalized patients with systemic autoimmune diseases (AD) [systemic lupus erythematosus (SLE) or anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV)] using a highly sensitive CMV assay. METHODS: Prospectively collected samples were obtained from AD hospitalized patients at study entry with a second sample collected 1 week later or at hospital discharge. Controls included age- and gender- matched inpatients without AD and outpatients with AD. All samples were tested in batch using the Abbott RealTime CMV for investigational use assay (RT assay), with a LLOD (LLOQ) at 21 IU/mL (32 IU/mL). RESULTS: Twenty-three inpatients (10 SLE, 8 AAV, 5 controls), and 31 outpatient controls were recruited. Subclinical CMV viremia was found in 61% (11/18) of inpatient AD subjects, 3% (1/31) of outpatient AD subjects, and in none of the five inpatient controls ($p < 0.001$). CMV viremia was associated with increased median length of ICU stay (13 vs. 4 days, $p = 0.033$), hospital stay (17 vs. 9 days, $p = 0.014$) and increased nosocomial infections (7 vs. 1, $p = 0.007$). CMV viremia was not associated with overall severity of illness nor with disease-specific activity or damage. CONCLUSION: Over one-half of hospitalized AD patients in our cohort had detectable CMV viremia, which was associated with increased length of hospital stay and nosocomial infections. These data suggest that further study of the immunomodulatory effects of subclinical CMV viremia in AD is warranted.

Radiation Oncology

Fucinari J, **Elshaikh MA**, Ruterbusch JJ, **Khalil R**, Dyson G, **Shultz D**, Ali-Fehmi R, and Cote ML. The impact of race, comorbid conditions and obesity on survival endpoints in women with high grade endometrial carcinoma. *Gynecol Oncol* 2021; Epub ahead of print. PMID: 33985795. Full Text

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OBJECTIVE: To estimate overall survival, disease-specific survival, and progression-free survival among high grade endometrial carcinoma cases and to determine factors impacting survival for non-Hispanic white and non-Hispanic black women. METHODS: We identified high grade endometrial carcinoma cases among non-Hispanic white and non-Hispanic black women from ongoing institutional studies, and determined eligibility through medical record and pathologic review. We estimated effects of demographic and clinical variables on survival outcomes using Kaplan Meier methods and Cox proportional hazards modelling. RESULTS: Non-Hispanic Black women with BMI <25.0 had poorest overall survival compared to non-Hispanic white women with BMI <25.0 (HR 3.03; 95% CI [1.35, 6.81]), followed by non-Hispanic

black women with BMI 25.0+ (HR 2.43; 95% CI [1.28, 4.60]). A similar pattern emerged for disease-specific survival. Non-Hispanic black women also had poorer progression-free survival than non-Hispanic white women (HR 1.40; 95% CI [1.01, 1.93]). Other significant factors impacting survival outcomes included receipt of National Cancer Center Network (NCCN) guideline-concordant treatment (GCT), earlier stage at diagnosis, and fewer comorbid conditions. CONCLUSIONS: BMI and race interact and modify the association with high grade endometrial carcinoma survival. Other potentially modifiable factors, such as reducing comorbidities and increasing access to GCT will potentially improve survival after diagnosis of high grade endometrial carcinomas. A better understanding of the molecular drivers of these high grade carcinomas may lead to targeted therapies that reduce morbidity and mortality associated with these aggressive tumors.

Radiation Oncology

Hall WA, Small C, Paulson E, Koay EJ, Crane C, Intven M, Daamen LA, Meijer GJ, Heerkens HD, Bassetti M, Rosenberg SA, Aitken K, Myrehaug S, Dawson LA, Lee P, Gani C, Chuong MD, **Parikh PJ**, and Erickson BA. Magnetic Resonance Guided Radiation Therapy for Pancreatic Adenocarcinoma, Advantages, Challenges, Current Approaches, and Future Directions. *Front Oncol* 2021; 11:628155. PMID: 34046339. Full Text

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INTRODUCTION: Pancreatic adenocarcinoma (PAC) has some of the worst treatment outcomes for any solid tumor. PAC creates substantial difficulty for effective treatment with traditional RT delivery strategies primarily secondary to its location and limited visualization using CT. Several of these challenges are uniquely addressed with MR-guided RT. We sought to summarize and place into context the currently available literature on MR-guided RT specifically for PAC. METHODS: A literature search was conducted to identify manuscript publications since September 2014 that specifically used MR-guided RT for the treatment of PAC. Clinical outcomes of these series are summarized, discussed, and placed into the context of the existing pancreatic literature. Multiple international experts were involved to optimally contextualize these publications. RESULTS: Over 300 manuscripts were reviewed. A total of 6 clinical outcomes publications were identified that have treated patients with PAC using MR guidance. Successes, challenges, and future directions for this technology are evident in these publications. MR-guided RT holds theoretical promise for the treatment of patients with PAC. As with any new technology, immediate or dramatic clinical improvements associated with its use will take time and experience. There remain no prospective trials, currently publications are limited to small retrospective experiences. The current level of evidence for MR guidance in PAC is low and requires significant expansion. Future directions and ongoing studies that are currently open and accruing are identified and reviewed. CONCLUSIONS: The potential promise of MR-guided RT for PAC is highlighted, the challenges associated with this novel therapeutic intervention are also reviewed. Outcomes are very early, and will require continued and long term follow up. MR-guided RT should not be viewed in the same fashion as a novel chemotherapeutic agent for which dosing, administration, and toxicity has been established in earlier phase studies. Instead, it should be viewed as a novel procedural intervention which must be robustly tested, refined and practiced before definitive conclusions on the potential benefits or detriments

can be determined. The future of MR-guided RT for PAC is highly promising and the potential implications on PAC are substantial.

Radiation Oncology

Jaworski EM, Yin H, Griffith KA, Pandya R, Mancini BR, Jolly S, Boike TP, Moran JM, Dominello MM, Wilson M, **Parker J**, Burmeister J, **Fraser C**, Miller L, Baldwin K, Mietzel MA, Grubb M, Kendrick D, Spratt DE, and Hayman JA. Contemporary practice patterns for palliative radiotherapy of bone metastases: Impact of a quality improvement project on extended fractionation. *Pract Radiat Oncol* 2021; Epub ahead of print. PMID: 34048938. Request Article

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PURPOSE/OBJECTIVES: Radiotherapy (RT) effectively palliates bone metastases, though variability exists in practice patterns. National recommendations advocate against using extended fractionation (EF) with courses greater than ten fractions. We previously reported EF utilization of 14.8%. We analyzed practice patterns within a statewide quality consortium to assess EF use in a larger patient population following implementation of a quality measure focused on reducing EF. MATERIALS/METHODS: Patients treated for bone metastases within a statewide radiation oncology quality consortium were prospectively enrolled from March 2018 through October 2020. The EF quality metric was implemented March 1, 2018. Data on patient, physician and facility characteristics, fractionation schedules, and treatment planning and delivery techniques were collected. Multivariable binary logistic regression was used to assess EF. RESULTS: 1,445 consecutive patients treated with 1,934 plans were enrolled by 28 facilities. The median number of treatment plans per facility was 52 (range, 7-307). 60 different fractionation schedules were utilized. EF was delivered in 3.4% of plans. Initially, EF use was lower than expected and remained low over time. Significant predictors for EF use included complicated metastasis (OR 2.04, 95% CI: 1.04-4.02, p=0.04), lack of associated CNS or visceral disease (OR 2.27, 95% CI: 1.2-4.2, p=0.01), non-teaching versus teaching facilities (OR 8.97, 95% CI: 2.1-38.5, p<0.01), and treating physicians with more years in practice (OR 12.82, 95% CI: 3.9-42.4, p<0.01). CONCLUSIONS: Within a large, prospective population-based dataset, fractionation schedules for palliative RT of bone metastases remain highly variable. Resource-intensive treatments including EF persist, though EF use was low following implementation of a quality measure. Complicated metastases, lack of CNS or visceral disease, treatment at non-teaching facilities or by physicians with more years in practice significantly predict use of EF. These results support ongoing efforts to more clearly understand and address barriers to high value radiation approaches in the palliative setting.

Research Administration

Kemp SB, Carpenter ES, Steele NG, Donahue KL, Nwosu ZC, Pacheco A, Velez-Delgado A, Menjivar RE, Lima F, The S, Espinoza CE, Brown K, Long D, Lyssiotis CA, Rao A, Zhang Y, Pasca di Magliano M, and **Crawford HC**. Apolipoprotein E promotes immune suppression in pancreatic cancer through NF-kB-mediated production of CXCL1. *Cancer Res* 2021; Epub ahead of print. PMID: 34049975. Full Text

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Pancreatic ductal adenocarcinoma (PDA) is a lethal malignancy with few effective therapeutic options. PDA is characterized by an extensive fibroinflammatory stroma that includes abundant infiltrating immune cells. Tumor-associated macrophages (TAM) are prevalent within the stroma and are key drivers of immunosuppression. TAMs in human and murine PDA are characterized by elevated expression of apolipoprotein E (ApoE), an apolipoprotein that mediates cholesterol metabolism and has known roles in cardiovascular and Alzheimer's disease but no known role in PDA. We report here that ApoE is also elevated in peripheral blood monocytes in PDA patients, and plasma ApoE protein levels stratify patient survival. Orthotopic implantation of mouse PDA cells into syngeneic wild-type or in ApoE-/- mice showed reduced tumor growth in ApoE-/- mice. Histological and mass cytometric (CyTOF) analysis of these tumors showed an increase in CD8+ T cells in tumors in ApoE-/- mice. Mechanistically, ApoE induced pancreatic tumor cell expression of Cxcl1 and Cxcl5, known immunosuppressive factors, through LDL receptor and NF-kB signaling. Taken together, this study reveals a novel immunosuppressive role of ApoE in the PDA microenvironment.

Rheumatology

Maksimowicz-McKinnon K, **Zhou J**, **Hudy J**, **Hegab S**, and **McKinnon JE**. Subclinical CMV viremia is associated with increased nosocomial infections and prolonged hospitalization in patients with systemic autoimmune diseases. *J Clin Virol* 2021; 140:104849. PMID: 34023574. Full Text

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OBJECTIVE: Subclinical cytomegalovirus (CMV) viremia has been associated with other infections, prolonged hospitalization, and mortality in select immunosuppressed populations. We examined the incidence and outcomes of subclinical CMV viremia in hospitalized patients with systemic autoimmune diseases (AD) [systemic lupus erythematosus (SLE) or anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV)] using a highly sensitive CMV assay. METHODS: Prospectively collected samples were obtained from AD hospitalized patients at study entry with a second sample collected 1 week later or at hospital discharge. Controls included age- and gender- matched inpatients without AD and outpatients with AD. All samples were tested in batch using the Abbott RealTime CMV for investigational use assay (RT assay), with a LLOD (LLOQ) at 21 IU/mL (32 IU/mL). RESULTS: Twenty-three inpatients (10 SLE, 8 AAV, 5 controls), and 31 outpatient controls were recruited. Subclinical CMV viremia was found in 61% (11/18) of inpatient AD subjects, 3% (1/31) of outpatient AD subjects, and in none of the five inpatient controls ($p < 0.001$). CMV viremia was associated with increased median length of ICU stay (13 vs. 4 days, $p = 0.033$), hospital stay (17 vs. 9 days, $p = 0.014$) and increased nosocomial infections (7 vs. 1, $p = 0.007$). CMV viremia was not associated with overall severity of illness nor with disease-specific activity or damage. CONCLUSION: Over one-half of hospitalized AD patients in our cohort had detectable CMV viremia, which was associated with increased length of hospital stay and nosocomial infections.

These data suggest that further study of the immunomodulatory effects of subclinical CMV viremia in AD is warranted.

Sleep Medicine
Huang Y, Mayer C, **Cheng P**, Siddula A, Burgess HJ, **Drake C**, Goldstein C, Walch O, and Forger DB. Predicting circadian phase across populations: a comparison of mathematical models and wearable devices. *Sleep* 2021; Epub ahead of print. PMID: 34013347. Full Text

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From smart work scheduling to optimal drug timing, there is enormous potential in translating circadian rhythms research results for precision medicine in the real world. However, the pursuit of such effort requires the ability to accurately estimate circadian phase outside of the laboratory. One approach is to predict circadian phase non-invasively using light and activity measurements and mathematical models of the human circadian clock. Most mathematical models take light as an input and predict the effect of light on the human circadian system. However, consumer-grade wearables that are already owned by millions of individuals record activity instead of light, which prompts an evaluation of the accuracy of predicting circadian phase using motion alone. Here, we evaluate the ability of four different models of the human circadian clock to estimate circadian phase from data acquired by wrist-worn wearable devices. Multiple datasets across populations with varying degrees of circadian disruption were used for generalizability. Though the models we test yield similar predictions, analysis of data from 27 shift workers with high levels of circadian disruption shows that activity, which is recorded in almost every wearable device, is better at predicting circadian phase than measured light levels from wrist-worn devices when processed by mathematical models. In those living under normal living conditions, circadian phase can typically be predicted to within 1 hour, even with data from a widely available commercial device (the Apple Watch). These results show that circadian phase can be predicted using existing data passively collected by millions of individuals with comparable accuracy to much more invasive and expensive methods.

Sleep Medicine
Kalmbach DA, **Ahmedani BK**, Gelaye B, **Cheng P**, and **Drake CL**. Nocturnal cognitive hyperarousal, perinatal-focused rumination, and insomnia are associated with suicidal ideation in perinatal women with mild to moderate depression. *Sleep Med* 2021; 81:439-442. PMID: 33839373. Full Text

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OBJECTIVES: This prospective study explored associations among insomnia, nocturnal cognitive hyperarousal, and nocturnal perinatal-focused rumination with suicidal ideation (SI) in perinatal women with depression. METHODS: From late pregnancy through early postpartum, 39 depressed women completed 17 weekly surveys assessing SI, insomnia, depression, stress, and cognitive arousal. RESULTS: Women with nocturnal cognitive hyperarousal at baseline, relative to those with low cognitive arousal, were at greater risk for new onset SI (33% vs 1%). Moreover, nocturnal perinatal-focused rumination was independently associated with SI. SI-risk was highest when women reported clinical insomnia combined with nocturnal cognitive hyperarousal (OR = 5.66, p = 0.037) or perinatal-focused rumination (OR = 11.63, p = 0.018). Daytime perseverative thinking was not uniquely associated with SI. CONCLUSIONS: Nocturnal cognitive arousal predicts the development of new onset SI, and perinatal-

focused rumination is also uniquely associated with SI-risk in late pregnancy and early parenting. Critically, SI-risk is highest when perinatal women endorsed insomnia and high cognitive arousal at the same time. Future research should determine whether alleviating nocturnal cognitive arousal, pregnancy- and fetal/infant-related concerns, and insomnia with psychotherapy reduces SI for women with perinatal depression.

Sleep Medicine
Kalmbach DA, O'Brien LM, **Pitts DS**, **Sagong C**, **Arnett LK**, **Harb NC**, **Cheng P**, and **Drake CL**. Mother-to-Infant Bonding is Associated with Maternal Insomnia, Snoring, Cognitive Arousal, and Infant Sleep Problems and Colic. *Behav Sleep Med* 2021;1-17. Epub ahead of print. PMID: 34047659. Request Article

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Objective: Emerging evidence links maternal and infant sleep problems to impairments in the mother-to-infant bond, but the independence and directionality of these associations remain unclear. The present study characterized concurrent and prospective effects of maternal sleep disturbances and poor infant sleep on the mother-infant relationship. As common sequalae of problematic sleep, nocturnal cognitive hyperarousal and daytime sleepiness were investigated as facilitating mechanisms.Participants: Sixty-seven pregnant women enrolled in a prospective study on maternal sleep.Methods: Sociodemographic information and clinical symptoms were measured prenatally then weekly across the first two postpartum months. Women reported insomnia symptoms, sleep duration, snoring, daytime sleepiness, nocturnal cognitive arousal (broadly focused and perinatal-specific), perseverative thinking, depression, infant colic, infant sleep quality, and mother-infant relationship quality. Mixed effects models were conducted to test hypotheses.Results: Prenatal snoring and weak maternal-fetal attachment augured poorer postpartum bonding. Poor infant sleep was associated with increased odds for maternal insomnia and short sleep. Impairments in the mother-to-infant bond were linked to maternal insomnia, nocturnal perinatal-focused rumination, daytime sleepiness, depression, and poor infant sleep. Postnatal insomnia predicted future decreases in mother-infant relationship quality, and nocturnal cognitive hyperarousal partially mediated this association.Conclusions: Both maternal and infant sleep problems were associated with poorer mother-to-infant bonding, independent of the effects of maternal depression and infant colic. Perseverative thinking at night, particularly on infant-related concerns, was linked to impaired bonding, rejection and anger, and infant-focused anxiety. Improving maternal and infant sleep, and reducing maternal cognitive arousal, may improve the maternal-to-infant bond.

Sleep Medicine
Tucker RM, Contreras DA, Carlson BR, Carter A, and **Drake CL**. Sleep Education for Elders Program (SLEEP): Promising Pilot Results of a Virtual, Health Educator-Led, Community-Delivered Sleep Behavior Change Intervention. *Nat Sci Sleep* 2021; 13:625-633. PMID: 34040471. Full Text

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PURPOSE: Sleep problems pose serious public health concerns, and evidence suggests that the problem is worsening. Both sufficient sleep quantity and quality are needed for optimal health, particularly among older adults, but access to sleep care can be difficult. This study examined the efficacy of a six-week sleep behavior change program designed for older adults that was delivered virtually by health educators. PARTICIPANTS AND METHODS: This quasi-experimental pilot study (intervention n = 22;

control n = 31) explored the effects of the Sleep Education for Elders Program (SLEEP) on sleep outcomes, which included: 1) sleep quality, measured by the Pittsburgh Sleep Quality Index (PSQI); 2) sleep duration, extracted from the PSQI; 3) insomnia symptoms, measured by the Insomnia Severity Index; 4) sleep hygiene behaviors, obtained from the Sleep Hygiene Index; and 5) excessive daytime sleepiness, measured by the Epworth Sleepiness Scale. RESULTS: After SLEEP, the intervention group experienced significantly improved sleep quality ($p < 0.001$), a reduction in maladaptive sleep hygiene behaviors ($p = 0.007$), and reduced daytime sleepiness ($p < 0.027$) compared to the control group. Effect sizes for all five sleep measures were medium or large. In the intervention group, all changes were judged to be clinically meaningful (≥ 0.5 SD) except for improvements in daytime sleepiness. CONCLUSION: These data support the efficacy of a group-based, virtual behavior change intervention in improving sleep outcomes among older adults.

Surgery

Basal Y, Oommen J, Faraj U, **Acho R**, and **Aravapally A**. Facklamia hominis in hidradenitis suppurativa. *JAAD Case Reports* 2021; 11:20-22. PMID: 33898677. Full Text

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Surgery

Ivanics T, Shwaartz C, Claasen M, Patel MS, Yoon P, Raschzok N, Wallace D, Muaddi H, Murillo F, Hansen BE, Selzner N, and Sapisochin G. Trends in Indications and Outcomes of Liver Transplantation in Canada: A Multi Centre Retrospective Study. *Transpl Int* 2021; Epub ahead of print. PMID: 33977568. Full Text

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BACKGROUND: The liver transplantation (LT) landscape is continuously evolving. We sought to evaluate trends in indications for LT in Canada and the impact of primary liver disease on post-LT outcomes using a national transplant registry. METHODS: Adult patients who underwent a primary LT between 2000 and 2018 were retrospectively identified in the Canadian Organ Replacement Registry. Outcomes included post-LT patient and graft survival. RESULTS: A total of 5,722 LTs were identified. The number of LT per year increased from 251 in 2000 to 349 in 2018. The proportion of patients transplanted for HCV decreased from 31.5% in 2000 to 3.4% in 2018. In contrast, the percentage of transplants for HCC increased from 2.3% in 2000 to 32.4% in 2018, and those performed for NASH increased from 0.4% in 2005 to 12.6% in 2018. Year of transplant (per 1-year) was protective for both patient (HR:0.96,95%CI:0.94-0.97;p<0.001) and graft survival (HR:0.97,95%CI:0.96-0.99;p=0.001). CONCLUSION: Post-LT outcomes have improved over time in this nation-wide analysis spanning 18 years. Moreover, trends in the indications for LT have changed, with HCC becoming the leading etiology. The decrease in the proportion of HCV patients and increase in those with NASH has implications on the evolving management of LT patients.

Surgery

Jeyarajah DR, **Abouljoud M**, Alseidi A, Berman R, D'Angelica M, Hagopian E, and Pawlik TM. Training Paradigms in Hepato-Pancreatico-Biliary Surgery: an Overview of the Different Fellowship Pathways. *J Gastrointest Surg* 2021; Epub ahead of print. PMID: 33948865. Full Text

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Hepato-pancreatico-biliary (HPB) surgery, and the training of HPB surgeons, has evolved significantly over the last several decades. The current state of training in HPB surgery in North America is defined through three main pathways: the Complex General Surgical Oncology (CGSO) ACGME fellowship, the American Society of Transplant Surgeons (ASTS) fellowship, and the Americas Hepatopancreaticobiliary Association (AHPBA) fellowship. These fellowships offer variable experiences in pancreas, liver, and biliary cases, and each pathway offers a unique perspective on HPB surgery. The CGSO ACGME, ASTS, and AHPBA fellowships represent decades of work by the three major surgical leadership stakeholders to improve and ensure quality training of future HPB surgeons. The best care is provided by the HPB surgeon who has been trained to understand the importance of all available treatment options within the context of a multidisciplinary setting. The three fellowship pathways are outlined in this paper with the nuances and variations characteristic of the different training programs highlighted.

Surgery
Leonard-Murali S, **Lezotte J**, **Kalu R**, **Blyden DJ**, **Patton JH**, **Johnson JL**, and **Gupta AH**. Necrotizing pancreatitis: A review for the acute care surgeon. *Am J Surg* 2021; 221(5):927-934. PMID: 32878690. Full Text

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BACKGROUND: Necrotizing pancreatitis is a common condition with high mortality; the acute care surgeon is frequently consulted for management recommendations. Furthermore, there has been substantial change in the timing, approach, and frequency of surgical intervention for this group of patients. METHODS: In this article we summarize key clinical and research developments regarding necrotizing pancreatitis, including current recommendations for treatment of patients requiring intensive care and those with common complications. Articles from all years were considered to provide proper historical context, and most recent management recommendations are identified. RESULTS: Epidemiology, diagnosis, treatment in the acute phase, and complications (both short-term and long-term) are discussed. Images of surgical interventions are included from our institutional experience. CONCLUSION: Necrotizing pancreatitis management remains heavily based on clinical judgement, although technological advances and clinical trials have made decision making more straightforward.

Surgery
Malinzak L, **McEvoy T**, **Denny J**, **Kim D**, Stracke J, **Jeong W**, and **Yoshida A**. Robot-assisted Transplant Ureteral Repair to treat transplant ureteral strictures in patients after Robot-assisted Kidney Transplant: a case series. *Urology* 2021; Epub ahead of print. PMID: 34058240. Full Text

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OBJECTIVE: To describe the use of robotic-assisted transplant ureteral repair (RATUR) for treating transplant ureteral stricture (TUS) in 3 patients who had undergone robot assisted kidney transplant (RAKT). METHOD: We reviewed the medical records of 3 patients who experienced TUS after RAKT and who underwent RATUR between 2017 and 2020. The patients' RAKT, post-transplant clinical course, endourological interventions, reoperation, and recovery were assessed. RESULTS: All patients diagnosed with TUS presented with deterioration of kidney function after RAKT. Method of diagnosis included ultrasound, antegrade ureterogram, and CT scan. All 3 patients had a short (<1 cm) area of TUS and underwent RATUR. For 2 patients, distal strictures were bypassed with modified Lich-Gregoir ureteroneocystostomy reimplantation. One patient was treated with pyelo-ureterostomy to the contralateral native ureter. No intraoperative complications, conversions to open surgery, or significant operative blood loss requiring blood transfusion for any patient were observed. Also, no patients had urine leaks in the immediate or late postoperative period. After RATUR, 2 patients developed Clavien grade II complications with rectus hematoma or urinary tract infection. CONCLUSION: RATUR is a technically feasible operation for kidney transplant patients with TUS after RAKT. This procedure may provide the same benefits of open operation without promoting certain comorbidities that may occur from open surgical procedures.

Surgery

Marshall-Goebel K, Macias BR, Kramer LA, Hasan KM, Ferguson C, Patel N, Ploutz-Snyder RJ, Lee SMC, Ebert D, Sargsyan A, **Dulchavsky S**, Hargens AR, Stenger MB, and Laurie S. Association of Structural Changes in the Brain and Retina After Long-Duration Spaceflight. *JAMA Ophthalmol* 2021; Epub ahead of print. PMID: 34014272. Full Text

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IMPORTANCE: Long-duration spaceflight induces structural changes in the brain and eye. Identification of an association between cerebral and ocular changes could help determine if there are common or independent causes and inform targeted prevention strategies or treatments. OBJECTIVE: To determine if there is an association between quantitative changes in intracranial compartment volumes and peripapillary total retinal thickness after spaceflight. DESIGN, SETTING, AND PARTICIPANTS: This cohort study included healthy International Space Station crew members before and immediately after long-duration spaceflight. Data on race were not collected. Analysis was conducted from September to November 2020. EXPOSURES: Long-duration spaceflight (mean [SD], 191 [55] days). MAIN OUTCOMES AND MEASURES: Optical coherence tomography-derived peripapillary total retinal thickness as a quantitative assessment and early sign of optic disc edema and magnetic resonance imaging-derived measures of lateral ventricle volume, white matter volume, and whole brain plus cerebrospinal fluid volume. RESULTS: In 19 healthy crew members included in this study (5 women [26.3%], 14 men [73.7%]; mean [SD] age, 45.2 [6.4] years), analyses revealed a positive, although not definitive, association between spaceflight-induced changes in total retinal thickness and lateral ventricle volume (4.7-µm increase in postflight total retinal thickness [95% CI, -1.5 to 10.8 µm; P = .13] per 1-mL postflight increase in lateral ventricle volume). Adjustments for mission duration improved the strength of association (5.1 µm; 95% CI, -0.4 to 10.5 µm; P = .07). No associations were detected between spaceflight-induced changes in total retinal thickness and white matter volume (0.02 µm; 95% CI, -0.5 to 0.5 µm; P = .94) or brain tissue plus cerebrospinal fluid volume, an estimate of intracranial volume (0.02 µm; 95% CI, -0.6 to 0.6 µm; P = .95). CONCLUSIONS AND RELEVANCE:

These results help characterize spaceflight-associated neuro-ocular syndrome and the physiologic associations of headward fluid shifts with outcomes during spaceflight on the central nervous system. The possibly weak association between increased total retinal thickness and lateral ventricle volume suggest that while weightlessness-induced fluid redistribution during spaceflight may be a common stressor to the brain and retina, the development of optic disc edema appears to be uncoupled with changes occurring in the intracranial compartment.

Surgery

Modi K, Segovia M, Mavis A, Schiano T, Patel Y, Boike J, Sudan D, **Nagai S**, and **Jafri SM**. Efficacy and Safety of Mammalian Target of Rapamycin Inhibitors Following Intestinal and Multivisceral Transplantation. *Clin Transplant* 2021;e14324. Epub ahead of print. PMID: 34046945. Full Text

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This is a descriptive study reviewing the outcomes of mammalian target of rapamycin inhibitors (mTORs) in intestinal (IT) and multivisceral transplantation (MVT). This study included 22 patients, 20 adults, and 2 children, and an overall mean age of 46 years old at the time of transplantation. Twelve patients (54.5%) received IT, and the remainder (45.5%) MVT. The mean time between transplantation and mTORs initiation was 24 months. The indication was worsening renal function in 13 patients (59%), with 9/13(69.2%) noted to have an increase in glomerular filtration rate of at least 10 mL/min/1.73m2. The indication for 4 patients (18.2%) was history of neuroendocrine tumor. After mTOR initiation, 50% of patients were reduced or weaned off tacrolimus and 13.7% off prednisone. mTORs were discontinued in 11/22 patients. Six patients (54.5%) stopped due to side effects, two (18.1%) for surgery, and one (9%) for acute cellular rejection. Side effects were edema (33.3%), headaches (33.3%), diarrhea (16.7%), and oral ulcers (16.7%). Average duration of mTORs prior to discontinuation due to side effects was 7 months. mTORs may function in their own niche of patients due to the potential renal safety profile, but use is most limited by tolerance to side effects.

Surgery

Nagai S, **Suzuki Y**, **Kitajima T**, **Ivanics T**, **Shimada S**, **Kuno Y**, **Shamaa MT**, **Yeddula S**, **Samaniego M**, **Collins K**, **Rizzari M**, **Yoshida A**, and **Abouljoud M**. Paradigm change in liver transplant practice after the implementation of the liver-kidney allocation policy. *Liver Transpl* 2021; Epub ahead of print. PMID: 34043869. Full Text

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The OPTN/UNOS policy regarding kidney allocation for liver transplant (LT) patients was implemented in August 2017. This study aimed to evaluate the effects of the simultaneous liver-kidney transplant policy on outcomes in LT alone (LTA) patients with kidney dysfunction. We analyzed adult primary LTA patients with kidney dysfunction at listing (estimated glomerular filtration rate [eGFR] less than 30mL/min or dialysis requirement) between January 2015 and March 2019 using the OPTN/UNOS registry. Waitlist practice and kidney transplant (KT) listing after LTA were compared between pre- and post-policy groups. 3,821 LTA listings with eGFR<30mL/min were included. The daily number of listings on dialysis was significantly higher in Era2 (post-policy group) than Era1 (pre-policy group) (1.21/day vs. 0.95/day, P<0.001). Of these LTA listings, 90-day LT waitlist mortality, LTA probability, and one-year post-LTA survival were similar between eras. LTA recipients in Era2 had a higher probability for KT listing post-LTA than those in Era1 (6.2% vs. 3.9%, odds ratio=3.30, P<0.001), especially those on dialysis (8.4% vs.

2.0%, odds ratio=4.38, P<0.001). Under the safety-net rule, there was a higher KT probability after LTA (26.7% and 53% at 6 months in Eras 1 and 2, respectively, P=0.017). Conclusion: After the implementation of the policy, the number of LTA listings among patients on dialysis significantly increased. While their post-transplant survival was not changed, KT listing after LTA increased. The safety-net rule led to high KT probability and low waitlist mortality rate in patients who were listed for KT after LTA. These results suggest that the policy successfully achieved the goals, which did not compromise LTA waitlist or post-transplant outcomes in patients with kidney dysfunction, and provided KT opportunities if they developed kidney failure after LTA.

Surgery

Nathanson SD, Detmar M, Padera TP, Yates LR, Welch DR, Beadnell TC, Scheid AD, Wrenn ED, and Cheung K. Mechanisms of breast cancer metastasis. *Clin Exp Metastasis* 2021; Epub ahead of print. PMID: 33950409. Full Text

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Invasive breast cancer tends to metastasize to lymph nodes and systemic sites. The management of metastasis has evolved by focusing on controlling the growth of the disease in the breast/chest wall, and at metastatic sites, initially by surgery alone, then by a combination of surgery with radiation, and later by adding systemic treatments in the form of chemotherapy, hormone manipulation, targeted therapy, immunotherapy and other treatments aimed at inhibiting the proliferation of cancer cells. It would be valuable for us to know how breast cancer metastasizes; such knowledge would likely encourage the development of therapies that focus on mechanisms of metastasis and might even allow us to avoid toxic therapies that are currently used for this disease. For example, if we had a drug that targeted a gene that is critical for metastasis, we might even be able to cure a vast majority of patients with breast cancer. By bringing together scientists with expertise in molecular aspects of breast cancer metastasis, and those with expertise in the mechanical aspects of metastasis, this paper probes interesting aspects of the metastasis cascade, further enlightening us in our efforts to improve the outcome from breast cancer treatments.

Surgery

Patel B, Wonski BT, Saliganan DM, **Rteil A**, **Kabbani LS**, and Lam MT. Decellularized dermis extracellular matrix alloderm mechanically strengthens biological engineered tunica adventitia-based blood vessels. *Sci Rep* 2021; 11(1):11384. PMID: 34059745. Full Text

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The ideal engineered vascular graft would utilize human-derived materials to minimize foreign body response and tissue rejection. Current biological engineered blood vessels (BEBVs) inherently lack the structure required for implantation. We hypothesized that an ECM material would provide the structure needed. Skin dermis ECM is commonly used in reconstructive surgeries, is commercially available and

FDA-approved. We evaluated the commercially-available decellularized skin dermis ECM Alloderm for efficacy in providing structure to BEBVs. Alloderm was incorporated into our lab's unique protocol for generating BEBVs, using fibroblasts to establish the adventitia. To assess structure, tissue mechanics were analyzed. Standard BEBVs without Alloderm exhibited a tensile strength of 67.9 ± 9.78 kPa, whereas Alloderm integrated BEBVs showed a significant increase in strength to 1500 ± 334 kPa. In comparison, native vessel strength is 1430 ± 604 kPa. Burst pressure reached 51.3 ± 2.19 mmHg. Total collagen and fiber maturity were significantly increased due to the presence of the Alloderm material. Vessels cultured for 4 weeks maintained mechanical and structural integrity. Low probability of thrombogenicity was confirmed with a negative platelet adhesion test. Vessels were able to be endothelialized. These results demonstrate the success of Alloderm to provide structure to BEBVs in an effective way.

Surgery

Quillin RC, 3rd, Cortez AR, Dageforde LA, Watkins A, **Collins KM**, Garonzik-Wang J, Glorioso JM, Tevar AD, Emond JC, and Segev DL. Transplant Surgery Pipeline: A Report from the American Society of Transplant Surgeons Pipeline Taskforce. *J Am Coll Surg* 2021; Epub ahead of print. PMID: 34015454. Full Text

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BACKGROUND: Transplant surgery fellowship has evolved over the years and today there are 66 accredited training programs in the United States and Canada. There is growing concern, however, regarding the number of U.S-trained general surgery residents pursuing transplant surgery. In this study, we examined the transplant surgery pipeline, comparing it to other surgical subspecialty fellowships, and characterized the resident transplant experience. METHODS: Datasets were compiled and analyzed from surgical fellowship match data obtained from NRMP and ACGME reports and relative fellowship competitiveness was assessed. The surgical resident training experience in transplantation was evaluated. RESULTS: From 2006 to 2018, 1094 applicants have applied for 946 transplant surgery fellowship positions, with 299 (27.3%) being U.S. graduates. Over this period, there was a 0.8% decrease per year in U.S.-trained surgical residents matching into transplant (p=0.042). Moreover, transplant surgery was one of the least competitive fellowships compared to other NRMP surgical subspeciality fellowships, as measured by the number of U.S. applicants per available fellowship position, average number of fellowship programs listed on each applicant's rank list, and proportion of unfilled fellowship positions (each p<0.05). Finally, from 2015 to 2017, there were 57 general surgery residency programs that produced 77 transplant fellows but nearly half of the fellows (n=36, 46.8%) came from 16 (28.1%) programs. CONCLUSIONS: Transplant surgery is one of the least competitive and sought after surgical fellowships for U.S. trained residents. These findings highlight the need for dedicated efforts to increase exposure, mentorship, and interest in transplantation to recruit strong U.S. graduates.

Surgery

Yan Y, John S, Meiliute J, **Kabbani L**, and Mehrmohammadi M. Efficacy of High Temporal Frequency Photoacoustic Guidance of Laser Ablation Procedures. *Ultrason Imaging* 2021; 43(3):149-156. PMID: 33966510. Full Text

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Inaccurate placement of the ablation catheter and the inability to monitor the real-time temperature within the tissue of interest such as veins curbs the treatment efficacy of laser ablation procedures during thermal therapies. Our previous studies have validated the efficacy of photoacoustic (PA) imaging during endovenous laser ablation (EVLA) procedures. However, the PA-guided therapies suffer from low temporal resolution, due to the low pulse repetition rates of pulsed lasers, which could cause a problem during fast catheter motion and rapid temperature changes. Herein, to enhance the accuracy and sensitivity for tracking the ablation catheter tip and temperature monitoring, we proposed to develop a high frame rate (500 Hz), combined ultrasound (US), and PA-guided ablation system. The proposed PA-guided ablation system was evaluated in a set of ex vivo tissue studies. The developed system provides a 2 ms temporal resolution for tracking and monitoring the ablation catheter tip's location and temperature, which is 50 times higher temporal resolution compared to the previously proposed 10 Hz system. The proposed system also provided more accurate feedback about the temperature variations during rapid temperature increments of 10°C per 250 ms. The co-registered US and PA images have an imaging resolution of about 200 µm and a field of view of 45 × 40 mm(2). Tracking the ablation catheter tip in an excised tissue layer shows higher accuracy during a relatively fast catheter motion (0.5-3 mm/s). The fast US/PA-guided ablation system will potentially enhance the outcome of ablation procedures by providing location and temperature feedback.

Urology

Alanee S, Sana S, El-Zawahry A, **Peabody J**, **Pearce T**, **Adams N**, **Deebajah M**, Crabtree J, Delfino K, McVary K, Robinson K, and Rao K. Phase I trial of intravesical Bacillus Calmette-Guérin combined with intravenous pembrolizumab in recurrent or persistent high-grade non-muscle-invasive bladder cancer after previous Bacillus Calmette-Guérin treatment. *World J Urol* 2021; Epub ahead of print. PMID: 33966128. Full Text

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OBJECTIVES: We conducted the first phase I dose-escalation trial (NCT02324582) of intravesical Bacillus Calmette-Guérin (BCG) in combination with systemic pembrolizumab in patients with high-grade non-muscle-invasive bladder cancer (HGNMIBC) who had persistent or recurrent disease after prior intravesical therapy with BCG. The primary endpoint was the safety of this combination. The secondary endpoint was clinical activity at three months following BCG treatment. METHODS: Eighteen patients were consented for the study, five of which were screen failures. Six doses of pembrolizumab were administered every 3 weeks over 16 weeks concurrently with six weekly doses of BCG beginning at week 7. Patient safety was evaluated from the time of consent through 30 days following pembrolizumab treatment. Clinical activity was determined using cystoscopy and biopsy of suspicious lesions. RESULTS: Treatment-related adverse events included one grade 4 adverse event (AEs) (adrenal insufficiency). There were nine grade 3 AEs (chest discomfort, pulmonary embolism, arthritis, wrist edema, injection site reaction, bilateral wrist pain, cardiomyopathy, hypokalemia, urinary tract infection). There were 49 grade 1 and 30 grade 2 AEs (88% of AEs). Eleven patients finished the treatment, and two patients died during the study. Of 13 patients treated, nine patients (69%) had no evidence of disease at 3 months following BCG treatment. CONCLUSIONS: We report for the first time that combining BCG and pembrolizumab in treating HGNMIBC is safe allowing complete treatment of most patients. A phase III trial has opened to test the efficacy of this combination in HGNMIBC (KEYNOTE-676).

Urology

Albawardi A, Livingstone J, Almarzooqi S, **Palanisamy N**, Houlahan KE, Awwad AAA, Abdelsalam RA, Boutros PC, and Bismar TA. Copy number profiles of prostate cancer in men of middle eastern ancestry. *Cancers* 2021; 13(10). PMID: Not assigned. Full Text

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Our knowledge of prostate cancer (PCa) genomics mainly reflects European (EUR) and Asian (ASN) populations. Our understanding of the influence of Middle Eastern (ME) and African (AFR) ancestry on the mutational profiles of prostate cancer is limited. To characterize genomic differences between ME, EUR, ASN, and AFR ancestry, fluorescent in situ hybridization (FISH) studies for NKX3-1 deletion and MYC amplification were carried out on 42 tumors arising in individuals of ME ancestry. These were supplemented by analysis of genome-wide copy number profiles of 401 tumors of all ancestries. FISH results of NKX3-1 and MYC were assessed in the ME cohort and compared to other ancestries. Gene level copy number aberrations (CNAs) for each sample were statistically compared between ancestry groups. NKX3-1 deletions by FISH were observed in 17/42 (17.5%) prostate tumors arising in men of ME ancestry, while MYC amplifications were only observed in 1/42 (2.3%). Using CNAs called from arrays, the incidence of NKX3-1 deletions was significantly lower in ME vs. other ancestries (20% vs. 52%; $p = 2.3 \times 10-3$). Across the genome, tumors arising in men of ME ancestry had fewer CNAs than those in men of other ancestries ($p = 0.014$). Additionally, the somatic amplification of 21 specific genes was more frequent in tumors arising in men of ME vs. EUR ancestry (two-sided proportion test; $Q < 0.05$). Those included amplifications in the glutathione S-transferase family on chromosome 1 (GSTM1, GSTM2, GSTM5) and the IQ motif-containing family on chromosome 3 (IQCF1, IQCF2, IQCF13, IQCF4, IQCF5, IQCF6). Larger studies investigating ME populations are warranted to confirm these observations.

Urology

Alhamar M, Jabbar A, Deebajah M, **Diaz M**, Alanee S, **Hassan O**, Williamson SR, **Schultz D**, and **Gupta N**. Prognostic significance of histomorphologic features of lymph node metastases in prostate cancer patients treated with radical prostatectomy: A single center study. *Urol Oncol* 2021; Epub ahead of print. PMID: 33985876. Full Text

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OBJECTIVE: We assessed the prognostic value of histomorphologic features of lymph node (LN) metastases in patients with prostate cancer treated with radical prostatectomy MATERIALS AND METHODS: We evaluated the effect of the features of LN metastasis on the risk of biochemical recurrence (BCR) in 280 LN-positive patients who underwent radical prostatectomy between 2006 to 2018. LN specific parameters recorded included number of metastatic LNs, size of the largest metastatic focus, Gleason Grade (GG) of the metastatic focus, and extranodal extension (ENE). RESULTS: A solitary positive LN was found in 166/280 (59%), 95/280 (34%) patients had 2-4 positive LNs, and 19/280 (7%) had 5 or more positive LNs. The size of the largest metastatic focus > 2 mm (macrometastasis) in 154/261 (59%). GG of the metastatic focus was as follows: GG 1-2: 29/224 (13%); GG 3: 27/224 (12%); and GG 4-5: 168/224 (75%). ENE was identified in 99/244 (41%). We found the number of LNs positive (2-4 vs. 1 Hazard ratio (HR) = 1.60; 95% CI: 1.02 to 2.5; P = 0.04) and GG of the metastatic focus (GG 4&5 vs. 1-3 HR = 1.90; 95% CI: 1.14-3.2; P= 0.014) to be independent predictors of the risk of BCR after surgery on multivariate analysis. CONCLUSIONS: Our study showed the number of LNs positive and GG of the LN metastatic focus to be significant independent predictors of BCR after radical prostatectomy. We recommend reporting histomorphologic parameters of LN metastasis as they may help in defining BCR risk categorization.

Urology
Fedrigon D, Faris A, **Kachroo N**, Jain R, Elia M, Wilkins L, Li J, De S, Noble M, Monga M, and Sivalingam S. Reply by Authors. *J Urol* 2021; Epub ahead of print. PMID: 33983827. Full Text

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Urology
Malinzak L, **McEvoy T**, **Denny J**, **Kim D**, Stracke J, **Jeong W**, and **Yoshida A**. Robot-assisted Transplant Ureteral Repair to treat transplant ureteral strictures in patients after Robot-assisted Kidney Transplant: a case series. *Urology* 2021; Epub ahead of print. PMID: 34058240. Full Text

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OBJECTIVE: To describe the use of robotic-assisted transplant ureteral repair (RATUR) for treating transplant ureteral stricture (TUS) in 3 patients who had undergone robot assisted kidney transplant (RAKT). METHOD: We reviewed the medical records of 3 patients who experienced TUS after RAKT and who underwent RATUR between 2017 and 2020. The patients' RAKT, post-transplant clinical course, endourological interventions, reoperation, and recovery were assessed. RESULTS: All patients diagnosed with TUS presented with deterioration of kidney function after RAKT. Method of diagnosis included ultrasound, antegrade ureterogram, and CT scan. All 3 patients had a short (<1 cm) area of TUS and underwent RATUR. For 2 patients, distal strictures were bypassed with modified Lich-Gregoir ureteroneocystostomy reimplantation. One patient was treated with pyelo-ureterostomy to the contralateral native ureter. No intraoperative complications, conversions to open surgery, or significant operative blood loss requiring blood transfusion for any patient were observed. Also, no patients had urine leaks in the immediate or late postoperative period. After RATUR, 2 patients developed Clavien grade II complications with rectus hematoma or urinary tract infection. CONCLUSION: RATUR is a technically feasible operation for kidney transplant patients with TUS after RAKT. This procedure may provide the same benefits of open operation without promoting certain comorbidities that may occur from open surgical procedures.

Urology
Sood A, **Wong P**, **Borchert A**, **Budzyn J**, **Keeley J**, **Heilbronn C**, **Eilender B**, **Littleton R**, and **Leavitt DA**. Use of ultra-low dose computed tomography versus abdominal plain film for assessment of stone-free rates after shock-wave lithotripsy: implications on emergency room visits, surgical procedures, and cost-effectiveness. *Urolithiasis* 2021; Epub ahead of print. PMID: 33993338. Full Text

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The aims of this investigation were: (1) to compare residual stone-fragment (RSF) detection rates of ultra-low dose computed tomography (ULD-CT) and abdominal plain film (KUB) in urolithiasis patients undergoing shock-wave lithotripsy (SWL), and (2) to evaluate the downstream sequelae of utilizing these two disparate imaging pathways of differing diagnostic fidelity. A retrospective chart-review of patients undergoing SWL at two high-volume surgical centers was undertaken (2013-2016). RSF diagnostic rates of ULD-CT and KUB were assessed, and the impact of imaging modality used on subsequent emergency room (ER) visits, unplanned procedures, and cost-effectiveness was investigated. Adjusted analyses examined association between imaging modality used and outcomes, and Markov decision-tree analysis was performed to identify a cost advantageous scenario for ULD-CT over KUB. Of 417 patients studied, 57 (13.7%) underwent ULD-CT while the remaining 360 underwent KUB. The RSF rates were 36.8% and 22.8% in the ULD-CT and KUB groups, respectively ($p = 0.019$). A 5.6% and 18% of the patients deemed stone-free on ULD-CT and KUB, respectively, returned to the ER ($p = 0.040$). Similarly, 2.8% and 15.1% needed an unplanned surgery ($p = 0.027$). These findings were confirmed on multivariable analyses, Odds ratios CT-ULD versus KUB: 0.19 and 0.10, respectively, $p < 0.05$. With regards to cost-effectiveness, at low ULD-CT charges, the ULD-CT follow-up pathway was economically more favorable, but with increasing ULD-CT charges, the KUB follow-up pathway superseded. ULD-CT seems to provide a more 'true' estimate of stone-free status, and in consequence mitigates unwanted emergency and operating room visits by reducing untimely stent removals and false patient reassurances. Further, at low ULD-CT costs, it may also be economically more favorable.

Urology

Wertheimer S, **Budzyn J**, **Perkins S**, **Borchert A**, **Rogers C**, and **Patel A**. Patient Tolerability with Office Transperineal Biopsy Using a Reusable Needle Guide. *Urology* 2021; Epub ahead of print. PMID: 34044025. Full Text

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INTRODUCTION: Transrectal ultrasound-guided (TRUS) prostate biopsy is associated with a 1-5% risk of severe sepsis, despite the use of prophylactic antibiotics. Recent studies have demonstrated the feasibility of transperineal (TP) prostate biopsy in the outpatient setting under local anesthetic (LA). We demonstrate the safety, efficacy, and tolerability of our technique for performing TP biopsy under LA in the clinic setting using a reusable needle guide. MATERIALS & METHODS: A biplanar ultrasound probe with an attached adjustable, reusable needle guide was evaluated for transperineal biopsy. A 17 gauge x 10 cm coaxial needle is attached to the needle guide. The skin is infiltrated, bilaterally, approximately 2 cm anterolateral to the anal verge with 1% lidocaine using a 25 gauge needle. A deeper prostatic block is then performed using a 20 gauge spinal needle. Administration of the anesthetic is delivered to the musculature of the pelvic floor, superficial-to-deep. Prostate samples are obtained using an 18 gauge x 25cm biopsy gun. All biopsies on a side can be obtained utilizing a single perineal skin puncture site. Patients who underwent office TP biopsy after May 2019 also completed a 10-item patient experience questionnaire regarding pain or discomfort experienced during the procedure. RESULTS: In 2019, a total of 74 patients underwent office TP prostate biopsy under local anesthesia using a reusable needle guide, while 564 underwent office TRUS biopsy. Prostate biopsy was positive for malignancy in 58.1% of TP patients vs 57.6% in TRUS patients ($p=0.93$). TP biopsy had a lower utilization of prophylactic antibiotics compared to TRUS biopsy: 33.8% vs 99.5% ($p<0.001$), yet there were no admissions, UTI, or sepsis for TP patients, compared to 6 admissions (1.1%) for TRUS biopsy ($p=0.01$)). The mean VAS score ± SD for pain or discomfort caused by the overall office TP biopsy was 3.68 ± 1.96. CONCLUSION: We demonstrate that office TP biopsy under LA with a reusable needle guide can be safely introduced with equivalent cancer detection rates whilst nearly eliminating the risk of urinary sepsis. This was achieved while also significantly reducing the use of prophylactic antibiotics. The procedure was well tolerated, with the most common complaint being local infiltration of anesthetic. We believe that office TP biopsy under LA can be performed with good patient tolerability, as almost 94% of patients were willing to undergo the procedure again. There is also the potential for reduction in overall cost with the use of a reusable needle guide.

Conference Abstracts

Administration

Lanfear DE, **Gui H**, **Hannawi B**, **Connolly T**, **Li J**, **She R**, **Pereira N**, **Adams K**, **Hernandez A**, **Luzum J**, **Francke S**, **Tang WH**, and **Williams LK**. PHARMACOGENOMIC ANALYSES IN ASCEND-HF INDICATE INFLUENCE OF NPR3ON NESIRITIDE BLOOD PRESSURE EFFECT. *Journal of the American College of Cardiology* 2021; 77(18):840.

Background The Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) randomized hospitalized HF patients to nesiritide or placebo and found no survival difference, but some data suggests genetic variation may influence nesiritide effect. We explored if genetic factors are associated with treatment effects on blood pressure (BP) in ASCEND-HF. Methods A genetic substudy was conducted including 2680 participants (2173 European Ancestry [EA] and 507 African Ancestry [AA]) that underwent genome-wide (GW) genotyping using Axiom Biobank Array (Affymetrix) and imputation via 1000 Genome reference panels. BP change was defined as systolic BP at 0.5 and 1 hour of nesiritide infusion minus baseline. We tested candidate SNPs in four genes of the BNP pathway (NPR1, NPR2, NPR3 and MME) and performed an unbiased GW association study. Linear mixed models, stratified by race, were used to estimate SNP*nesiritide interaction effects on BP change adjusting for SNP, nesiritide, sex, BMI, HTN, and top five genetic principal components. Overall results (both races) were obtained by meta-analysis. Significance was set at 0.0125 and 5.0x10-8 for candidate and GW study, respectively. Analysis of mortality or re-hospitalization was performed for significant SNPs. Results Candidate gene analysis showed two SNPs (rs3792761, minor allele frequency (MAF)=0.18 in EA, 0.37 in AA; rs817893, MAF=0.22 in EA, 0.42 in AA) that had significant interactions with nesiritide on BP (β=2.87, p=0.005 for rs3792761; β=2.26, p=0.012 for rs817893). However, these SNPs were not linked to mortality or re-hospitalization (HR=1.09, p=0.26 for rs3792761; HR=1.07, p=0.34 for rs817893). There were no loci meeting GW significance in either ancestral group nor in the meta-analysis, though a few suggestive hits were identified with p<1x10-5. Conclusion Our data indicate there could be pharmacogenomic interactions where NPR3 sequence variants modify the impact of BNP infusion. Further investigation to define responders vs. non-responders may be warranted.

Cardiology/Cardiovascular Research

Al-Darzi W, **Michaels A**, and **Cowger J**. A RARE CASE OF EOSINOPHILIC MYOCARDITIS PRESENTING WITH REFRACTORY VENTRICULAR TACHYCARDIA AND CARDIOGENIC SHOCK. *Journal of the American College of Cardiology* 2021; 77(18):2254.

Background Eosinophilic myocarditis (EM) is a rare etiology of cardiogenic shock. There are few reports of eosinophilic myositis associated with orbital myositis. Herein, we present a rare case of EM presented with refractory ventricular tachycardia (VT). Case 55-Year-old female with medical history of orbital myositis on chronic oral prednisone, bicuspid aortic valve, abdominal aortic aneurysm. She presented to an outside hospital with palpitations and found to have a wide complex tachycardia with atrioventricular dissociation requiring subsequent cardioversions. Echocardiogram showed left ventricle ejection fraction at 51% and normal right ventricle. Coronary angiogram showed non-obstructive coronary artery disease. Course was complicated by refractory VT, intubation, and cardiogenic shock that warranted escalation of care. On arrival, patient was in VT storm and required multiple shocks despite anti-arrhythmics. Patient was placed on venoarterial extracorporeal membrane oxygenation(VA-ECMO). Decision-making Due to rapid progression of her cardiogenic shock, giant cell myocarditis was suspected. Other differential included sarcoidosis, viral or other acute myocarditis. Due to instability, cardiac magnetic resonance was not performed. Endomyocardial biopsy revealed a small focus of eosinophils infiltrating a focus with myocardial cell damage and edema consistent with EM. There was no peripheral eosinophilia. Extensive rheumatological and autoimmune workup in addition to viral panels were negative. Patient was started on high dose steroids that was gradually tapered down to oral prednisone. Due persistent VT, VT ablation attempt was unsuccessful. Patient was deemed not a candidate for heart transplant. Eventually, with mexilitine, amiodarone and steroids, VA-ECMO was weaned off. Unfortunately, her course was also complicated by acute renal injury requiring hemodialysis, sepsis, and shock liver. Patient enrolled in

hospice and expired. Conclusion EM can be presented without peripheral eosinophilia. EM should be suspected in patients presenting with arrhythmia or cardiogenic shock and have history of orbital myositis for early immunosuppressive therapy.

Cardiology/Cardiovascular Research
Alqam B, Habash F, Gheith Z, Vallurupalli S, and **Maskoun W**. LONG TERM OUTCOMES OF TAKOTSUBO CARDIOMYOPATHY IN MEN COMPARED TO WOMEN IN THE US VETERAN AFFAIRS HEALTHCARE SYSTEM. *Journal of the American College of Cardiology* 2021; 77(18):867.

Background Takotsubo cardiomyopathy is characterized by significant transient left ventricular dysfunction. Differences in long term outcome in men compared to women is not well described in the literature. Methods We performed a retrospective study using chart review for patients diagnosed with Takotsubo Cardiomyopathy between 2005 and 2018 in the Veteran Affairs (VA) national database. We included patients who met the Mayo Clinic diagnostic criteria for Takotsubo Cardiomyopathy. We compared the long term outcomes in men vs women patients. Results 641 patients were included, of those 69.3% were males, median age was 64 years, median ejection fraction at the time of diagnosis was 35. On Kaplan-Meier analysis there was no significant difference between men and women in the rates of recurrence of Takotsubo at median follow up of 4 years, or arrhythmia at 1 year (Figure-1 A and B respectively). However, men had higher mortality rate over 10 year follow up period (Figure-1 C). Conclusion In patients with Takotsubo cardiomyopathy at the VA system, men had higher mortality rates but there was not significant difference in rates of recurrence or arrhythmias when compared to women. [Formula presented]

Cardiology/Cardiovascular Research
Cerrud-Rodriguez R, Wiley K, **Villablanca-Spinetto P**, and Wiley J. POSTPROCEDURAL MONOTHERAPY WITH ASPIRIN VS DAPT AFTER TAVI - AN UPDATED META-ANALYSIS OF RANDOMIZED, CONTROL TRIALS. *Journal of the American College of Cardiology* 2021; 77(18):978.

Background Multiple studies have evaluated whether monotherapy with aspirin is superior to DAPT in patients who have undergone transcatheter aortic valve implantation (TAVI) Methods A systematic review of Medline, Cochrane, and Embase was performed for RCTs that reported outcomes of patients undergoing TAVI who received post-procedural aspirin only vs those who received DAPT. Four RCTs met the eligibility criteria Results This meta-analysis includes 1,086 patients with a mean age 80.0±0.75 years; 50.3% were male. After a mean follow-up of 9.0±3.5 months, there was a significant benefit in the aspirin only group, when compared with the DAPT group, in all bleeding events (Risk Ratio [RR] 0.58, 95% Confidence Interval [CI] 0.44-0.76, p<0.0001, relative risk reduction [RRR] 42%, absolute risk reduction [ARR] 9.1%). No statistically significant differences between groups were found in the other outcomes: all-cause mortality (RR 1.01, 95% CI 0.63-1.61, p=0.97), cardiovascular mortality (RR 1.07, 95% CI 0.54-2.12, p=0.84) or all stroke (RR 0.93, 95% CI 0.54-1.61, p=0.79) Conclusion Monotherapy with aspirin following TAVI is associated with a lower risk of all bleeding events when compared with post-procedural DAPT. No differences between groups were seen in the other studied outcomes. However, the short mean follow-up period is an important limitation of the present study. Further studies with longer follow-up periods are needed before changes are implemented in the current TAVI guidelines% [Formula presented]

Cardiology/Cardiovascular Research
Duran AT, Kronish I, **Keteyian SJ**, Ye SQ, Stavrolakes K, West H, and Moise N. The implications of COVID-19 on cardiac rehabilitation: The need for theory-driven, telehealth-enhanced, non-traditional models. *Implementation Science* 2021; 16(SUPPL 1):1.

[Duran, Andrea T.; Kronish, Ian; Ye, Siqin; Moise, Nathalie] Columbia Univ, Irving Med Ctr, New York, NY USA. [Keteyian, Steven J.] Henry Ford Hosp, Detroit, MI 48202 USA. [Stavrolakes, Kimberly] New York Presbyterian Hosp, New York, NY USA. [West, Harry] Columbia Univ, New York, NY USA. atd2127@cumc.columbia.edu

Cardiology/Cardiovascular Research

Jain A, Aggarwal A, Mehta A, and **Qaqi O**. SUCCESSFUL USE OF POLYURETHANE COVERED CORONARY STENT (PCCS) FOR MANAGEMENT OF GIANT CORONARY ANEURYSM. *Journal of the American College of Cardiology* 2021; 77(18):1912.

Background Coronary Artery Aneurysm(CAA) is defined as localized dilatation of coronary artery exceeding 50% of its reference diameter. Although CAA is uncommon, it is associated with a poor prognosis. At present, there are no guidelines on its management. By presenting this case, we acknowledge the scarcity of data on this topic and support the use of PCCS for clinical situations that may mimic our case. Case 71 year old female with multiple comorbidities presented with NSTEMI. Coronary angiogram showed 95% stenosis of proximal RCA with a large aneurysm distal to the stenotic segment. Due to multiple comorbidities, patient was deemed a poor surgical candidate. Thereafter, a staged PCI of proximal RCA and simultaneous repair of coronary aneurysm using a single covered coronary stent was planned. A 4mmx26mm PCCS was deployed successfully. At 6-month follow-up, the patient had no major adverse cardiovascular event. Decision-making PCCS were originally approved to treat coronary perforations. Data on its use in treating CAA is not sufficient. Our patient had prohibitive surgical risk. Clinical presentation was complicated with the presence of a large aneurysm in conjunction with significant subtotal stenosis. We decided to intervene percutaneously and fix both lesions simultaneously. Conclusion Giant CAA although occurs infrequently, it may have dreaded complications like rupture and death. PCCS could potentially be used to seal-off CAA, if hemodynamically indicated in a poor surgical candidate. [Formula presented]

Cardiology/Cardiovascular Research

Jebbawi LA, Jia KQ, and Ruzieh M. EFFECT OF CLASS OF BETA-BLOCKERS, CARDIOSELECTIVE VERSUS NON-CARDIOSELECTIVE, ON COPD EXACERBATIONS IN PATIENT WITH COPD AND CARDIOVASCULAR DISEASES. *Journal of the American College of Cardiology* 2021; 77(18):1687.

Background Several guideline committees and experts advocate cardioselective beta-blockers (βB) over non-cardioselective βB use in patients with heart disease and chronic obstructive pulmonary disease (COPD), as a safer option to reduce COPD exacerbations. We sought to test this hypothesis using a meta-analysis and meta-regression of available studies. Methods Pubmed, and MEDLINE were searched for relevant studies. Risk ratio (RR) of COPD exacerbations was calculated using the Mantel Haenszel random effect model and a meta-regression analysis was performed using the percentage of patients using cardioselective βB in each trial as a moderator variable. Results Data from 10 studies comprising 75,504 patients were included. There was no statistically significant difference in the rate of COPD exacerbations and/or COPD related hospitalizations with cardioselective vs non-cardioselective βB (RR: 1.02, 95% CI: 0.88 - 1.18), figure 1A. When controlling for the percentage of cardioselective βB use in each trial as a moderate variable, there was no significant change in heterogeneity (Tau2: 0.09, $p < 0.001$) and there was no correlation between the percentage of patients used cardioselective βB in each study and the change in COPD exacerbations and/or COPD related hospitalizations, figure 1B. Conclusion We found no evidence to support that cardioselective βB were associated with a lower risk of COPD exacerbations compared to non-cardioselective βB. [Formula presented]

Cardiology/Cardiovascular Research

Jebbawi LA, Jia KQ, and Ruzieh M. EFFECT OF BETA-BLOCKERS CLASS, CARDIOSELECTIVE VERSUS NON-CARDIOSELECTIVE, ON MORTALITY IN PATIENTS WITH COPD AND CARDIOVASCULAR DISEASE. *Journal of the American College of Cardiology* 2021; 77(18):1684.

Background Chronic obstructive pulmonary disease (COPD) and cardiovascular disease often coexist, and the presence of heart disease increases mortality in patients with COPD and vice versa. Whenever indicated, cardioselective beta-blockers (βB) are often recommended over non-cardioselective βB in patients with COPD. We sought to clarify the evidence supporting this approach. Methods We searched Pubmed and MEDLINE for relevant studies. We calculated the risk ratio (RR) of mortality using the Mantel Haenszel random effect model. We performed a meta-regression analysis using the percentage of patients using cardioselective βB in each trial as a moderator variable. Results Data from 14 studies comprising 91,714 patients were included. There was no significant difference in overall mortality between patients who received cardioselective vs. non-cardioselective βB (RR: 1.01, 95% CI: 0.90 -

1.12), figure 1A. However, when using the percentage of patients taking cardioselective βB as a moderator variable, heterogeneity became moderate (Tau2: 0.01, P: 0.01, R2: 0.79), and there was a strong correlation between the percentage of cardioselective βB used in each trial and the reduction in mortality, such as when the percentage of patients using cardioselective βB in the study increases, the reduction in mortality is higher, figure 1B. Conclusion Cardioselective βB use may be associated with lower mortality in COPD patients. This hypothesis should be tested in a formal randomized controlled trial. [Formula presented]

Cardiology/Cardiovascular Research

Lanfear DE, **Gui H**, **Hannawi B**, **Connolly T**, **Li J**, **She R**, **Pereira N**, **Adams K**, **Hernandez A**, **Luzum J**, **Francke S**, **Tang WH**, and **Williams LK**. PHARMACOGENOMIC ANALYSES IN ASCEND-HF INDICATE INFLUENCE OF NPR3ON NESIRITIDE BLOOD PRESSURE EFFECT. *Journal of the American College of Cardiology* 2021; 77(18):840.

Background The Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) randomized hospitalized HF patients to nesiritide or placebo and found no survival difference, but some data suggests genetic variation may influence nesiritide effect. We explored if genetic factors are associated with treatment effects on blood pressure (BP) in ASCEND-HF. Methods A genetic substudy was conducted including 2680 participants (2173 European Ancestry [EA] and 507 African Ancestry [AA]) that underwent genome-wide (GW) genotyping using Axiom Biobank Array (Affymetrix) and imputation via 1000 Genome reference panels. BP change was defined as systolic BP at 0.5 and 1 hour of nesiritide infusion minus baseline. We tested candidate SNPs in four genes of the BNP pathway (NPR1, NPR2, NPR3 and MME) and performed an unbiased GW association study. Linear mixed models, stratified by race, were used to estimate SNP*nesiritide interaction effects on BP change adjusting for SNP, nesiritide, sex, BMI, HTN, and top five genetic principal components. Overall results (both races) were obtained by meta-analysis. Significance was set at 0.0125 and 5.0x10-8 for candidate and GW study, respectively. Analysis of mortality or re-hospitalization was performed for significant SNPs. Results Candidate gene analysis showed two SNPs (rs3792761, minor allele frequency (MAF)=0.18 in EA, 0.37 in AA; rs817893, MAF=0.22 in EA, 0.42 in AA) that had significant interactions with nesiritide on BP (β=2.87, p=0.005 for rs3792761; β=2.26, p=0.012 for rs817893). However, these SNPs were not linked to mortality or re-hospitalization (HR=1.09, p=0.26 for rs3792761; HR=1.07, p=0.34 for rs817893). There were no loci meeting GW significance in either ancestral group nor in the meta-analysis, though a few suggestive hits were identified with p<1x10-5. Conclusion Our data indicate there could be pharmacogenomic interactions where NPR3 sequence variants modify the impact of BNP infusion. Further investigation to define responders vs. non-responders may be warranted.

Cardiology/Cardiovascular Research

Mohammed M, **Sirdenis N**, **Gorgis S**, **Azzo Z**, and **Parikh S**. TWO VARIANTS OF TAKOTSUBO CARDIOMYOPATHY IN A YOUNG WOMAN WITH ALCOHOL WITHDRAWAL. *Journal of the American College of Cardiology* 2021; 77(18):2250.

Background Takotsubo cardiomyopathy (TCM) is characterized by transient left ventricular dysfunction and often mimics acute coronary syndrome. Although there are four echocardiographic patterns of TCM, patients typically present with one variant. Case A 32-year-old woman with alcohol use disorder presented with shortness of breath, nausea, vomiting, and malaise. She had tremors concerning for alcohol withdrawal and was found to be hypoxic with a chest X-ray showing pulmonary edema. She had elevated troponin, BNP, and lactate. Electrocardiogram showed no ischemic changes. The patient developed acute respiratory failure and required intubation. Transthoracic echocardiogram (TTE) showed an ejection fraction (EF) of 22% with global hypokinesis of the left ventricle, apical ballooning and preserved basal function. Cardiac catheterization showed no coronary artery disease. Decision-making The patient made hemodynamic and symptomatic improvement and in three days the EF improved to 50%. She was diagnosed with classical TCM in the setting of alcohol withdrawal. Four months after the initial presentation, she presented again with palpitations, diaphoresis, tremors and sharp chest pain. The patient reported alcohol cessation for three days following two months of heavy alcohol use. She had elevated BNP, troponin and lactate. Electrocardiogram showed ST segment depression in leads V3-V5. TTE showed an EF of 38% with severe hypokinesis of basal to mid left ventricular wall consistent with

reverse TCM. The patient was treated for acute decompensated heart failure in the setting of alcohol withdrawal and had symptomatic improvement in few days. Conclusion TCM has been described to occur in various morphologies but only rare cases have shown multiple variants in one individual. We present a rare case of one patient with two distinct variants of TCM during two separate episodes of alcohol withdrawal. Although the mechanism is unclear, we suspect that the combination of genetic predisposition and adrenergic response in substance abuse may play a role in our case.

Cardiology/Cardiovascular Research

Nowak RM, Peacock F, **Jacobsen G**, Limkakeng AT, Christenson R, Singer AJ, **McCord J**, Apple FS, and DeFilippi C. Indeterminate zone high-sensitivity troponin levels in a rapid acute myocardial infarction assessment algorithm and patient dispositions. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S206.

R.M. Nowak, Henry Ford Health System

Background and Objectives: The multicenter High Sensitivity Cardiac Troponin I (hs-cTnI) in the United States (HIGH-US) study reported a 1-hour Emergency Department (ED) hs-cTnI algorithm for the assessment of acute myocardial infarction (AMI). However, 783 (37.1%) patients were placed in the algorithm's indeterminate zone, not meeting the rule-out or rule-in criteria. Our objectives were to describe the AMI and 30-day AMI/death rates and clinical characteristics of these patients placed in observation/inpatient beds (OBS/ADM) compared to having an ED discharge (EDD). Methods: In this prospective cohort study 2113 consenting adults with any symptoms suspicious for AMI were enrolled from 2015-2016 in 29 US medical centers. There were no patient exclusion criteria. Baseline and 1-hour plasma samples were analyzed using the Siemens Atellica hs-cTnI assay (99th % = 47.0 ng/L), with results not available to the treating physician. AMI diagnosis was independently adjudicated using local contemporary troponin assays and all 30-day clinical data available. Patients were placed in OBS/ADM or had EDD according to each site's clinical practice. Stepwise logistic regression modeling was used to determine which of 25 clinical patient characteristics were associated with OBS/ADM disposition decisions. Results: Of 763 (30.3%) of the intermediate zone placed patients with complete data available, 532 (69.7 %) were placed in OBS/ ADM and 231 (30.3%) had an EDD. Adjudicated AMI rates and 30-day AMI/death rates were different in these 2 groups (41 [7.7%], 2 [0.9%], p = 0.001 and 15 [2.8%], 1 [0.4%] respectively, p = 0.050). The clinical variables associated with OBS/ADM placement were age, hypertension, eGFR < 60, abnormal ECG, and previous revascularization (odds ratio estimates of 1.027, 1.764, 1.955, 1.700 and 1.620 respectively). The OBS/ADM to EDD ratios varied widely amongst the participating centers (100.0-50.0%). Conclusion: The correct disposition decision for patients not ruling out or ruling in for AMI using a 1-hour hs-cTnI algorithm remains unclear. ED physicians, using contemporary troponin assays and clinical evaluations for 231 patients with EDD but who were placed in the hs-cTnI algorithm intermediate zone, missed 1 (0.4%) AMI, with 15 (2.8%) patients having 30-day AMI/death. The absence of our reported cardiac risk factors likely contributed to the EDD decision. Further studies are needed to validate our results.

Cardiology/Cardiovascular Research

Patel S, **Magbanua MLP**, and **Ananthasubramaniam K**. PSEUDO WELLEN'S SYNDROME : THINK OUTSIDE THE HEART TOO. *Journal of the American College of Cardiology* 2021; 77(18):2797.

Background Wellen's syndrome (WS) is a characteristic ECG pattern in patients with acute coronary syndrome (ACS) and critical left anterior descending artery stenosis. We present a case of pseudo Wellen's syndrome (PWS) with submassive pulmonary embolism (PE) mimicking acute coronary syndrome. Case A 63 yr old man with a history of venous thromboembolism presented with acutely worsening dyspnea. He denied chest pain, syncope or heart failure symptoms. He was acutely short of breath with limited speech and tachycardic to 101 beats/min; remaining exam and vitals were unremarkable. Intake blood work was notable for high sensitivity troponin I of 129ng/L with a repeat level of 115 ng/dL. Initial ECG is shown below (Figure 1A). Decision-making ECG was concerning for WS though lack of risk factors, decreasing troponin levels and acute dyspnea raised suspicion of a nonischemic etiology. Urgent echocardiogram found a dilated and hypokinetic right ventricle (RV) and normal left ventricular function and wall motion (Figure 1B-C). Chest CT showed extensive bilateral PE

involving both main pulmonary arteries (Figure 1D-E). ECG findings were attributed to RV strain and coronary angiography was not pursued. Catheter-directed thrombolysis was performed with improvement in symptoms. Conclusion ECG changes are common and varied in PE. This case underscores the importance and awareness of acute right heart strain from PE as a cause of PWS, enabling timely diagnosis and treatment of a life threatening emergency. [Formula presented]

Cardiology/Cardiovascular Research
Patel S, **Mohammed M**, **Gorgis S**, **Zakhour S**, **Aurora L**, **Bhasin S**, and **Parikh S**. PRIMARY CARDIAC BURKITT LYMPHOMA PRESENTING WITH ABDOMINAL PAIN. *Journal of the American College of Cardiology* 2021; 77(18):2672.

Background Primary cardiac lymphomas are rare, carry high mortality rates and are often due to aggressive B cell lymphomas, including Burkitt Lymphoma (BL). BL is rare in the immunocompetent though more prevalent among AIDS patients. Case A 41yo man with a history of alcohol abuse presented with 1 month of B-symptoms and abdominal pain. Initial labs found a positive HIV-1 antibody, elevated viral load and low CD4 count. CT chest and abdomen on arrival revealed a large infiltrating lobulated right atrial mass (RAM)(Figure 1A). Decision-making Cardiac masses are often due to metastatic disease and warrant evaluation for extra-cardiac origin. TTE, TEE (Figures 1B & 1C) and cardiac magnetic resonance imaging identified a 2.8cm subcarinal lymph node and found the RAM to be infiltrating the inter-atrial septum, partially surrounding the pulmonary veins, obstructing the superior vena cava and extending to the aortic root (Figure 1D). Cytology of the subcarinal lymph node biopsy was consistent with BL. Highly active anti-retroviral therapy and chemotherapy were initiated. CT chest after 1 treatment cycle showed a marked reduction in RAM size (Figure 1E). Conclusion Our case underscores the central role of advanced imaging in the evaluation of cardiac masses by identifying a malignant etiology, staging, identifying a target for pathologic diagnosis and monitoring treatment response. Early use of multimodality imaging for cardiac masses in the HIV population allows for timely use of lifesaving therapies. [Formula presented]

Cardiology/Cardiovascular Research
Sadat B, **Saleem M**, **Lemor A**, **Qintar M**, **Frisoli T**, **Eng M**, **O'Neill B**, **Wang DD**, **Alaswad K**, **Basir M**, **Lee J**, **O'Neill W**, and **Villablanca P**. LARGE SINGLE CENTER EXPERIENCE WITH MANTA VASCULAR CLOSURE DEVICE IN TRANSCATHETER AORTIC VALVE REPLACEMENT AND MECHANICAL CIRCULATORY SUPPORT. *Journal of the American College of Cardiology* 2021; 77(18):1154.

Background Transcatheter aortic valve replacement (TAVR) and mechanical circulatory support (MCS) are common procedures requiring large-bore arterial access. Data on suture-based VCD for large-bore arterial access closure have been comprehensive. The safety and efficacy of the MANTA VCD using real-world data are scarce. The present study aims to evaluate the safety and efficacy of the MANTA vascular closure device (VCD) (Teleflex, Morrisville, NC, USA) in arterial transfemoral large-bore sheath size from 14 to 24 Fr using real-world data in a tertiary-care center. Methods A single-center evaluation of patients who underwent TAVR and MCS with the use of Manta VCD from June 2019 to September 2020. The primary efficacy outcome is defined as immediate hemostasis post closure in absence of major bleeding or access site endovascular or surgical intervention. The secondary safety outcomes assessed using Valve Academic Research Consortium-2 (VARC-2) criteria, including major and minor bleeding and vascular complications. Results Twelve different operators consecutively treated 174 patients with the MANTA device. TAVR was performed in 94 (54%), percutaneous MCS was performed in 76 (43.6%), and other structural interventions in five (3%) of patients. The 14Fr MANTA was used in 59 cases (34%) and the 18Fr was used in 115 cases (66%). The median sheath size was 14 Fr. A single device was deployed in 173 (99.4%) of cases. The primary efficacy outcome was obtained in 92.6% of cases. The secondary safety outcomes using VARC-2 criteria were major bleeding 0.5%, minor bleeding 4.5%, major vascular complication 1.13%, minor vascular complication 4.5%. To achieve hemostasis 6.7% of the cases required endovascular balloon tamponade and 1.7% required covered stents. There was no access site infection, collagen-plug embolization, surgical repair, and retroperitoneal bleeding. Conclusion In this single-center experience, the use of MANTA VCD can safely and effectively close large bore

arteriotomies, including TAVR and MCS. Larger multicenter studies of efficacy, safety, and cost-effectiveness are needed.

Cardiology/Cardiovascular Research

Singh-Kucukarslan G, **Raad M**, **Al-Darzi W**, **Cowger J**, **Brice L**, **Basir M**, **O'Neill W**, **Alaswaad K**, and **Eng M**. EXTRACORPOREAL MEMBRANE OXYGENATION WITH BI-ATRIAL UNLOADING TO TREAT BIVENTRICULAR DYSFUNCTION. *Journal of the American College of Cardiology* 2021; 77(18):2382.

Background Veno-arterial extracorporeal membrane deoxygenation (ECMO) is increasingly used in patients with cardiogenic shock and myocardial injury. Case A 59-year old male with a history of coronary artery bypass graft presented with a lateral ST-elevation myocardial infarction. He received thrombolytics however had persistent ST elevations requiring angiography, and a salvage-percutaneous intervention was performed. Despite successful angioplasty, he spiraled into cardiogenic shock prompting placement of a transfemoral Impella CP, after which he was transferred to our center. Echocardiogram revealed a left ventricular ejection fraction of 25%, moderate right ventricular dysfunction, and severe mitral regurgitation with frequent ventricular tachycardia requiring cardioversion. Decision-making He was in cardiogenic shock SCAI stage D. With maximal impella support, his kidney, liver enzyme, and lactate levels were within normal limits. The ventricular tachycardia became less frequent. However, given his progressively increasing pulmonary artery (PA) pressures, increasing vasopressor requirements, and borderline low cardiac index, the decision was to upgrade his hemodynamic support. A left atrial veno-arterial (LAVA) cannulation strategy was considered for additional left ventricular offloading given his biventricular dysfunction and severe mitral regurgitation. Intracardiac echocardiography was used to guide balloon septostomy and placement of an Edwards Lifesciences VFEM024 24Fr cannula that traversed both left and right atria. The Impella CP was exchanged for a 19Fr arterial cannula. Immediately after cannulation, his mean PA pressure decreased from 38 to 25 mmHg, and cardiac index increased from 2 L/min/m2 to 5-6 L/min/m2. Despite improved hemodynamics, he was unable to be weaned from LAVA ECMO. He underwent orthotopic heart transplantation 11 days post-cannulation. Conclusion This case demonstrates the benefits of early hemodynamic support with a LAVA cannulation strategy. LAVA is a safe and viable option that offers ECMO support with additional left ventricular offloading using a single inflow cannula.

Center for Individualized and Genomic Medicine Research

Lanfear DE, **Gui H**, **Hannawi B**, **Connolly T**, **Li J**, **She R**, **Pereira N**, **Adams K**, **Hernandez A**, **Luzum J**, **Francke S**, **Tang WH**, and **Williams LK**. PHARMACOGENOMIC ANALYSES IN ASCEND-HF INDICATE INFLUENCE OF NPR3ON NESIRITIDE BLOOD PRESSURE EFFECT. *Journal of the American College of Cardiology* 2021; 77(18):840.

Background The Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) randomized hospitalized HF patients to nesiritide or placebo and found no survival difference, but some data suggests genetic variation may influence nesiritide effect. We explored if genetic factors are associated with treatment effects on blood pressure (BP) in ASCEND-HF. Methods A genetic substudy was conducted including 2680 participants (2173 European Ancestry [EA] and 507 African Ancestry [AA]) that underwent genome-wide (GW) genotyping using Axiom Biobank Array (Affymetrix) and imputation via 1000 Genome reference panels. BP change was defined as systolic BP at 0.5 and 1 hour of nesiritide infusion minus baseline. We tested candidate SNPs in four genes of the BNP pathway (NPR1, NPR2, NPR3 and MME) and performed an unbiased GW association study. Linear mixed models, stratified by race, were used to estimate SNP*nesiritide interaction effects on BP change adjusting for SNP, nesiritide, sex, BMI, HTN, and top five genetic principal components. Overall results (both races) were obtained by meta-analysis. Significance was set at 0.0125 and 5.0x10-8 for candidate and GW study, respectively. Analysis of mortality or re-hospitalization was performed for significant SNPs. Results Candidate gene analysis showed two SNPs (rs3792761, minor allele frequency (MAF)=0.18 in EA, 0.37 in AA; rs817893, MAF=0.22 in EA, 0.42 in AA) that had significant interactions with nesiritide on BP (β=2.87, p=0.005 for rs3792761; β=2.26, p=0.012 for rs817893). However, these SNPs were not linked to mortality or re-hospitalization (HR=1.09, p=0.26 for rs3792761; HR=1.07, p=0.34 for rs817893). There were no loci meeting GW significance in either ancestral group nor in the meta-analysis, though a few suggestive hits were identified with p<1x10-5. Conclusion Our data indicate there could be

pharmacogenomic interactions where NPR3 sequence variants modify the impact of BNP infusion. Further investigation to define responders vs. non-responders may be warranted.

Dermatology

Dimitrion P, **Yin C**, **Subedi K**, **Khalasawi N**, **Yao Y**, **Miller A**, **Veenstra J**, **Vellaichamy G**, **Lim H**, **Hamzvi I**, **Zhou L**, and **Mi Q**. 222 Whole-blood immune profile in hidradenitis suppurativa. *Journal of Investigative Dermatology* 2021; 141(5):S39.

Hidradenitis suppurativa (HS), a chronic inflammatory skin condition with a multifactorial etiology, has a complex cutaneous immune reaction localized around the hair follicles in intertriginous skin. HS pathogenesis remains enigmatic, although some hypotheses have been proposed. Increasing evidence of the association between HS and other inflammatory conditions (e.g. inflammatory bowel disease) and cardiovascular disease suggests that patients with HS have underlying systemic inflammation. To date, few studies have sought to understand the systemic changes that occur in the immune system of HS patients. One recent study performed bulk RNA-sequencing on peripheral blood mononuclear and showed minor differences in transcriptomes of peripheral blood mononuclear cells, but bulk RNA-sequencing does not have the capacity to identify specific changes in cellular subsets. To determine whether specific systemic changes occur in HS patients we performed CyTOF using a standardized panel that identifies 37 immune cell subpopulations in whole blood. We analyzed whole blood samples from 8 HS and 7 healthy controls. Compared to healthy controls, HS patients had an increased frequency of plasmablasts and a decreased frequency of CD66b- neutrophils. Furthermore, marked differences in monocyte subclasses showed a shift from classical monocytes (CD14+ CD16-) towards intermediate (CD14+ CD16+) and non-classical subsets (CD14dim CD16+) in HS. We also identified a large population of CDR45RO+ CCR6+ CD38+ intermediate monocytes in HS, which was largely absent in healthy controls. Taken together our results support previous studies highlighting the role of neutrophils and B cells in HS pathogenesis, and identify newly discovered monocyte dynamics in peripheral blood of HS patients further supporting widespread inflammation as a feature of HS.

Emergency Medicine

Chan JC, Davenport M, Schmitt TW, Lee HM, Abbas T, Hayes AK, Adamakos FJ, **Axelson DJ**, and Salvo MB. Slack intern curriculum supports intern preparedness and bridges curriculum gaps due to COVID-19 pandemic. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S346-S347.

J.C. Chan, St. John's Riverside Hospital

Background and Objectives: Transitioning to residency involves translation of academic knowledge into clinical acumen, and is complicated by variable medical school experiences. The COVID-19 pandemic presented a new challenge by displacing students from clinical rotations. Virtual educational modalities such as the Slack Intern Curriculum (SIC) have increased newly-matched pre-intern perceived preparedness (PP) for residency in prior years, but the SIC had never been implemented or evaluated in a pandemic with disrupted medical education. Assess the effectiveness of social media implementation of an Accreditation Council for Graduate Medical Education (ACGME) milestone-based curriculum during the spring 2020 U.S. COVID-19 surge. The hypothesis is that pre-interns will report improvements in PP regarding multiple ACGME milestone topics. Methods: The SIC was constructed using topics from 8 ACGME milestones in emergency medicine (EM), incorporated into 8 clinical scenarios. Residency recruitment occurred via national EM listservs; of 276 programs, 27 enrolled. Curricular implementation was on Slack workspaces. Cases included stimulus images and clinical questions. Ample discussion time, answers, and resources were provided. Trends in PP were calculated with descriptive statistics and the Wilcoxon Rank Sum test. Results: Of 311 total pre-interns contacted, 289 (92.9%) completed a presurvey in April/May 2020, and 240 (77.2%) completed a post-survey in June/July 2020; an 83.9% follow-through rate. Pre-interns reported statistically significant increases in PP both overall and regarding 14 of 21 milestone topics, including the areas of diagnosis, pharmacotherapy, disposition, airway management, and procedures. Conclusion: Amidst the educational disruption of the COVID-19 pandemic, pre-interns participating in the SIC reported statistically significant increases in PP. Limitations include absence of control or pre-pandemic data. Future directions include adapting the SIC to other specialties' ACGME milestones for generalizability across all fields.

Emergency Medicine

Do AP, and **Holbrook M**. A RARE CASE OF EARLY CARDIAC TAMPONADE CAUSED BY SEVERE POSTOPERATIVE HYPOTHYROIDISM TWO YEARS AFTER OPERATION. *Journal of the American College of Cardiology* 2021; 77(18):2287.

Background Hypothyroidism (HT) is a disease with many clinical presentations. Among those, pericardial effusion (PEff) is a rare presenting finding detected in patients with severe HT. It is typically mild but rarely can cause cardiac tamponade. This case will highlight that severe HT can manifest as myxedema with heart failure symptoms and PEff. Case A 49 years old female with HT from total thyroidectomy two years prior, presented with shortness of breath and orthopnea. The patient ran out of levothyroxine several months ago. She was found to be hypoxic requiring oxygen. Physical exam showed expiratory wheezes, bilateral lower extremity non-pitting edema. TSH was 260uIU/mL and free T4<0.25ng/dL. BNP and troponin were unremarkable. CXR showed marked enlargement of the cardiac silhouette which were confirmed to be moderate PEff with findings of early tamponade on transthoracic echocardiogram (TTE). This was determined to be due to severe HT. She was started on IV levothyroxine which was transitioned to oral medication with improvement of symptoms. Serial TTE showed stable effusion without evidence of tamponade. She was discharged to follow up TTE in the next month. Decision-making Etiology of non-traumatic PEff is most commonly due to infarction, pericarditis, malignancy, infection or uremia. Rarely, severe HT represents itself as moderate size PEff as demonstrated in this case. The initial echo showed early signs of cardiac tamponade which can be a detrimental complication if it continues to worsen. When cardiac tamponade occurs, urgent TTE with pericardiocentesis or creation of a pericardial window along with IV thyroxine therapy is the treatment of choice. The IV administration of both T3 and T4 is important as gut absorption might be impaired in this patient population. If tamponade has not occurred, conservative treatment with thyroid supplementation and follow-up TTE to monitor for resolution of the effusion is often enough. Conclusion Even though uncommon, PEff in the setting of severe HT is a potential cause of tamponade if it went undiagnosed. Prompt TTE to determine the severity of the effusion and IV thyroxine is the remained the most crucial steps in management.

Emergency Medicine

Grahf D, **Dandashi J**, **Vohra T**, **Deledda J**, and **Vallee P**. Health care provider absences and intervenable areas during a COVID-19 surge. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S155.

D. Grahf, Henry Ford Hospital

Background and Objectives: Health care provider (HCP) absenteeism during the initial phase of an epidemic or pandemic can lead to significant understaffing during a critical time. There is a paucity of literature that describes the effect that the initial phases of a pandemic have on emergency department (ED) HCP absences, or possible interventions that may curb the number of absences. This lack of data places frontline departments at undue risk for inadequate HCP staffing at a time when patient care needs are greatest. This study aimed to quantify HCP absenteeism in the ED during the initial Coronavirus Disease 2019 (COVID-19) surge and to identify potential interventions that may mitigate absences. Methods: This was a retrospective, descriptive record review that included 82 resident physicians, physician assistants, and staff physicians who were scheduled to work more than 3 clinical shifts during March 2020 in an urban, academic ED that received a high number of COVID-19 patients in March. The department created an external database during the pandemic to assist with staffing given the sudden increase in HCP absenteeism. This database included date of COVID-19 exposure, symptom onset, absence from and return to work, testing with result, age, gender, travel history, and admission history. Descriptive statistics and graphical representations superimposed with dated institutional policy changes were used in framing the progression of dependent variables. Results: During March 2020, of 82 ED HCPs, 28 (34%) required an absence from clinical duties, totaling 152 absentee calendar days (n = 13 women [46%]; n = 15 men [54%]). Median age was 32 years (interquartile range 28-39). Median number of days absent was 4 (interquartile range 3-7). While 16 (57%) of the total absences were secondary to a known exposure, 12 (43%) were symptomatic without a known exposure. A total of 25 (89%) absent HCPs received COVID-19 testing (n = 5 positive [20%]; n = 20 negative [80%]) with test results returning in 1 to 10 days. Eleven (39%) symptomatic HCPs had traveled domestically or internationally in the past

30 days. Conclusion: EDs should anticipate substantial HCP absenteeism during the initial surge of a pandemic. Possible interventions to mitigate absences include early and broad use of personal protective equipment, planning for many asymptomatic HCP absences secondary to exposures, prioritizing HCP testing, and mandating early travel restrictions.

Emergency Medicine

Hagerman TK, and Houtrow A. Prevalence of adversities related to social determinants of health among children with multiple emergency department visits. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S210.

T.K. Hagerman, Henry Ford Health System

Background and Objectives: The emergency department (ED) is an important screening site for social determinants of health (SDH) among children. Therefore, we aimed to determine the prevalence of multiple SDH among children with frequent ED visits. Methods: This is a cross-sectional study of data from the 2016-2018 National Surveys of Children's Health (NSCH), an annual nationally representative survey from the CDC including 102,341 children ages 0-17 in the United States. Survey weights were used for generation of population estimates. Children with ≥2 ED visits as reported by parent respondents were compared to children with 1 or 0 ED visits in the last year. Chi squared statistics and 95% confidence intervals of population estimates from the survey were used for statistical comparison. Results: Overall, 80.1% of children ages 0-17 had no ED visit in the last year, 15.1% had 1 ED visit, and 4.8% had ≥2 ED visits in the last year. Compared to those with no ED visits, children with ≥2 ED visits were generally younger, of Black non-Hispanic race/ethnicity, experienced poverty (40.4% with ≥2 ED visits were at ≤100% of the federal poverty level versus 18.3% with no ED visit, $p < 0.05$), had public insurance, lived in unsafe communities (11.2% of children with ≥2 ED versus 4.6% of those with 0 ED visits, $p < 0.05$). Significantly more children with ≥2 ED visits were food insecure [13.3% (95% CI 11.0-15.7) ≥2 ED visits versus 5.2% (95% CI 4.7-5.6) no ED visit], had housing instability with ≥3 lifetime moves [34.4% (95% CI 29.6-39.3) ≥2 ED visits versus 24.6% (95% CI 23.8-25.3) no ED visit], and had ≥3 adverse childhood experiences [ACEs, 19.4% (95% CI 16.5-22.2) versus 8.9% (95% CI 8.4-9.3) no ED visit] compared to children with no ED visits. Children with ≥2 ED visits had nearly three times the unmet needs [7.7% (95% CI 6.1-9.3)] compared to those with no ED visits [2.7% (95% CI 2.4-3.0)]. Most children with ≥2 ED visits with unmet needs specifically identified unmet medical needs [44% (95% CI 30.7-57.2)]. Conclusion: Children with multiple ED visits have higher rates of adversity related to social determinants of health than do children with no ED visits, with notably higher rates of food and housing insecurity, ACEs, exposure to unsafe communities, and unmet medical needs. Support is necessary for interventions that screen and connect patients to resources at both an ED and national level.

Emergency Medicine

Hagerman TK, **Lee MS**, **Miller J**, and **Manteuffel J**. Improving linkage to care in an emergency department hepatitis C screening program with text messaging. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S153-S154.

T.K. Hagerman, Henry Ford Health System

Background and Objectives: Effective hepatitis C (HCV) screening programs in EDs depend on reliable means to contact patients after discharge. Phone calls are the standard means of communication for these efforts, yet many patients are lost to follow up when they are unreachable by telephone. To increase rates of linkage to care for patients with positive HCV screening tests, we utilized text messaging as an adjunct to telephone calls. Methods: Patients identified as lost to follow up with a positive HCV screening test from 8/2018 to 9/2020 in our opt-out ED HCV screening program were included in this study. A text message asking the patient or family member to call an ED physician regarding a test results was sent 11/2020 -1/ 2021 to phone numbers listed in the electronic medical record. The rate of linkage to care using text messaging was determined as of percentage of patients linked to care of all patients messaged. Results: A total of 381 messages were sent for 153 patients that were lost to follow up with a median of 2 messages per patient. A response from either the patient or patient contact person(s) was received for 42 patients (27.5% of all patients messaged). More patient contact persons (27, 64.3%)

responded to messages compared to patients themselves (15, 35.7%). A direct phone call response (30, 71.4%) to the text message was more common than a text message response (12, 28.6%). At the time of abstract submission, 13 patients previously lost to follow up were pending specialist appointment scheduling, 2 were scheduled for a future specialist appointment, 1 attended their first appointment, and 5 were pending a lab visit for RNA testing. The median time to the first scheduled specialist appointment from referral placement was 23 days. Of those originally lost to follow up from 8/2018 to 9/2020, upon re-establishing communication 6 patients reported being treated previously, 3 were currently being treated or evaluated, and 6 were deceased/ hospice. Overall, we re-established contact with 36 (23.5%) of the 153 total patients using text messaging. Conclusion: Text messaging is a valuable adjunct to phone call-based result notification. Family members and contact persons are an especially useful resource to enhance connection to care for this patient population. Providers may consider the routine use of multiple methods of communication and contacting family members to connect patients to care following ED visits.

Emergency Medicine

Hagerman TK, **Mumby K**, Brar I, Markowitz N, **Miller J**, and **Manteuffel J**. Connecting patients diagnosed with human immunodeficiency virus in the emergency department to care during the COVID-19 pandemic. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S173-S174.

T.K. Hagerman, Henry Ford Health System

Background and Objectives: The ED has been identified as an important location for HIV screening, yet little is known about the impact of the COVID-19 pandemic on ED based HIV screening programs. We hypothesized that our electronic medical record (EMR) triggered HIV screening program would continue to identify new HIV positive patients and link them to care during the COVID-19 pandemic. Methods: We conducted a retrospective chart review of ED patients screened for HIV and compared the average monthly tests performed, number of confirmed HIV positive cases, and rates of linkage to care before and after the onset of the COVID-19 pandemic. We used 3/13/2020 as the start date for the pandemic and compared data in a 5-month period prior to the pandemic (limited to initiation of EMR triggered HIV screening) and a 9-month period during the pandemic. Two tailed t-tests were used for comparison of means. Results: A total of 20,825 patients were screened for HIV from 11/18/2019 to 12/12/2020 (8,417 pre-pandemic and 12,408 during the pandemic). On average, more HIV screening tests were performed in the pre-pandemic period compared to the pandemic period (1,683/month pre-pandemic versus 1,379/month during pandemic). However, when accounting for ED volume changes, a similar rate of patients in the pre-pandemic period (35.8% of all patients seen in the ED) were screened compared to during the pandemic (34.7% of all patients seen). In the pre-pandemic period 11/18/2020 -3/ 12/2020, a total of 25 patients were diagnosed with HIV and all patients were linked to care. In the pandemic period 3/13/2020 -12/ 12/2020, 27 patients were diagnosed with HIV. Of the 27 patients diagnosed, 22 (81%) were linked to care. Two patients died prior to attending specialist appointments during the pandemic (88% linkage to care accounting for deaths). The average time to the first attended specialist appointments for non-admitted patients was not significantly greater during the pandemic period (6.0 days pre-pandemic vs. 6.9 days during pandemic, $p = 0.55$). Conclusion: EMR generated HIV screening allows for continued efforts to diagnose and link patients to care despite the global disruptions caused by the COVID-19 pandemic. These efforts are critical to the mission to end the HIV epidemic by 2030.

Emergency Medicine

Haidar D, **Khanna N**, Fung C, Burkhardt JC, Theyyunni NR, and Huang R. Effect of a longitudinal preclinical point-of-care ultrasound course on medical student performance. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S115-S116.

D. Haidar, University of Michigan

Background and Objectives: Undergraduate medical educators have incorporated point of care ultrasound training (POCUS) to enhance specific components of basic science medical curricula. Literature on objective outcome data on curriculum efficacy is limited. Our study aims to address this deficit by comparing the preclinical performance of medical students participating in a POCUS curriculum to those who did not. We hypothesized that POCUS would improve scores in sections with clear

ultrasound (US) applications but not in other areas where the US curriculum was not as well matched. Methods: At our institution the curriculum is divided into blocks by organ system. Students were offered a voluntary longitudinal POCUS course that was paired with organ system blocks and the exam performance of those enrolled in the curriculum was retroactively compared to those who did not participate. Multivariate linear regression analyses were used to evaluate the relationship between participation in the POCUS course and exam performance in cardiovascular, gastroenterology, and neurology blocks. Results were controlled for gender, MCAT score, and science versus non-science undergraduate degree. Grades in organ blocks were assigned independently by faculty not involved in this project. Results: We compared 51 students who completed the curriculum to 127 who did not participate from the same medical school class. Students who participated in the curriculum had a higher mean cardiovascular anatomy exam score (92.1 vs 88.5, $p < 0.05$) but this difference was not seen with cumulative cardiovascular block scores. No statistically significant differences in anatomy practical or cumulative exam scores were seen with the gastroenterology or neurology blocks. Conclusion: Medical students enrolled in a longitudinal POCUS curriculum demonstrated improved performance in cardiovascular anatomy exam scores. Our study failed to demonstrate a significant difference in performance in two other organ system sequences within the curriculum. These results suggest that ultrasound education may be most beneficial in specific aspects of undergraduate medical education where the connection between organ system material and US application is strongest. Future directions include evaluating the differences in student performance in the musculoskeletal block, as well as analysis of differences in USMLE scores between participants and non-participants.

Emergency Medicine

Joyce K, **Irvin E**, **Vohra T**, **Champagne S**, and **Goyal N**. Voting is a public health issue: Addressing voter participation and engagement among trainees. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S91.

K. Joyce, Henry Ford Health System

Background and Objectives: Practicing physicians vote less than the general public despite policy implications on patient care and physician practice. There is no published data on voting rates (VTR) of trainees or barriers they may face. Residency programs and teaching hospitals may have unique opportunities to promote trainee civic engagement. Our objectives were to measure voter registration rates (VRR) and VTR for trainees, identify barriers, and determine interventions to improve VRR and VTR. Methods: Trainees (n~895) at 3 Henry Ford Health System (HFHS) hospitals were surveyed in 2018 and 2020. They were asked about VRR status, voting habits and barriers to voting. Based on 2018 survey results, voter registration and absentee ballot request forms were provided to new trainees during 2020 orientation and 2 informational sessions were held in subsequent months. In 2020, VRR and VTR were compared to survey results from 2158 trainees at local hospitals who did not receive the intervention. Additional comparisons matched trainees to GP age/gender cohorts. Analysis used descriptive statistics, chi-square or Fisher's exact tests, and univariate analyses. Free-text responses were categorized into themes with iterative discussion. Results: 37.6% and 34.5% of HFHS trainees responded in 2018 and 2020, respectively. VRR was higher among trainees than GP in 2018 (91% vs 67%). VTR among trainees in 2016 primary (53%), 2016 general (79%), 2018 primary (39%) and 2018 general (73%) were also higher than GP (26%, 61%, 20%, 53% respectively, $p < 0.001$ compared to general population and age/gender matched cohorts). Preliminary analyses of 2020 HFHS trainee data after intervention show VRR and VTR for primary and general elections increased over 2016 and 2018, with 98% of trainees registered and 91% voting in the 2020 general election. Forgetting to request absentee ballots and apathy were the most common barriers. Further 2020 analyses including non-HFHS trainees who did not receive the intervention and GP comparisons will be included in the final presentation. Conclusion: Residents and fellows are more engaged in state and national elections compared to the GP. Programs may be able to further improve trainee civic participation by encouraging VRR and absentee balloting, and providing informational sessions. Limitations included a low response rate. Generalizability to other states may be limited due to unique voting regulations.

Emergency Medicine

Klausner HA, **Rockoff S**, **Beyer M**, and **Clayton P**. Review of patient care at the TCF Center Alternative Care Facility during the COVID-19 pandemic. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S393-S394.

H.A. Klausner, Henry Ford Hospital

Background and Objectives: The first confirmed case of COVID-19 in The U.S. was on January 19, 2020 and by the end of March, COVID-19 was in all 50 states. In Michigan, the first confirmed case was on March 10 and later that day a state of emergency was declared. Given the exponential growth of the pandemic, and with concern that hospital resources would be overwhelmed, local hospitals determined that the TCF Center (local convention center) in Detroit, MI would function as a site for an Alternative Care Facility. Methods: Admission criteria included patients accepted as transfers from local hospitals, must be inpatient >48 hours, hemodynamically stable, >14 days from symptom onset (later reduced to 10 days) and requiring no more than 4L NC. The TCF Center was equipped to administer oxygen, IV fluids, perform ACLS, and send iSTAT and POC glucose labs, but there were no imaging capabilities, telemetry, consultants or critical care providers. Results: 39 patients were admitted (one patient twice and another four times for total of 43 admissions). 23 were male and 16 were female, range of ages were 33-95 with an average of 66. The highest census was 21 patients. 14 patients required oxygen, and 25 did not. Length of stay (LOS) ranged from 1-19 days with an average LOS of 7.2 days. Of the 43 admissions, 13 were discharged to a private home, 1 to a homeless shelter, 14 to a nursing home, and 15 were sent back to the hospital. Of these 15 patients transferred back to a hospital reasons included fever (3) and chest pain (2) as the most common reasons. Other reasons include inability to take oral meds, dehydration, lethargy, atrial fibrillation, worsening dyspnea, falls, hyperkalemia, anemia and altered mental status. Conclusion: The TCF Center had a capacity of 970 patients, but only admitted 39, much fewer than anticipated. At the time of design and construction of the facility, the COVID-19 pandemic was in an exponential growth phase and the facility was designed for a surge that never materialized. This may be due to difficulty of scientific models in predicting a novel pandemic course, the ability of hospitals to better care for a larger number of COVID-19 patients than anticipated due to an unprecedented decrease in routine hospital volume, and the beneficial effects of social distancing. Apart from the Javits Center in New York City, which saw 1,095 patients, other field hospitals throughout the country built in response to the COVID-19 pandemic saw equally few patients.

Emergency Medicine

Rafique Z, Safdar B, Duanmu Y, Boone S, Bischof JJ, Beiser DG, D'Etienne J, Driver BE, Fermann GJ, **Klausner HA**, Lagina A, Robinson D, Singer AJ, Stopyra JP, and Peacock F. Standardizing emergency department hyperkalemia management: The PLATINUM study. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S203-S204.

Z. Rafique, Baylor College of Medicine

Background and Objectives: Although hyperkalemia (HK) is common and potentially life-threatening, there is limited data defining an ED standard of care (SoC). ED treatment is mostly based on small studies, anecdotal experience, and historical standards. The lack of a SoC has resulted in wide practice variability and created challenges for the control arm of any investigation. The PLATINUM (Patiromer utiLity as an Adjunct Treatment In patients Needing Urgent hyperkalemia Management) study has proposed an ED SoC HK treatment regimen. Methods: This is a multicenter, randomized, double-blind, placebo-controlled, parallel group study. After informed consent, ED subjects ≥18 years old with potassium (K) ≥ 5.8 mEq/L are enrolled. Exclusions are clinically significant arrhythmia, hemodynamic instability, overdose on K, known bowel obstruction, K binder use within 7 days, expected dialysis within 6 hours of enrollment, hypersensitivity to patiromer, participation in another study <30 days prior, inability to take study drug, life expectancy of <6 months, or pregnant/breastfeeding. No more than 50% will be current hemodialysis recipients. Upon enrollment, subjects are randomized to treatment or control in a 1:1 ratio, and all receive SoC therapy defined as regular insulin 5U IV plus dextrose 25 g IV plus albuterol 10 mg nebulized. Controls receive blinded placebo and the treatment group receives blinded patiromer 25.2 g by mouth. Serum K is drawn at baseline and every 2 hours up to 10 hours or until ED discharge. Efficacy will be evaluated by comparing Net Clinical Benefit (NCB) at 6 hours between study arms as

defined by the mean change in number of interventions less mean change in serum K. Safety analysis will include frequency and severity of adverse events, ECG changes, hypokalemia and hypomagnesemia. Results: A total of 300 subjects will be enrolled from 30 sites across the United States. A modified intention to treat analysis will be used for the primary endpoint. Proportions will be analyzed using Cochran-Mantel- Haenszel methods while continuous variables will be analyzed using analysis of covariance. Conclusion: The Platinum study is the first randomized controlled trial to evaluate the efficacy and safety of a standard combination of insulin, dextrose, and albuterol with or without an oral K binder for treatment of HK. In addition, the 150-patient control arm may help define the optimal ED HK SoC management.

Emergency Medicine

Rykulski N, Berger D, Paxton J, **Klausner HA**, Smith GC, Chen NW, and Swor RA. Impact of missing data on measurement of cardiac arrest outcomes according to race. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S265.

N. Rykulski, William Beaumont Hospital

Background and Objectives: Complete high-quality data is important to understanding racial differences in outcome following out of hospital cardiac arrest (OHCA). Previous studies have shown differences in OHCA outcomes according to both race and socioeconomic status, independent of bystander CPR or EMS care. EMS reporting of data on race is often incomplete. We aim to determine the impact of missing data on the determination of racial differences in outcomes for OHCA patients who survive to hospital admission. Methods: We performed a secondary analysis of a data set developed by probabilistically linking the Michigan Cardiac Arrest Registry to Enhance Survival (CARES) and the Michigan Inpatient Database (MIDB). Adult OHCA patients (age >18) who survived to hospital admission between 2014-2017 were included. Both datasets recorded patient race and ethnicity. Patients were categorized as Caucasian (C), African American (AA), Other, or Missing. Due to the small number of Hispanic patients, these patients were excluded. The outcome measures of interest were survival to hospital discharge (Survive) and survival to discharge with Cerebral Performance Category 1 or 2 (Good Outcome). Outcomes were stratified according to EMS-or hospital-documented race. Results: We included 3,756 matched patients, after excluding 34 Hispanic patients from analysis. Documentation of patient race was missing in 892 (22.1%) of CARES and 212 (5.6%) of MIDB patients. Moderate agreement in race documentation was found between data sets ($\kappa = 0.471$). Caucasian patients were more likely to have a Good Outcome than AA in both the CARES (27.3% vs 14.8%) and MIDB (26.9% vs 16.1%) databases (both $p < 0.001$), but were not more likely to Survive (30.8% vs 27.3% $p = 0.22$; 30.3% vs 28.1%, $p = 0.07$). Moreover, we found no significant difference in outcome measures based on race documentation for C vs AA patients (Good Outcome [27.3 vs 26.9% (MIDB)] and [16.1% vs 14.8% (CARES)] respectively and Survive [30.8% vs 30.3% (MIDB)] and [27.3 vs 28.1% (CARES)] respectively). Conclusion: Despite missing EMS documentation in 22% of OHCA cases, and only modest agreement between methods of race documentation, our analysis did not show significant variation in OHCA outcome measures between databases. Further analysis is needed to determine the true impact of missing documentation of race on the study of racial outcome measures following OHCA.

Infectious Diseases

Hagerman TK, **Mumby K**, Brar I, Markowitz N, **Miller J**, and **Manteuffel J**. Connecting patients diagnosed with human immunodeficiency virus in the emergency department to care during the COVID-19 pandemic. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S173-S174.

T.K. Hagerman, Henry Ford Health System

Background and Objectives: The ED has been identified as an important location for HIV screening, yet little is known about the impact of the COVID-19 pandemic on ED based HIV screening programs. We hypothesized that our electronic medical record (EMR) triggered HIV screening program would continue to identify new HIV positive patients and link them to care during the COVID-19 pandemic. Methods: We conducted a retrospective chart review of ED patients screened for HIV and compared the average monthly tests performed, number of confirmed HIV positive cases, and rates of linkage to care before and

after the onset of the COVID-19 pandemic. We used 3/13/2020 as the start date for the pandemic and compared data in a 5-month period prior to the pandemic (limited to initiation of EMR triggered HIV screening) and a 9-month period during the pandemic. Two tailed t-tests were used for comparison of means. Results: A total of 20,825 patients were screened for HIV from 11/18/2019 to 12/12/2020 (8,417 pre-pandemic and 12,408 during the pandemic). On average, more HIV screening tests were performed in the pre-pandemic period compared to the pandemic period (1,683/month pre-pandemic versus 1,379/month during pandemic). However, when accounting for ED volume changes, a similar rate of patients in the pre-pandemic period (35.8% of all patients seen in the ED) were screened compared to during the pandemic (34.7% of all patients seen). In the pre-pandemic period 11/18/2020 -3/ 12/2020, a total of 25 patients were diagnosed with HIV and all patients were linked to care. In the pandemic period 3/13/2020 -12/ 12/2020, 27 patients were diagnosed with HIV. Of the 27 patients diagnosed, 22 (81%) were linked to care. Two patients died prior to attending specialist appointments during the pandemic (88% linkage to care accounting for deaths). The average time to the first attended specialist appointments for non-admitted patients was not significantly greater during the pandemic period (6.0 days pre-pandemic vs. 6.9 days during pandemic, p = 0.55). Conclusion: EMR generated HIV screening allows for continued efforts to diagnose and link patients to care despite the global disruptions caused by the COVID-19 pandemic. These efforts are critical to the mission to end the HIV epidemic by 2030.

Internal Medicine

Do AP, and **Holbrook M**. A RARE CASE OF EARLY CARDIAC TAMPONADE CAUSED BY SEVERE POSTOPERATIVE HYPOTHYROIDISM TWO YEARS AFTER OPERATION. *Journal of the American College of Cardiology* 2021; 77(18):2287.

Background Hypothyroidism (HT) is a disease with many clinical presentations. Among those, pericardial effusion (PEff) is a rare presenting finding detected in patients with severe HT. It is typically mild but rarely can cause cardiac tamponade. This case will highlight that severe HT can manifest as myxedema with heart failure symptoms and PEff. Case A 49 years old female with HT from total thyroidectomy two years prior, presented with shortness of breath and orthopnea. The patient ran out of levothyroxine several months ago. She was found to be hypoxic requiring oxygen. Physical exam showed expiratory wheezes, bilateral lower extremity non-pitting edema. TSH was 260uIU/mL and free T4<0.25ng/dL. BNP and troponin were unremarkable. CXR showed marked enlargement of the cardiac silhouette which were confirmed to be moderate PEff with findings of early tamponade on transthoracic echocardiogram (TTE). This was determined to be due to severe HT. She was started on IV levothyroxine which was transitioned to oral medication with improvement of symptoms. Serial TTE showed stable effusion without evidence of tamponade. She was discharged to follow up TTE in the next month. Decision-making Etiology of non-traumatic PEff is most commonly due to infarction, pericarditis, malignancy, infection or uremia. Rarely, severe HT represents itself as moderate size PEff as demonstrated in this case. The initial echo showed early signs of cardiac tamponade which can be a detrimental complication if it continues to worsen. When cardiac tamponade occurs, urgent TTE with pericardiocentesis or creation of a pericardial window along with IV thyroxine therapy is the treatment of choice. The IV administration of both T3 and T4 is important as gut absorption might be impaired in this patient population. If tamponade has not occurred, conservative treatment with thyroid supplementation and follow-up TTE to monitor for resolution of the effusion is often enough. Conclusion Even though uncommon, PEff in the setting of severe HT is a potential cause of tamponade if it went undiagnosed. Prompt TTE to determine the severity of the effusion and IV thyroxine is the remained the most crucial steps in management.

Internal Medicine

Gupta K, Nagalli S, Kalra R, Zhou W, Gupta R, Prabhu S, and Bajaj N. ASSOCIATION BETWEEN BASELINE CARDIOVASCULAR RISK AND SLEEP DURATION IN AMBULATORY US ADULTS: INSIGHTS FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY. *Journal of the American College of Cardiology* 2021; 77(18):10.

Background Baseline CV risk may partially explain the significant variability in sleep duration across a population. We evaluated the association between baseline CV risk and self-reported sleep duration. Methods We used data from National Health and Nutrition Examination Survey (NHANES) 2005-2010 and linked cause of death from National Center for Health Statistics for adults aged ≥18 years. The 10-

year atherosclerotic CV disease risk score (ASCVD) was used to assess baseline CV risk and self-reported sleep duration was the outcome. We excluded participants with prevalent CV disease, defined as self-reported coronary artery disease, heart failure or stroke. Continuous variables were represented as medians with interquartile range (IQR). Non-linearity was accounted for using restricted cubic spline models. Results There were 14,079 eligible participants. Mean age was 46±19 years with 52% women and 46% non-Hispanic Whites. The median 10-year ASCVD risk was 3.5% (0.5, 14.4). There was a U-shaped relationship with 10-year ASCVD risk score and the sleep duration such that participants with a sleep-duration of 6-7 hours had the lowest risk (P-trend<0.001, Figure). The median 10-year ASCVD risk among participants with <6, 6-7 and >7 hours of sleep were 4.6% (0.9, 15.7), 3.3% (0.6, 12.3) and 3.3% (0.4, 17.3), respectively. Conclusion Least 10-year ASCVD risk is associated with a self-reported sleep duration of 6-7 hours in ambulatory US adults without prevalent CV disease. [Formula presented]

Internal Medicine

Mohammed M, **Sirdenis N**, **Gorgis S**, **Azzo Z**, and **Parikh S**. TWO VARIANTS OF TAKOTSUBO CARDIOMYOPATHY IN A YOUNG WOMAN WITH ALCOHOL WITHDRAWAL. *Journal of the American College of Cardiology* 2021; 77(18):2250.

Background Takotsubo cardiomyopathy (TCM) is characterized by transient left ventricular dysfunction and often mimics acute coronary syndrome. Although there are four echocardiographic patterns of TCM, patients typically present with one variant. Case A 32-year-old woman with alcohol use disorder presented with shortness of breath, nausea, vomiting, and malaise. She had tremors concerning for alcohol withdrawal and was found to be hypoxic with a chest X-ray showing pulmonary edema. She had elevated troponin, BNP, and lactate. Electrocardiogram showed no ischemic changes. The patient developed acute respiratory failure and required intubation. Transthoracic echocardiogram (TTE) showed an ejection fraction (EF) of 22% with global hypokinesis of the left ventricle, apical ballooning and preserved basal function. Cardiac catheterization showed no coronary artery disease. Decision-making The patient made hemodynamic and symptomatic improvement and in three days the EF improved to 50%. She was diagnosed with classical TCM in the setting of alcohol withdrawal. Four months after the initial presentation, she presented again with palpitations, diaphoresis, tremors and sharp chest pain. The patient reported alcohol cessation for three days following two months of heavy alcohol use. She had elevated BNP, troponin and lactate. Electrocardiogram showed ST segment depression in leads V3-V5. TTE showed an EF of 38% with severe hypokinesis of basal to mid left ventricular wall consistent with reverse TCM. The patient was treated for acute decompensated heart failure in the setting of alcohol withdrawal and had symptomatic improvement in few days. Conclusion TCM has been described to occur in various morphologies but only rare cases have shown multiple variants in one individual. We present a rare case of one patient with two distinct variants of TCM during two separate episodes of alcohol withdrawal. Although the mechanism is unclear, we suspect that the combination of genetic predisposition and adrenergic response in substance abuse may play a role in our case.

Public Health Sciences

Lanfear DE, **Gui H**, **Hannawi B**, **Connolly T**, **Li J**, **She R**, **Pereira N**, **Adams K**, **Hernandez A**, **Luzum J**, **Francke S**, **Tang WH**, and **Williams LK**. PHARMACOGENOMIC ANALYSES IN ASCEND-HF INDICATE INFLUENCE OF NPR3ON NESIRITIDE BLOOD PRESSURE EFFECT. *Journal of the American College of Cardiology* 2021; 77(18):840.

Background The Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) randomized hospitalized HF patients to nesiritide or placebo and found no survival difference, but some data suggests genetic variation may influence nesiritide effect. We explored if genetic factors are associated with treatment effects on blood pressure (BP) in ASCEND-HF. Methods A genetic substudy was conducted including 2680 participants (2173 European Ancestry [EA] and 507 African Ancestry [AA]) that underwent genome-wide (GW) genotyping using Axiom Biobank Array (Affymetrix) and imputation via 1000 Genome reference panels. BP change was defined as systolic BP at 0.5 and 1 hour of nesiritide infusion minus baseline. We tested candidate SNPs in four genes of the BNP pathway (NPR1, NPR2, NPR3 and MME) and performed an unbiased GW association study. Linear mixed models, stratified by race, were used to estimate SNP*nesiritide interaction effects on BP change adjusting for SNP, nesiritide, sex, BMI, HTN, and top five genetic principal components. Overall results

(both races) were obtained by meta-analysis. Significance was set at 0.0125 and 5.0x10-8 for candidate and GW study, respectively. Analysis of mortality or re-hospitalization was performed for significant SNPs. Results Candidate gene analysis showed two SNPs (rs3792761, minor allele frequency (MAF)=0.18 in EA, 0.37 in AA; rs817893, MAF=0.22 in EA, 0.42 in AA) that had significant interactions with nesiritide on BP (β=2.87, p=0.005 for rs3792761; β=2.26, p=0.012 for rs817893). However, these SNPs were not linked to mortality or re-hospitalization (HR=1.09, p=0.26 for rs3792761; HR=1.07, p=0.34 for rs817893). There were no loci meeting GW significance in either ancestral group nor in the meta-analysis, though a few suggestive hits were identified with p<1x10-5. Conclusion Our data indicate there could be pharmacogenomic interactions where NPR3 sequence variants modify the impact of BNP infusion. Further investigation to define responders vs. non-responders may be warranted.

Public Health Sciences

Nowak RM, Peacock F, **Jacobsen G**, Limkakeng AT, Christenson R, Singer AJ, **McCord J**, Apple FS, and DeFilippi C. Indeterminate zone high-sensitivity troponin levels in a rapid acute myocardial infarction assessment algorithm and patient dispositions. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S206.

R.M. Nowak, Henry Ford Health System

Background and Objectives: The multicenter High Sensitivity Cardiac Troponin I (hs-cTnI) in the United States (HIGH-US) study reported a 1-hour Emergency Department (ED) hs-cTnI algorithm for the assessment of acute myocardial infarction (AMI). However, 783 (37.1%) patients were placed in the algorithm's indeterminate zone, not meeting the rule-out or rule-in criteria. Our objectives were to describe the AMI and 30-day AMI/death rates and clinical characteristics of these patients placed in observation/inpatient beds (OBS/ADM) compared to having an ED discharge (EDD). Methods: In this prospective cohort study 2113 consenting adults with any symptoms suspicious for AMI were enrolled from 2015-2016 in 29 US medical centers. There were no patient exclusion criteria. Baseline and 1-hour plasma samples were analyzed using the Siemens Atellica hs-cTnI assay (99th % = 47.0 ng/L), with results not available to the treating physician. AMI diagnosis was independently adjudicated using local contemporary troponin assays and all 30-day clinical data available. Patients were placed in OBS/ADM or had EDD according to each site's clinical practice. Stepwise logistic regression modeling was used to determine which of 25 clinical patient characteristics were associated with OBS/ADM disposition decisions. Results: Of 763 (30.3%) of the intermediate zone placed patients with complete data available, 532 (69.7 %) were placed in OBS/ ADM and 231 (30.3%) had an EDD. Adjudicated AMI rates and 30-day AMI/death rates were different in these 2 groups (41 [7.7%], 2 [0.9%], p = 0.001 and 15 [2.8%], 1 [0.4%] respectively, p = 0.050). The clinical variables associated with OBS/ADM placement were age, hypertension, eGFR < 60, abnormal ECG, and previous revascularization (odds ratio estimates of 1.027, 1.764, 1.955, 1.700 and 1.620 respectively). The OBS/ADM to EDD ratios varied widely amongst the participating centers (100.0-50.0%). Conclusion: The correct disposition decision for patients not ruling out or ruling in for AMI using a 1-hour hs-cTnI algorithm remains unclear. ED physicians, using contemporary troponin assays and clinical evaluations for 231 patients with EDD but who were placed in the hs-cTnI algorithm intermediate zone, missed 1 (0.4%) AMI, with 15 (2.8%) patients having 30-day AMI/death. The absence of our reported cardiac risk factors likely contributed to the EDD decision. Further studies are needed to validate our results.

HFHS Publications on COVID-19

Cardiology/Cardiovascular Research
Duran AT, Kronish I, **Keteyian SJ**, Ye SQ, Stavrolakes K, West H, and Moise N. The implications of COVID-19 on cardiac rehabilitation: The need for theory-driven, telehealth-enhanced, non-traditional models. *Implementation Science* 2021; 16(SUPPL 1):1.

Cardiology/Cardiovascular Research
Rizik DG, Rao SV, Stone GW, Burke RF, Hermiller JB, and **O'Neill WW**. Re-instituting a live cardiology meeting without symptomatic COVID-19 transmission. *Catheter Cardiovasc Interv* 2021; Epub ahead of print. PMID: 33984174. Full Text

Dermatology
Narla S, Watchmaker J, **Ozog DM**, and Rohrer TE. Cosmetic Practices in the COVID-19 Era. *Advances in Cosmetic Surgery* 2021; 4(1):109-121. PMID: Not assigned. Full Text

Dermatology
Rodrigues M, Pandya AG, **Hamzavi I**, Ezzedine K, Bekkenk MW, and Harris JE. Treatment recommendations for patients with vitiligo during COVID-19. *Australas J Dermatol* 2021; Epub ahead of print. PMID: 34028796. Full Text

Emergency Medicine
Chan JC, Davenport M, Schmitt TW, Lee HM, Abbas T, Hayes AK, Adamakos FJ, **Axelson DJ**, and Salvo MB. Slack intern curriculum supports intern preparedness and bridges curriculum gaps due to COVID-19 pandemic. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S346-S347.

Emergency Medicine
Grahf D, **Dandashi J**, **Vohra T**, **Deledda J**, and **Vallee P**. Health care provider absences and intervenable areas during a COVID-19 surge. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S155.

Emergency Medicine
Hagerman TK, **Mumby K**, Brar I, Markowitz N, **Miller J**, and **Manteuffel J**. Connecting patients diagnosed with human immunodeficiency virus in the emergency department to care during the COVID-19 pandemic. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S173-S174.

Emergency Medicine
Klausner HA, **Rockoff S**, **Beyer M**, and **Clayton P**. Review of patient care at the TCF Center Alternative Care Facility during the COVID-19 pandemic. *Academic Emergency Medicine* 2021; 28(SUPPL 1):S393-S394.

Gastroenterology
Siddiqui MA, **Suresh S**, **Simmer S**, **Abu-Ghanimeh M**, **Karrick M**, **Nimri F**, **Musleh M**, **Mediratta V**, **Al-Shammari M**, **Russell S**, **Jou J**, **Dang D**, **Salgia R**, and **Zuchelli T**. Increased Morbidity and Mortality in COVID-19 Patients with Liver Injury. *Dig Dis Sci* 2021;1-7. Epub ahead of print. PMID: 33945064. Full Text

Hematology-Oncology
Hwang C, Izano MA, Thompson MA, **Gadgeel SM**, Weese JL, **Mikkelsen T**, Schrag A, Teka M, Walters S, Wolf FM, Hirsch J, Rivera DR, Kluetz PG, Singh H, and Brown TD. Rapid real-world data analysis of patients with cancer, with and without COVID-19, across distinct health systems. *Cancer Rep (Hoboken)* 2021;e1388. Epub ahead of print. PMID: 34014037. Full Text

Infectious Diseases

Heldman MR, Kates OS, Safa K, Kotton CN, Georgia SJ, Steinbrink JM, Alexander BD, Hemmersbach-Miller M, Blumberg EA, Crespo MM, Multani A, Lewis AV, Beaird OE, Haydel B, La Hoz RM, Moni L, Condor Y, Flores S, Munoz CG, Guitierrez J, Diaz EI, Diaz D, Vianna R, Guerra G, Loebe M, Rakita RM, Malinis M, Azar MM, Hemmige V, McCort ME, **Chaudhry ZS**, Singh P, Hughes K, Velioglu A, Yabu JM, Morillis JA, Mehta SA, Tanna SD, Ison MG, Tomic R, Derenge AC, van Duin D, Maximin A, Gilbert C, Goldman JD, Sehgal S, Weisshaar D, Girgis RE, Nelson J, Lease ED, Fisher CE, and Limaye AP. Covid-19 in hospitalized lung and non-lung solid organ transplant recipients: a comparative analysis from a multicenter study. *Am J Transplant* 2021; Epub ahead of print. PMID: 34008917. Full Text

Neurology

Hwang C, Izano MA, Thompson MA, **Gadgeel SM**, Weese JL, **Mikkelsen T**, Schrag A, Teka M, Walters S, Wolf FM, Hirsch J, Rivera DR, Kluetz PG, Singh H, and Brown TD. Rapid real-world data analysis of patients with cancer, with and without COVID-19, across distinct health systems. *Cancer Rep (Hoboken)* 2021;e1388. Epub ahead of print. PMID: 34014037. Full Text

Pharmacy

Kalus JS, Dagam JK, Hoying M, Erdman D, Mieure KD, Melroy MJ, Beehrle-Hobbs D, and Silvester JA. Enhancing pharmacy residency training program quality and efficiency through alignment of pharmacy residency programs within a multihospital health system. *Am J Health Syst Pharm* 2021; Epub ahead of print. PMID: 33999157. Full Text

Pharmacy

Kwiatkowski S, **Mulugeta S**, **Davis S**, **Kenney R**, **Kalus J**, Walton L, and **Patel N**. Optimizing preoperative antibiotics in patients with β-lactam allergies: A role for pharmacy. *Am J Health Syst Pharm* 2021; Epub ahead of print. PMID: 34037708. Full Text