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Henry Ford Health System

Henry Ford Health System Publication List – September 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 **149 unique citations** listed this month, with **12 articles** and **3 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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Articles

Conference Abstracts

Articles

Anesthesiology

Acho C, **Morita Y**, **Fernandez V**, **Safwan M**, **Galusca D**, **Abouljoud M**, **Yoshida A**, **El-Bashir J**, and **Nagai S**. Immediate Postoperative Extubation Decreases Pulmonary Complications in Liver Transplant Patients. *Transplantation* 2021; 105(9):2018-2028. PMID: 32890127. Full Text

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BACKGROUND: Fast-track anesthesia in liver transplantation (LT) has been discussed over the past few decades; however, factors associated with immediate extubation after LT surgery are not well defined. This study aimed to identify predictive factors and examine impacts of immediate extubation on post-LT outcomes. METHODS: A total of 279 LT patients between January 2014 and May 2017 were included. Primary outcome was immediate extubation after LT. Other postoperative outcomes included reintubation, intensive care unit stay and cost, pulmonary complications within 90 days, and 90-day graft survival. Logistic regression was performed to identify factors that were predictive for immediate extubation. A matched control was used to study immediate extubation effect on the other postoperative outcomes. RESULTS: Of these 279 patients, 80 (28.7%) underwent immediate extubation. Patients with anhepatic time >75 minutes and with total intraoperative blood transfusion ≥12 units were less likely to be immediately extubated (odds ratio [OR], 0.48; 95% confidence interval [CI], 0.26-0.89; P = 0.02; OR, 0.11; 95% CI, 0.05-0.21; P < 0.001). The multivariable analysis showed immediate extubation significantly decreased the risk of pulmonary complications (OR, 0.34; 95% CI, 0.15-0.77; P = 0.01). According to a matched case-control model (immediate group [n = 72], delayed group [n = 72]), the immediate group had a significantly lower rate of pulmonary complications (11.1% versus 27.8%; P = 0.012). Intensive care unit stay and cost were relatively lower in the immediate group (2 versus 3 d; P = 0.082; $5700 versus $7710; P = 0.11). Reintubation rates (2.8% versus 2.8%; P > 0.9) and 90-day graft survival rates (95.8% versus 98.6%; P = 0.31) were similar. CONCLUSIONS: Immediate extubation post-LT in appropriate patients is safe and may improve patient outcomes and resource allocation.

Behavioral Health Services/Psychiatry/Neuropsychology

Bryce R, WolfsonBryce JA, CohenBryce A, Milgrom N, Garcia D, Steele A, **Yaphe S**, Pike D, **Valbuena F**, and **Miller-Matero LR**. A pilot randomized controlled trial of a fruit and vegetable prescription program at a federally qualified health center in low income uncontrolled diabetics. *Prev Med Rep* 2021; 23:101410. PMID: 34150472. Full Text

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Eating a healthy diet is important for managing diabetes. Although there are high rates of diabetes in low-income urban areas, these patients often have limited access to fruits and vegetables. The 15-week Fresh Prescription (Fresh Rx) program was designed to improve access and consumption of fruits and vegetables among low-income patients with diabetes in Detroit, MI. The purpose of this study was to evaluate the effects of a fruit and vegetable prescription program on changes in hemoglobin A1C

(HbA(1)C), blood pressure (BP), and body mass index (BMI) in patients with diabetes in a randomized controlled trial at a federally qualified health center (FQHC). Patients randomized to the Fresh Rx group (n = 56) were allotted up to $80 ($10 for up to eight weeks) for purchase of produce from a farmers market based at the FQHC. The control group (n = 56) received standard treatment plus information on community resources to improve health. Outcomes were compared at baseline and within three months of program completion. There were no significant between-group differences for any of the outcomes at program completion (p > .05); however, there was a small effect size for HbA1c (partial η(2) = 0.02). Within the Fresh Rx group, HbA1c significantly decreased from 9.64% to 9.14% (p = 0.006). However, no changes were noted within the control group (9.38 to 9.41%, p = 0.89). BMI and BP did not change from pre- to post-study in either group (p > .05). Results from this study offer preliminary evidence that produce prescription programs may reduce HbA(1)C in low-income patients with diabetes.

Behavioral Health Services/Psychiatry/Neuropsychology
Katato HK, **Gautam M**, and **Akinyemi EO**. The Danger of Face Masks on an Inpatient Psychiatric Unit: New Protocol to Prevent Self-harm. *Prim Care Companion CNS Disord* 2021; 23(5). PMID: 34474509. Request Article

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Behavioral Health Services/Psychiatry/Neuropsychology
MacLean L, and Prabhakar D. Attention-Deficit/Hyperactivity Disorder and Sports: A Lifespan Perspective. *Psychiatr Clin North Am* 2021; 44(3):419-430. PMID: 34372998. Full Text

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Attention-deficit/hyperactivity disorder (ADHD), characterized by inattention, impulsivity and hyperactivity is a major health problem. This paper discusses ADHD across the life span and looks at the impact of debilitating symptoms, diagnosis, and treatment in athletes. Psychosocial interventions, with or without psychopharmacology including stimulants and nonstimulants, are discussed to help athletes achieve their highest level of symptom abatement and functioning. The age of the patient, the sport played, the athlete's overall health, and the regulations of the sport-governing body play a role in determining the most appropriate treatment.

Cardiology/Cardiovascular Research
Alonso WW, Kupzyk KA, Norman JF, Lundgren SW, Fisher A, Lindsey ML, **Keteyian SJ**, and Pozehl BJ. The HEART Camp Exercise Intervention Improves Exercise Adherence, Physical Function, and Patient-Reported Outcomes in Adults With Preserved Ejection Fraction Heart Failure. *J Card Fail* 2021; Epub ahead of print. PMID: 34534664. Full Text

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BACKGROUND: Despite exercise being one of few strategies to improve outcomes for individuals with heart failure with preserved ejection fraction (HFpEF), exercise clinical trials in HFpEF are plagued by poor interventional adherence. Over the last 2 decades, our research team has developed, tested, and refined Heart failure Exercise And Resistance Training (HEART) Camp, a multicomponent behavioral intervention to promote adherence to exercise in HF. We evaluated the effects of this intervention designed to promote adherence to exercise in HF focusing on subgroups of participants with HFpEF and heart failure with reduced ejection fraction (HFrEF). METHODS AND RESULTS: This randomized controlled trial included 204 adults with stable, chronic HF. Of those enrolled, 59 had HFpEF and 145 had HFrEF. We tested adherence to exercise (defined as ≥120 minutes of moderate-intensity [40%-80% of heart rate reserve] exercise per week validated with a heart rate monitor) at 6, 12, and 18 months. We also tested intervention effects on symptoms (Patient-Reported Outcomes Measurement Information System-29 and dyspnea-fatigue index), HF-related health status (Kansas City Cardiomyopathy Questionnaire), and physical function (6-minute walk test). Participants with HFpEF (n = 59) were a mean of 64.6 ± 9.3 years old, 54% male, and 46% non-White with a mean ejection fraction of 55 ± 6%. Participants with HFpEF in the HEART Camp intervention group had significantly greater adherence compared with enhanced usual care at both 12 (43% vs 14%, phi = 0.32, medium effect) and 18 months (56% vs 0%, phi = 0.67, large effect). HEART Camp significantly improved walking distance on the 6-minute walk test ($\eta(2) = 0.13$, large effect) and the Kansas City Cardiomyopathy Questionnaire overall ($\eta(2) = 0.09$, medium effect), clinical summary ($\eta(2) = 0.16$, large effect), and total symptom ($\eta(2) = 0.14$, large effect) scores. In the HFrEF subgroup, only patient-reported anxiety improved significantly in the intervention group. CONCLUSIONS: A multicomponent, behavioral intervention is associated with improvements in long-term adherence to exercise, physical function, and patient-reported outcomes in adults with HFpEF and anxiety in HFrEF. Our results provide a strong rationale for a large HFpEF clinical trial to validate these findings and examine interventional mechanisms and delivery modes that may further promote adherence and improve clinical outcomes in this population. CLINICAL TRIAL REGISTRATION: URL: https://clinicaltrials.gov/. Unique identifier: NCT01658670.

Cardiology/Cardiovascular Research

Arman P, **Basir MB**, Gupta A, Choi JW, Khatri JJ, Jaffer FA, Poomipanit P, Forouzandeh F, Koutouzis M, Tsiafoutis I, Patel M, Mahmud E, Vemmou E, Nikolakopoulos I, Karacsonyi J, ElGuindy A, Goktekin O, Abi Rafeh N, Brilakis ES, and **Alaswad K**. Procedural and In-Hospital Outcomes of Chronic Total Occlusion Percutaneous Coronary Interventions in Patients With Acute Myocardial Infarction: Insights From a Prospective Multicenter International Registry. *J Invasive Cardiol* 2021; 33(9):E670-e676. PMID: 34473071. Request Article

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BACKGROUND: We sought to examine the procedural and clinical outcomes of patients who underwent chronic total occlusion (CTO) percutaneous coronary intervention (PCI) in the setting of acute myocardial infarction (AMI). METHODS: We assessed the clinical and procedural characteristics, technical success, procedural success, and in-hospital outcomes of 2314 patients who underwent CTO-PCI at 20 experienced centers between 2012 and 2017, classified according to whether or not they presented with AMI. RESULTS: Mean patient age was 65 ± 10 years, 85% were men, and 154 (6.7%) presented with AMI (5.5% with non-ST segment elevation myocardial infarction, 1.1% with ST-segment elevation myocardial infarction). Compared with non-AMI patients who underwent CTO-PCI, AMI patients had higher prevalence of diabetes (56% vs 42%; P<.01) and lower median left ventricular ejection fraction (48% vs 54%; P<.001). The CTO angiographic characteristics were similar between the 2 groups. Compared with non-AMI patients undergoing CTO-PCI, AMI patients had more frequent use of antegrade wire escalation (86.0% vs 78.9%; P=.03) and more frequent use of hemodynamic support devices (16.2% vs 3.4%; P<.01), and were more likely to have a non-CTO lesion treated (34.0% vs 26.6%; P=.03). AMI and non-AMI patients had similar technical success (90% vs 87%; P=.26), procedural success (88% vs 85%; P=.38), and incidence of in-hospital MACE (2.6% vs 2.5%; P=.94). CONCLUSION: CTO-PCI is performed infrequently in AMI patients and is associated with similar technical and procedural success rates and in-hospital major adverse cardiovascular event rates when compared with CTO-PCI performed in non-AMI patients.

Cardiology/Cardiovascular Research

Arno S, and **Cowger J**. The genetics of cardiac amyloidosis. *Heart Fail Rev* 2021; Epub ahead of print. PMID: 34518987. Full Text

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Heritable cardiac amyloidosis (CA) is an underrecognized cause of morbidity and mortality in the USA. It results from the accumulation of the misfolded protein transthyretin within the myocardium, resulting in amyloid transthyretin-associated cardiomyopathy (ATTR-CM). Over 150 different pathologic point mutations within the transthyretin gene have been identified, each carrying variable clinical phenotypes and penetrance. In the USA, the most common cause of hereditary ATTR is the Val122Ile point mutation, with a prevalence of 3.4-4.0% in North Americans of African and Caribbean descent. Among Caucasians with hereditary ATTR-CM, the V30M mutation is the most commonly identified variant. Overall, the incidence of ATTR disease in the USA has been increasing, likely due to an increase in practitioner awareness, utilization of new non-invasive imaging technologies for ATTR diagnosis, and the growth of multidisciplinary amyloid programs across the country. Yet significant numbers of patients with evidence of left ventricular thickening on cardiac imaging, senile aortic stenosis, and/or symptoms of heart failure with preserved ejection fraction likely have undiagnosed CA, especially within the African American population. With the emergence of new disease-modifying therapies for ATTR, recognition and the prompt diagnosis of CA is important for patients and their potentially affected progeny. Herein, we review the genetics of heritable CA as well as the importance of genetic counseling and testing for patients and their families.

Cardiology/Cardiovascular Research

Beatty AL, Brown TM, Corbett M, Diersing D, **Keteyian SJ**, Mola A, Stolp H, Wall HK, and Sperling LS. Million Hearts Cardiac Rehabilitation Think Tank: Accelerating New Care Models. *Circ Cardiovasc Qual Outcomes* 2021; Epub ahead of print. PMID: 34587751. Full Text

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This article describes the October 2020 proceedings of the Million Hearts Cardiac Rehabilitation Think Tank: Accelerating New Care Models, convened with representatives from professional organizations, cardiac rehabilitation (CR) programs, academic institutions, federal agencies, payers, and patient representative groups. As CR delivery evolves, terminology is evolving to reflect not where activities occur (eg, center, home) but how CR is delivered: in-person synchronous, synchronous with real-time audiovisual communication (virtual), or asynchronous (remote). Patients and CR staff may interact through ≥1 delivery modes. Though new models may change how CR is delivered and who can access CR, new models should not change what is delivered-a multidisciplinary program addressing CR core components. During the coronavirus disease 2019 (COVID-19) public health emergency, Medicare issued waivers to allow virtual CR; it is unclear whether these waivers will become permanent policy post-public health emergency. Given CR underuse and disparities in delivery, new models must equitably address patient and health system contributors to disparities. Strategies for implementing new CR care models address safety, exercise prescription, monitoring, and education. The available evidence supports the efficacy and safety of new CR care models. Still, additional research should study diverse populations, impact on patient-centered outcomes, effect on long-term outcomes and health care utilization, and implementation in diverse settings. CR is evolving to include in-person synchronous,

virtual, and remote modes of delivery; there is significant enthusiasm for implementing new care models and learning how new care models can broaden access to CR, improve patient outcomes, and address health inequities.

Cardiology/Cardiovascular Research
Chu DJ, Ahmed AM, Qureshi WT, **Brawner CA**, **Keteyian SJ**, Nasir K, Blumenthal RS, Blaha MJ, **Ehrman JK**, Cainzos-Achirica M, Patel KV, Rifai MA, and Al-Mallah MH. Prognostic Value of Cardiorespiratory Fitness in Patients with Chronic Kidney Disease: The FIT (Henry Ford Exercise Testing) Project. *Am J Med* 2021; Epub ahead of print. PMID: 34509447. Full Text

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PURPOSE: To study the association of cardiorespiratory fitness (cardiorespiratory fitness) and all-cause mortality among patients with chronic kidney disease. METHODS: We studied a retrospective cohort of patients from the Henry Ford Health System who underwent clinically indicated exercise stress testing with baseline cardiorespiratory fitness and estimated glomerular filtration rate measurement. Cardiorespiratory fitness was expressed as metabolic equivalents of task and kidney function was categorized into stages according to estimated glomerular filtration rate. Multivariable-adjusted Cox proportional hazard models were used to examine the association between metabolic equivalents of task and all-cause mortality among patients with chronic kidney disease stages 3 to 5. Discrimination of mortality was assessed using receiver operating characteristic curves, while reclassification was evaluated using net reclassification index (NRI). RESULTS: Among 50,121 participants, the mean age was 55 ± 12.6 years, 47.5% were women, 64.5% were white, and 6,877 (13.7%) participants had chronic kidney disease stage 3-5. Over a median follow-up of 6.7 years, 6,308 participants died (12.6%). Each 1-unit higher metabolic equivalents of task was associated with a significant 15% reduction in all-cause mortality (Hazard Ratio = 0.85, 95% Confidence Interval [CI] 0.84-0.87). Metabolic equivalents of task improved discriminatory ability of mortality prediction when added to traditional risk factors and estimated glomerular filtration rate (area under the curve=0.7996; 95% CI 0.789-0.810 vs 0.759; 95% CI 0.748-0.770, respectively; p-value <0.001). The addition of metabolic equivalents of task to traditional risk factors resulted in significant reclassification (6% for events, 5% for non-events: NRI = 0.13, p-value <0.001). CONCLUSIONS: Cardiorespiratory fitness improves mortality risk prediction among patients with chronic kidney disease. Cardiorespiratory fitness provides incremental prognostic information when added to traditional risk factors and may help guide treatment options among patients with renal dysfunction.

Cardiology/Cardiovascular Research
Kandzari DE, **Alaswad K**, Jaffer FA, Brilakis E, Croce K, Kearney K, Spaedy A, Yeh R, Thompson C, Nicholson W, Wyman RM, Riley R, Lansky A, Buller C, and Karmpaliotis D. Safety and efficacy of dedicated guidewire, microcatheter, and guide catheter extension technologies for chronic total coronary occlusion revascularization: Primary results of the Teleflex Chronic Total Occlusion Study. *Catheter Cardiovasc Interv* 2021; Epub ahead of print. PMID: 34582080. Full Text

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BACKGROUND: Description of procedural outcomes using contemporary techniques that apply specialized coronary guidewires, microcatheters, and guide catheter extensions designed for chronic total occlusion (CTO) percutaneous revascularization is limited. METHODS: A prospective, multicenter, single-arm study was conducted to evaluate procedural and in-hospital outcomes among 150 patients undergoing attempted CTO revascularization utilizing specialized guidewires, microcatheters and guide extensions. The primary endpoint was defined as successful guidewire recanalization and absence of in-hospital cardiac death, myocardial infarction (MI), or repeat target lesion revascularization (major adverse cardiac events, MACE). RESULTS: The prevalence of diabetes was 32.7%; prior MI, 48.0%; and previous bypass surgery, 32.7%. Average (mean ± standard deviation) CTO length was 46.9 ± 20.5 mm, and mean J-CTO score was 1.9 ± 0.9. Combined radial and femoral arterial access was performed in 50.0% of cases. Device utilization included: support microcatheter, 100%; guide catheter extension, 64.0%; and mean number of study guidewires/procedure was 4.8 ± 2.6. Overall, procedural success was achieved in 75.3% of patients. The rate of successful guidewire recanalization was 94.7%, and in-hospital MACE was 19.3%. Achievement of TIMI grade 2 or 3 flow was observed in 93.3% of patients. Crossing strategies included antegrade (54.0%), retrograde (1.3%) and combined antegrade/retrograde techniques (44.7%). Clinically significant perforation resulting in hemodynamic instability and/or requiring intervention occurred in 16 (10.7%) patients. CONCLUSIONS: In a multicenter, prospective registration study, favorable procedural success was achieved despite high lesion complexity using antegrade and retrograde guidewire maneuvers and with acceptable safety, yet with comparably higher risk than conventional non-CTO PCI.

Cardiology/Cardiovascular Research

Lampert BC, Teuteberg JJ, **Cowger J**, Mokadam NA, Cantor RS, Benza RL, Ganapathi AM, Myers SL, Hiesinger W, Woo J, Pagani F, Kirklin JK, and Whitson BA. Impact of thoracotomy approach on right ventricular failure and length of stay in left ventricular assist device implants: an intermacs registry analysis. *J Heart Lung Transplant* 2021; 40(9):981-989. PMID: 34229917. Full Text

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INTRODUCTION: Traditionally, implantation of Left Ventricular Assist Devices (LVADs) is performed via median sternotomy. Recently, less invasive thoracotomy approaches are growing in popularity as they involve less surgical trauma, potentially less bleeding, and may preserve right ventricular function. We hypothesized implantation of LVADs via thoracotomy has less perioperative right ventricular failure (RVF) and shorter postoperative length of stay (LOS). METHODS: Continuous flow LVAD implants from Intermacs between February 6, 2014 - December 31, 2018 were identified. Patients implanted via

thoracotomy were propensity matched in a 1:1 ratio with patients implanted via sternotomy. Outcomes were compared between sternotomy and thoracotomy approach and by device type (axial, centrifugal-flow with hybrid levitation (CF-HL), centrifugal-flow with full magnetic levitation devices (CF-FML)). The primary outcome was time to first moderate or severe RVF. Secondary outcomes included survival and LOS. RESULTS: Overall 978 thoracotomy patients were matched with 978 sternotomy patients. Over the study period, 242 thoracotomy patients and 219 sternotomy patients developed RVF with no significant difference in time to first moderate to severe RVF by surgical approach overall (p = 0.27) or within CF-HL (p = 0.36) or CF-FML devices (p = 0.25). Survival did not differ by implant technique (150 deaths in thoracotomy group, 154 deaths in sternotomy group; p = 0.58). However, sternotomy approach was associated with a significantly shorter LOS (17 Vs 18 days, p = 0.009). CONCLUSION: As compared to sternotomy, implantation of continuous flow LVADs via thoracotomy approach does not reduce moderate to severe RVF or improve survival but does reduce post-operative LOS. Device type did not influence outcomes and most centers did a small volume of thoracotomy implants.

Cardiology/Cardiovascular Research

Lumbers RT, Shah S, Lin H, Czuba T, Henry A, Swerdlow DI, Mälarstig A, Andersson C, Verweij N, Holmes MV, Ärnlöv J, Svensson P, Hemingway H, Sallah N, Almgren P, Aragam KG, Asselin G, Backman JD, Biggs ML, Bloom HL, Boersma E, Brandimarto J, Brown MR, Brunner-La Rocca HP, Carey DJ, Chaffin MD, Chasman DI, Chazara O, Chen X, Chen X, Chung JH, Chutkow W, Cleland JGF, Cook JP, de Denus S, Dehghan A, Delgado GE, Denaxas S, Doney AS, Dörr M, Dudley SC, Engström G, Esko T, Fatemifar G, Felix SB, Finan C, Ford I, Fougerousse F, Fouodjio R, Ghanbari M, Ghasemi S, Giedraitis V, Giulianini F, Gottdiener JS, Gross S, Guðbjartsson DF, **Gui H**, Gutmann R, Haggerty CM, van der Harst P, Hedman Å K, Helgadottir A, Hillege H, Hyde CL, Jacob J, Jukema JW, Kamanu F, Kardys I, Kavousi M, Khaw KT, Kleber ME, Køber L, Koekemoer A, Kraus B, Kuchenbaecker K, Langenberg C, Lind L, Lindgren CM, London B, Lotta LA, Lovering RC, Luan J, Magnusson P, Mahajan A, Mann D, Margulies KB, Marston NA, März W, McMurray JJV, Melander O, Melloni G, Mordi IR, Morley MP, Morris AD, Morris AP, Morrison AC, Nagle MW, Nelson CP, Newton-Cheh C, Niessner A, Niiranen T, Nowak C, O'Donoghue ML, Owens AT, Palmer CNA, Paré G, Perola M, Perreault LL, Portilla-Fernandez E, Psaty BM, Rice KM, Ridker PM, Romaine SPR, Roselli C, Rotter JI, Ruff CT, Sabatine MS, Salo P, Salomaa V, van Setten J, Shalaby AA, Smelser DT, Smith NL, Stefansson K, Stender S, Stott DJ, Sveinbjörnsson G, Tammesoo ML, Tardif JC, Taylor KD, Teder-Laving M, Teumer A, Thorgeirsson G, Thorsteinsdottir U, Torp-Pedersen C, Trompet S, Tuckwell D, Tyl B, Uitterlinden AG, Vaura F, Veluchamy A, Visscher PM, Völker U, Voors AA, Wang X, Wareham NJ, Weeke PE, Weiss R, White HD, Wiggins KL, Xing H, Yang J, Yang Y, Yerges-Armstrong LM, Yu B, Zannad F, Zhao F, Wilk JB, Holm H, Sattar N, Lubitz SA, **Lanfear DE**, Shah S, Dunn ME, Wells QS, Asselbergs FW, Hingorani AD, Dubé MP, Samani NJ, Lang CC, Cappola TP, Ellinor PT, Vasan RS, and Smith JG. The genomics of heart failure: design and rationale of the HERMES consortium. *ESC Heart Fail* 2021; Epub ahead of print. PMID: 34480422. Full Text

AIMS: The HERMES (HEart failure Molecular Epidemiology for Therapeutic targetS) consortium aims to identify the genomic and molecular basis of heart failure. METHODS AND RESULTS: The consortium currently includes 51 studies from 11 countries, including 68 157 heart failure cases and 949 888 controls, with data on heart failure events and prognosis. All studies collected biological samples and performed genome-wide genotyping of common genetic variants. The enrolment of subjects into participating studies ranged from 1948 to the present day, and the median follow-up following heart failure diagnosis ranged from 2 to 116 months. Forty-nine of 51 individual studies enrolled participants of both sexes; in these studies, participants with heart failure were predominantly male (34-90%). The mean age at diagnosis or ascertainment across all studies ranged from 54 to 84 years. Based on the aggregate sample, we estimated 80% power to genetic variant associations with risk of heart failure with an odds ratio of ≥1.10 for common variants (allele frequency ≥ 0.05) and ≥1.20 for low-frequency variants (allele frequency 0.01-0.05) at P < 5 × 10(-8) under an additive genetic model. CONCLUSIONS: HERMES is a global collaboration aiming to (i) identify the genetic determinants of heart failure; (ii) generate insights into the causal pathways leading to heart failure and enable genetic approaches to target prioritization; and (iii) develop genomic tools for disease stratification and risk prediction.

Cardiology/Cardiovascular Research

Mahmood S, **Nona P**, **Villablanca P**, Nunez-Gil I, and Ramakrishna H. The Meta-Analysis in Evidence-Based Medicine: High-Quality Research When Properly Performed. *J Cardiothorac Vasc Anesth* 2021; 35(9):2556-2558. PMID: 34127359. Full Text

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Cardiology/Cardiovascular Research

Meraj PM, and **O'Neill WW**. Cardiogenic Shock Management Should Be a Team Sport. *J Am Coll Cardiol* 2021; 78(13):1318-1320. PMID: 34556317. Full Text

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Cardiology/Cardiovascular Research

O'Neill BP, **Wang DD**, Caranasos TG, Chitwood WR, Jr., **O'Neill WW**, and Stack R. Initial in-human experience with the conveyor cardiovascular system for the delivery of large profile transcatheter valve devices. *Catheter Cardiovasc Interv* 2021; Epub ahead of print. PMID: 34534413. Full Text

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OBJECTIVES: To determine the safety and efficacy of the conveyor cardiovascular system (CCS) to facilitate the delivery of large profile transcatheter valve devices. BACKGROUND: Transcatheter valve devices rely on force provided by the operator to be delivered to their intended position. This delivery may be challenging in a variety of anatomic scenarios. The ability to provide steering from the tip of the device by forming an arterial venous loop may help overcome these challenges. METHODS: Between May, 2019 and October, 2020, five patients were recruited for delivery of transcatheter valve devices with the CCS. These patients were deemed by the operators to have challenging anatomy which could make conventional valve delivery difficult or impossible. These patients were recruited as part of an FDA approved early feasibility study or through an institutional review board approved compassionate use protocol. RESULTS: Three patients underwent transcatheter mitral valve replacement with a SAPIEN-3 valve. One patient each underwent transcatheter aortic valve (TAVR) implantation with a SAPIEN 3 and 1 patient underwent TAVR implantation with a Lotus valve. All patients underwent successful implantation of the valve and removal of the CCS and valve delivery systems. There was no more than trivial mitral regurgitation post procedure in any patient and there was no more than trivial paravavular leak. There were no major in-hospital complications. CONCLUSIONS: The CCS facilitates the delivery of large profile transcatheter valve devices in challenging anatomic scenarios. Further studies are needed with additional valve technologies.

Cardiology/Cardiovascular Research

Osman M, Syed M, Patel B, Munir MB, Kheiri B, Caccamo M, Sokos G, Balla S, **Basir MB**, Kapur NK, Mamas MA, and Bianco CM. Invasive Hemodynamic Monitoring in Cardiogenic Shock Is Associated With Lower In-Hospital Mortality. *J Am Heart Assoc* 2021; 10(18):e021808. PMID: 34514850. Full Text

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Background There is increasing utilization of cardiogenic shock treatment algorithms. The cornerstone of these algorithms is the use of invasive hemodynamic monitoring (IHM). We sought to compare the in-hospital outcomes in patients who received IHM versus no IHM in a real-world contemporary database. Methods and Results Patients with cardiogenic shock admitted during October 1, 2015 to December 31, 2018, were identified from the National Inpatient Sample. Among this group, we compared the outcomes among patients who received IHM versus no IHM. The primary end point was in-hospital mortality. Secondary end points included vascular complications, major bleeding, need for renal replacement therapy, length of stay, cost of hospitalization, and rate of utilization of left ventricular assist devices and heart transplantation. Propensity score matching was used for covariate adjustment. A total of 394 635 (IHM=62 565; no IHM=332 070) patients were included. After propensity score matching, 2 well-matched groups were compared (IHM=62 220; no IHM=62 220). The IHM group had lower in-hospital mortality (24.1% versus 30.6%, P<0.01), higher percentages of left ventricular assist devices (4.4% versus 1.3%, P<0.01) and heart transplantation (1.3% versus 0.7%, P<0.01) utilization, longer length of hospitalization and higher costs. There was no difference between the 2 groups in terms of vascular complications, major bleeding, and the need for renal replacement therapy. Conclusions Among patients with cardiogenic shock, the use of IHM is associated with a reduction in in-hospital mortality and increased utilization of advanced heart failure therapies. Due to the observational nature of the current study, the results should be considered hypothesis-generating, and future prospective studies confirming these findings are needed.

Cardiology/Cardiovascular Research

Peacock WF, Levy PD, Diercks DB, Li S, **McCord J**, Newby LK, Osborne A, Ross M, Winchester DE, Kontos MC, Deitelzweig S, and Bhatt DL. The Impact of American College of Cardiology Chest Pain Center Accreditation on Guideline Recommended Acute Myocardial Infarction Management. *Crit Pathw Cardiol* 2021; Epub ahead of print. PMID: 34494982. Full Text

Baylor College of Medicine Wayne State School of Medicine, Detroit, MI University of Texas, Southwestern NCDR employee Henry Ford Health System, Department of Medicine, Division of Cardiology, Duke University School of Medicine Emory University School of Medicine University of Florida Virginia Commonwealth University, Ochsner Health System Brigham and Women's Hospital Heart & Vascular Center, Harvard Medical School, Boston, MA.

BACKGROUND: Whether American College of Cardiology (ACC) Chest Pain Center (CPC) accreditation alters guidelines adherence rates is unclear. METHODS: We analyzed patient-level, hospital-reported, quality metrics for myocardial infarction (MI) patients from 644 hospitals collected in the ACC's Chest Pain-MI Registry from 1/1/19 to 12/31/20, stratified by CPC accreditation for >1 year. RESULTS: Of 192,374 MI patients, 67,462 (35.1%) received care at an accredited hospital. In general, differences in guideline adherence rates between accredited and non-accredited hospitals were numerically small, though frequently significant. Patients at accredited hospitals were more likely to undergo coronary angiography (98.6% vs 97.9%, p<0.0001), percutaneous coronary intervention (PCI) for NSTEMI (55.4% vs 52.3%, p<0.0001), have overall revascularization for NSTEMI (63.5% vs 61.0%, p<0.0001), and receive P2Y12 inhibitor on arrival (63.5% vs. 60.2%, p<0.0001). Non-accredited hospitals more ECG within 10 minutes (62.3% vs. 60.4%, p<0.0001) and first medical contact to device activation ≤ 90 minutes

(66.8% vs. 64.8%, p<0.0001). Accredited hospitals had uniformly higher discharge medication guideline adherence, with patients more likely receiving aspirin (97.8% vs. 97.4%, p<0.0001), angiotensin converting enzyme inhibitor (46.7% vs. 45.3%, p<0.0001), beta blocker (96.6% vs. 96.2%, p<0.0001), P2Y12 inhibitor (90.3% vs. 89.2%, p<0.0001), and statin (97.8% vs. 97.5%, p<0.0001). Interaction by accredited status was significant only for length of stay (LOS), which was slightly shorter at accredited facilities for specific subgroups. CONCLUSIONS: ACC CPC accreditation was associated with small consistent improvement in adherence to guideline-based treatment recommendations of catheter-based care (catheterization and PCI) for NSTEMI and discharge medications, and shorter hospital stays.

Cardiology/Cardiovascular Research
Qintar M, **Wang DD**, **O'Neill WW**, and **O'Neill B**. Vacuum to the Rescue: Aspiration of a Large Mobile Aortic Arch Thrombus With the AngioVac System Utilizing Transcaval Access. *J Invasive Cardiol* 2021; 33(9):E756-e757. PMID: 34473079. Request Article

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Multiple case reports have been published on using the AngioVac system for right-sided clots or vegetations and few others report AngioVac in the aorta. Our case is the first to utilize transcaval access for a successful aspiration of the mobile part of a large aortic arch thrombus. Future studies are needed to further define this approach.

Cardiology/Cardiovascular Research
Raad M, **Gorgis S**, Abshire C, Yost M, **Dabbagh MF**, Chehab O, **Aurora L**, **Patel S**, **Nona P**, **Yan J**, **Singh G**, Syrjamaki J, **Kaatz S**, and **Parikh S**. COVID-19 risk index (CRI): a simple and validated emergency department risk score that predicts mortality and the need for mechanical ventilation. *J Thromb Thrombolysis* 2021; 1-9. Epub ahead of print. PMID: 34554359. Full Text

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Although certain risk factors have been associated with morbidity and mortality, validated emergency department (ED) derived risk prediction models specific to coronavirus disease 2019 (COVID-19) are lacking. The objective of this study is to describe and externally validate the COVID-19 risk index (CRI). A large retrospective longitudinal cohort study was performed to analyze consecutively hospitalized patients with COVID-19. Multivariate regression using clinical data elements from the ED was used to create the CRI. The results were validated with an external cohort of 1799 patients from the MI-COVID19 database. The primary outcome was the composite of the need for mechanical ventilation or inpatient mortality, and the secondary outcome was inpatient mortality. A total of 1020 patients were included in the derivation cohort. A total of 236 (23%) patients in the derivation cohort required mechanical ventilation or died. Variables independently associated with the primary outcome were age ≥ 65 years, chronic obstructive pulmonary disease, chronic kidney disease, cerebrovascular disease, initial D-dimer > 1.1 µg/mL, platelet count < 150 K/µL, and severity of SpO2:FiO2 ratio. The derivation cohort had an area under the receiver operator characteristic curve (AUC) of 0.83, and 0.74 in the external validation cohort Calibration shows close adherence between the observed and expected primary outcomes within the validation cohort. The CRI is a novel disease-specific tool that assesses the risk for mechanical ventilation or death in hospitalized patients with COVID-19. Discrimination of the score may change given continuous updates in contemporary COVID-19 management and outcomes.

Cardiology/Cardiovascular Research
Rogers JH, Sorajja P, Thourani VH, Sharma RP, Chehab B, **Cowger J**, Heimansohn D, Badhwar V, Guerrero M, and Ailawadi G. Randomized Trials Are Needed for Transcatheter Mitral Valve Replacement. *JACC Cardiovasc Interv* 2021; 14(18):2039-2046. PMID: 34556279. Full Text

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Transcatheter mitral valve replacement (TMVR) is a new therapy for treating symptomatic mitral regurgitation (MR) and stenosis. The proposed benefit of TMVR is the predictable, complete elimination of MR, which is less certain with transcatheter repair technologies such as TEER (transcatheter edge-to-edge repair). The potential benefit of MR elimination with TMVR needs to be rigorously evaluated against its risks which include relative procedural invasiveness, need for anticoagulation, and chronic structural valve deterioration. Randomized controlled trials (RCTs) are a powerful method for evaluating the safety and effectiveness of TMVR against current standard of care transcatheter therapies, such as TEER. RCTs not only help with the assessment of benefits and risks, but also with policies for determining operator or institutional requirements, resource utilization, and reimbursement. In this paper, the authors provide recommendations and considerations for designing pivotal RCTs for first-in-class TMVR devices.

Cardiology/Cardiovascular Research

Shero ST, Benzo R, Cooper LS, Finkelstein J, Forman DE, Gaalema DE, Joseph L, **Keteyian SJ**, Peterson PN, Punturieri A, Zieman S, and Fleg JL. Update on RFA Increasing Use of Cardiac and Pulmonary Rehabilitation in Traditional and Community Settings NIH-Funded Trials: ADDRESSING CLINICAL TRIAL CHALLENGES PRESENTED BY THE COVID-19 PANDEMIC. *J Cardiopulm Rehabil Prev* 2021; Epub ahead of print. PMID: 34508036. Full Text

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Cardiology/Cardiovascular Research

Sparrow RT, Sanjoy SS, Lindman BR, Tang GHL, Kaneko T, Wasfy JH, Pershad A, **Villablanca PA**, Guerrero M, Alraies MC, Choi YH, Sposato LA, Mamas MA, and Bagur R. Racial, ethnic and socioeconomic disparities in patients undergoing transcatheter mitral edge-to-edge repair. *Int J Cardiol* 2021; Epub ahead of print. PMID: 34555446. Full Text

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BACKGROUND: Transcatheter mitral edge-to-edge repair (TEER) is an increasingly common procedure performed on patients with severe mitral regurgitation. This study assessed the impact of race/ethnicity and socioeconomic status on in-hospital complications after TEER. METHODS: Cohort-based observational study using the National Inpatient Sample between October 2013 and December 2018. The population was stratified into 4 groups based on race/ethnicity and quartiles of neighborhood income levels. The primary outcome was in-hospital complications, defined as the composite of death, bleeding, cardiac and vascular complications, acute kidney injury, and ischemic stroke. RESULTS: 3795 hospitalizations for TEER were identified. Patients of Black and Hispanic race/ethnicity comprised 7.4% and 6.4%, respectively. We estimated that White patients received TEER with a frequency of 38.0/100,000, compared to 29.7/100,000 for Blacks and 30.5/100,000 for Hispanics. In-hospital complications occurred in 20.2% of patients and no differences were found between racial/ethnic groups (P = 0.06). After multilevel modelling, Black and Hispanic patients had similar rate of overall in-hospital complications (OR: 0.84, CI:0.67-1.05 and OR: 0.84, CI:0.66-1.07, respectively) as compared to White patients, however, higher rates of death were observed in Black patients. Individuals living in income quartile-1 had worse in-hospital outcomes as compared to quartile-4 (OR: 1.19, CI:0.99-1.42). CONCLUSION: In this study assessing racial/ethnic disparities in TEER outcomes, aged-adjusted race/ethnicity minorities were less underrepresented as compared to other structural heart interventions. Black patients experienced a higher rate of in-hospital death, but similar overall rate of post-procedural adverse events as compared to White patients. Lower income levels appear to negatively impact on in-hospital outcomes. BRIEF SUMMARY: This study appraises race/ethnic and socioeconomical disparities in access and outcomes following transcatheter mitral edge-to-edge repair. Racial minority groups were less underrepresented as compared to other structural heart interventions. While Black patients experienced a higher rate of in-hospital death, they experienced similar overall rate of post-procedural complications compared to White patients. Lower income levels also appeared to negatively impact on outcomes.

Cardiology/Cardiovascular Research

Ya'Qoub L, Jneid H, and Elgendy IY. Transcatheter edge-to-edge repair of the mitral valve: A promising bridge to heart transplant for select patients? *Int J Cardiol* 2021; Epub ahead of print. PMID: 34509533.
Full Text

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Center for Health Policy and Health Services Research

Beidas RS, **Ahmedani BK**, Linn KA, Marcus SC, Johnson C, **Maye M**, **Westphal J**, Wright L, Beck AL, Buttenheim AM, Daley MF, Davis M, **Elias ME**, Jager-Hyman S, Hoskins K, Lieberman A, **McArdle B**, Ritzwoller DP, Small DS, Wolk CB, Williams NJ, and Boggs JM. Study protocol for a type III hybrid effectiveness-implementation trial of strategies to implement firearm safety promotion as a universal suicide prevention strategy in pediatric primary care. *Implement Sci* 2021; 16(1):89. PMID: 34551811. Full Text

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BACKGROUND: Insights from behavioral economics, or how individuals' decisions and behaviors are shaped by finite cognitive resources (e.g., time, attention) and mental heuristics, have been underutilized in efforts to increase the use of evidence-based practices in implementation science. Using the example of firearm safety promotion in pediatric primary care, which addresses an evidence-to-practice gap in universal suicide prevention, we aim to determine: is a less costly and more scalable behavioral economic-informed implementation strategy (i.e., "Nudge") powerful enough to change clinician behavior or is a more intensive and expensive facilitation strategy needed to overcome implementation barriers? METHODS: The Adolescent and child Suicide Prevention in Routine clinical Encounters (ASPIRE) hybrid type III effectiveness-implementation trial uses a longitudinal cluster randomized design. We will test the comparative effectiveness of two implementation strategies to support clinicians' use of an evidence-based firearm safety practice, S.A.F.E. Firearm, in 32 pediatric practices across two health systems. All pediatric practices in the two health systems will receive S.A.F.E. Firearm materials, including training and cable locks. Half of the practices (k = 16) will be randomized to receive Nudge; the other half (k = 16) will be randomized to receive Nudge plus 1 year of facilitation to target additional practice and clinician implementation barriers (Nudge+). The primary implementation outcome is parent-reported clinician fidelity to the S.A.F.E Firearm program. Secondary implementation outcomes include reach and cost. To understand how the implementation strategies work, the primary mechanism to be tested is practice adaptive reserve, a self-report practice-level measure that includes relationship infrastructure, facilitative leadership, sense-making, teamwork, work environment, and culture of learning. DISCUSSION: The ASPIRE trial will integrate implementation science and behavioral economic approaches to advance our understanding of methods for implementing evidence-based firearm safety promotion practices in pediatric primary care. The study answers a question at the heart of many practice change efforts: which strategies are sufficient to support change, and why? Results of the trial will offer valuable insights into how best to implement evidence-based practices that address sensitive health matters in pediatric primary care. TRIAL REGISTRATION: ClinicalTrials.gov, NCT04844021 . Registered 14 April 2021.

Center for Health Policy and Health Services Research

Li J, **Lu M**, **Zhou Y**, Bowlus CL, Lindor K, Rodriguez-Watson C, Romanelli RJ, Haller IV, Anderson H, VanWormer JJ, Boscarino JA, Schmidt MA, Daida YG, Sahota A, Vincent J, **Wu KH**, **Trudeau S**, **Rupp LB**, **Melkonian C**, and **Gordon SC**. Dynamic Risk Prediction of Response to Ursodeoxycholic Acid Among Patients with Primary Biliary Cholangitis in the USA. *Dig Dis Sci* 2021; Epub ahead of print. PMID: 34499271. Full Text

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BACKGROUND: Ursodeoxycholic acid (UDCA) remains the first-line therapy for primary biliary cholangitis (PBC); however, inadequate treatment response (ITR) is common. The UK-PBC Consortium developed the modified UDCA Response Score (m-URS) to predict ITR (using alkaline phosphatase [ALP] > 1.67 times the upper limit of normal [*ULN]) at 12 months post-UDCA initiation). Using data from the US-based Fibrotic Liver Disease Consortium, we assessed the m-URS in our multi-racial cohort. We then used a dynamic modeling approach to improve prediction accuracy. METHODS: Using data collected at the time of UDCA initiation, we assessed the m-URS using the original formula; then, by calibrating coefficients to our data, we also assessed whether it remained accurate when using Paris II criteria for ITR. Next, we developed and validated a dynamic risk prediction model that included post-UDCA initiation laboratory data. RESULTS: Among 1578 patients (13% men; 8% African American, 9% Asian American/American Indian/Pacific Islander; 25% Hispanic), the rate of ITR was 27% using ALP > 1.67*ULN and 45% using Paris II criteria. M-URS accuracy was "very good" (AUROC = 0.87, sensitivity = 0.62, and specificity = 0.82) for ALP > 1.67*ULN and "moderate" (AUROC = 0.74, sensitivity = 0.57, and specificity = 0.70) for Paris II. Our dynamic model significantly improved accuracy for both definitions of ITR (ALP > 1.67*ULN: AUROC = 0.91; Paris II: AUROC = 0.81); specificity approached 100%. Roughly 9% of patients in our cohort were at the highest risk of ITR. CONCLUSIONS: Early identification of patients who will not respond to UDCA treatment using a dynamic prediction model based on longitudinal, repeated risk factor measurements may facilitate earlier introduction of adjuvant treatment.

Center for Health Policy and Health Services Research
Macki M, **Hamilton T**, **Lim S**, **Mansour TR**, **Telemi E**, **Bazydlo M**, **Schultz L**, **Nerenz DR**, Park P, **Chang V**, **Schwalb J**, and **Abdulhak MM**. The role of postoperative antibiotic duration on surgical site infection after lumbar surgery. *J Neurosurg Spine* 2021;1-7. Epub ahead of print. PMID: 34534952. Full Text

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OBJECTIVE: Despite a general consensus regarding the administration of preoperative antibiotics, poorly defined comparison groups and underpowered studies prevent clear guidelines for postoperative antibiotics. Utilizing a data set tailored specifically to spine surgery outcomes, in this clinical study the authors aimed to determine whether there is a role for postoperative antibiotics in the prevention of surgical site infection (SSI). METHODS: The Michigan Spine Surgery Improvement Collaborative registry was queried for all lumbar operations performed for degenerative spinal pathologies over a 5-year period from 2014 to 2019. Preoperative prophylactic antibiotics were administered for all surgical procedures. The study population was divided into three cohorts: no postoperative antibiotics, postoperative antibiotics

≤ 24 hours, and postoperative antibiotics > 24 hours. This categorization was intended to determine 1) whether postoperative antibiotics are helpful and 2) the appropriate duration of postoperative antibiotics. First, multivariable analysis with generalized estimating equations (GEEs) was used to determine the association between antibiotic duration and all-type SSI with adjusted odds ratios; second, a three-tiered outcome-no SSI, superficial SSI, and deep SSI-was calculated with multivariable multinomial logistical GEE analysis. RESULTS: Among 37,161 patients, the postoperative antibiotics > 24 hours cohort had more men with older average age, greater body mass index, and greater comorbidity burden. The postoperative antibiotics > 24 hours cohort had a 3% rate of SSI, which was significantly higher than the 2% rate of SSI of the other two cohorts (p = 0.004). On multivariable GEE analysis, neither postoperative antibiotics > 24 hours nor postoperative antibiotics ≤ 24 hours, as compared with no postoperative antibiotics, was associated with a lower rate of all-type postoperative SSIs. On multivariable multinomial logistical GEE analysis, neither postoperative antibiotics ≤ 24 hours nor postoperative antibiotics > 24 hours was associated with rate of superficial SSI, as compared with no antibiotic use at all. The odds of deep SSI decreased by 45% with postoperative antibiotics ≤ 24 hours (p = 0.002) and by 40% with postoperative antibiotics > 24 hours (p = 0.008). CONCLUSIONS: Although the incidence of all-type SSI was highest in the antibiotics > 24 hours cohort, which also had the highest proportions of risk factors, duration of antibiotics failed to predict all-type SSI. On multinomial subanalysis, administration of postoperative antibiotics for both ≤ 24 hours and > 24 hours was associated with decreased risk of only deep SSI but not superficial SSI. Spine surgeons can safely consider antibiotics for 24 hours, which is equally as effective as long-term administration for prophylaxis against deep SSI.

Center for Health Policy and Health Services Research

Maye M, Boyd BA, Martínez-Pedraza F, Halladay A, Thurm A, and Mandell DS. Biases, Barriers, and Possible Solutions: Steps Towards Addressing Autism Researchers Under-Engagement with Racially, Ethnically, and Socioeconomically Diverse Communities. *J Autism Dev Disord* 2021; Epub ahead of print. PMID: 34529251. Full Text

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Autistic individuals who are also people of color or from lower socioeconomic strata are historically underrepresented in research. Lack of representation in autism research has contributed to health and healthcare disparities. Reducing these disparities will require culturally competent research that is relevant to under-resourced communities as well as collecting large nationally representative samples, or samples in which traditionally disenfranchised groups are over-represented. To achieve these goals, a diverse group of culturally competent researchers must partner with and gain the trust of communities to identify and eliminate barriers to participating in research. We suggest community-academic partnerships as one promising approach that results in high-quality research built on cultural competency, respect, and shared decision making.

Center for Individualized and Genomic Medicine Research

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AIMS: The HERMES (HEart failure Molecular Epidemiology for Therapeutic targetS) consortium aims to identify the genomic and molecular basis of heart failure. METHODS AND RESULTS: The consortium currently includes 51 studies from 11 countries, including 68 157 heart failure cases and 949 888 controls, with data on heart failure events and prognosis. All studies collected biological samples and performed genome-wide genotyping of common genetic variants. The enrolment of subjects into participating studies ranged from 1948 to the present day, and the median follow-up following heart failure diagnosis ranged from 2 to 116 months. Forty-nine of 51 individual studies enrolled participants of both sexes; in these studies, participants with heart failure were predominantly male (34-90%). The mean age at diagnosis or ascertainment across all studies ranged from 54 to 84 years. Based on the aggregate sample, we estimated 80% power to genetic variant associations with risk of heart failure with an odds ratio of ≥1.10 for common variants (allele frequency ≥ 0.05) and ≥1.20 for low-frequency variants (allele frequency 0.01-0.05) at P < 5 × 10(-8) under an additive genetic model. CONCLUSIONS: HERMES is a global collaboration aiming to (i) identify the genetic determinants of heart failure; (ii) generate insights into the causal pathways leading to heart failure and enable genetic approaches to target prioritization; and (iii) develop genomic tools for disease stratification and risk prediction.

Dermatology

Anderson J, **Maghfour J**, Hamp A, Christensen A, and Dellavalle RP. From the Cochrane Library: Emollients and Moisturizers for Eczema. *Dermatology* 2021; 1-3. Epub ahead of print. PMID: 34511590. Full Text

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Dermatology

Elbuluk N, Grimes P, Chien A, **Hamzavi I**, Alexis A, Taylor S, Gonzalez N, Weiss J, Desai SR, and Kang S. The Pathogenesis and Management of Acne-Induced Post-inflammatory Hyperpigmentation. *Am J Clin Dermatol* 2021; Epub ahead of print. PMID: 34468934. Request Article

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Acne vulgaris is a common inflammatory disease. Among patients with darker skin phototypes (Fitzpatrick III-VI), the inflammatory processes of acne stimulate excess melanogenesis and abnormal melanin deposition, leading to pigmentary sequelae known as post-inflammatory hyperpigmentation and post-inflammatory erythema in all skin tones, although post-inflammatory hyperpigmentation is more common in darker skin and post-inflammatory erythema in lighter skin. These pigmentary alterations can be long lasting and are often more distressing to patients than the active acne lesions. This article discusses what is known about acne-related pigmentation, much of which is extrapolated from general study of nonspecific pigment deposition. Because dyspigmentation poses both a significant clinical concern to patients and a therapeutic challenge to clinicians, we formed a working group consisting of pigmentary experts with the aim of increasing awareness and education of acne-related pigmentary sequelae.

Dermatology
Fathy RA, McMahon DE, Lee C, Chamberlin GC, Rosenbach M, Lipoff JB, Tyagi A, Desai SR, French LE, **Lim HW**, Thiers BH, Hruza GJ, Fassett M, Fox LP, Greenberg HL, Blumenthal K, and Freeman EE. Varicella Zoster and Herpes Simplex Virus Reactivation Post-COVID-19 Vaccination: A Review of 40 Cases in an International Dermatology Registry. *J Eur Acad Dermatol Venereol* 2021; Epub ahead of print. PMID: 34487581. Full Text

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Since December 2020, the American Academy of Dermatology and the International League of Dermatologic Societies' COVID-19 Dermatology Registry has tracked dermatologic reactions post-COVID-19 vaccination. Within months, a variety of cutaneous manifestations were reported after the Moderna and Pfizer-BioNTech COVID-19 vaccines.(1) As of April 2021, a total of 672 possible vaccine-related skin reactions have been reported by healthcare providers. Here, we evaluate the first 40 cases of varicella zoster virus (VZV) and herpes simplex virus (HSV) reported in the registry after COVID-19 vaccination with either the Moderna or Pfizer-BioNTech vaccines.

Dermatology
Ko D, **Lyons AB**, **Kohli I**, Narla S, Torres AE, **Miller A**, **Ozog D**, **Hamzavi I**, and **Lim HW**. The value of photomedicine in a global health crisis: Utilizing ultraviolet C to decontaminate N95 respirators during the COVID-19 pandemic. *Photodermatol Photoimmunol Photomed* 2021; Epub ahead of print. PMID: 34467568. Full Text

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One early problem during the height of the COVID-19 global pandemic, caused by severe acute respiratory syndrome 2 (SARS-CoV-2), was the shortage of personal protective equipment donned by healthcare workers, particularly N95 respirators. Given the known virucidal, bactericidal, and fungicidal properties of ultraviolet irradiation, in particular ultraviolet C (UVC) radiation, our photomedicine and photobiology unit explored the role of ultraviolet germicidal irradiation (UVGI) using UVC in effectively decontaminating N95 respirators. The review highlights the important role of photobiology and photomedicine in this pandemic. Namely, the goals of this review were to highlight: UVGI as a method of respirator disinfection-specifically against SARS-CoV-2, adverse reactions to UVC and precautions to protect against exposure, other methods of decontamination of respirators, and the importance of respirator fit testing.

Dermatology

Lyons AB, Zubair R, **Kohli I**, Nahhas AF, **Braunberger TL**, Mokhtari M, Ruvolo E, **Lim HW**, and **Hamzavi IH**. Mitigating Visible Light and Long Wavelength UVA1-Induced Effects with Topical Antioxidants. *Photochem Photobiol* 2021; Epub ahead of print. PMID: 34549819. Request Article

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The role of topical antioxidants (AO) on visible light plus ultraviolet A1 (VL+UVA1)-induced skin changes were evaluated. Twenty subjects with skin phototypes (SPT) I-VI had placebo and concentrations of an AO blend applied to their back (AO 0.5, 1.0, and 2.0%). Treated and control sites were irradiated with VL+UVA1. Colorimetric and diffuse reflectance spectroscopy (DRS) assessments were performed immediately, 24 hours, and 7 days after irradiation. Subjects with SPT I-III had erythema that faded within 24 hours, while SPT IV-VI had persistent pigmentation. SPT I-III demonstrated significantly less erythema at the 2% AO site while SPT IV-VI demonstrated significantly less immediate pigmentation at 2% AO site and less pigmentation (approaching significance, p=0.07) on day 7 compared to control. Immunohistochemistry from biopsies of 2% AO and placebo at 24 hours did not demonstrate a significant change in COX-2 or MART-1 for any SPT. There was a decrease in cyclin D1 for SPT IV-VI which was approaching significance (p=0.06) but not for SPT I-III. The results indicate that topical AO inhibits erythema in SPT I-III and reduces pigmentation in SPT IV-VI caused by VL+UVA1. AO may help prevent worsening of pigmentary disorders and should be incorporated into photoprotection.

Dermatology

McMahon DE, Kovarik CL, Damsky W, Rosenbach M, Lipoff JB, Tyagi A, Chamberlin G, Fathy R, Nazarian RM, Desai SR, **Lim HW**, Thiers BH, Hruza GJ, French LE, Blumenthal K, Fox LP, and Freeman EE. Clinical and Pathologic Correlation of Cutaneous COVID-19 Vaccine Reactions including V-REPP: A Registry Based Study. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34517079. Full Text

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BACKGROUND: Cutaneous reactions after COVID-19 vaccination have been commonly reported. However, histopathologic features and clinical correlations have not been well characterized. METHODS: From an international registry, we evaluated all reports of COVID-19 associated vaccination reactions for history of skin biopsy. When histopathology reports were available, we categorized them by reaction patterns. RESULTS: Of 803 vaccine reactions reported, 58 cases (7%) had biopsy reports available for review. The most common histopathologic reaction pattern was spongiotic dermatitis, which clinically ranged from robust papules with overlying crust, to pityriasis-rosea like eruptions, to pink papules with fine scale. We propose the acronym V-REPP (vaccine-related eruption of papules and plaques) for this spectrum. Other clinical patterns included bullous pemphigoid-like (n=12), dermal hypersensitivity (n=4), herpes zoster (n=4), lichen planus-like (n=4), pernio (n=3), urticarial (n=2), neutrophilic dermatosis (n=2), leukocytoclastic vasculitis (n=2), morbilliform (n=2), delayed large local (n=2), erythromelalgia (n=1), and other (n=5). LIMITATION: Cases in which histopathology was available represented a minority of registry entries. Analysis of registry data cannot measure incidence. CONCLUSION: Clinical and histopathologic correlation allowed for categorization of cutaneous COVID-19 vaccine reactions. We propose defining a subset of vaccine-related eruption of papules and plaques (V-REPP), as well as 12 other patterns, following COVID-19 vaccination.

Dermatology

Novice M, **Novice T**, Henry NL, Johnson K, Jeruss JS, Kidwell KM, and Burness ML. Identifying Barriers and Facilitators to Scalp Cooling Therapy Through a National Survey of the Awareness, Practice Patterns, and Attitudes of Oncologists. *JCO Oncol Pract* 2021; Epub ahead of print. PMID: 34529505.
Request Article

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PURPOSE: Scalp cooling therapy (SCT) is the most effective method to reduce chemotherapy-induced alopecia (CIA), a highly distressing side effect of cancer treatment. Despite data supporting SCT efficacy and safety, SCT use in the United States is not widespread. Oncologists' interactions with scalp cooling were examined to identify facilitators and barriers to SCT implementation. METHODS: A 33-question survey was distributed through the ASCO Research Survey Pool to a nationally representative, random sample of 600 oncology providers. Outcome measures included knowledge of SCT, frequency of initiating conversations about SCT with patients, degree of support, and barriers for SCT. Significance was defined as $P < .001$. RESULTS: Of 155 (25.8%) responding providers, 62% of providers were in favor of SCT always or most of the time, but only 26% reported initiating discussions about SCT always or most of the time. Providers who treat breast cancer ($P \leq .0001$), those who report being very familiar with SCT ($P \leq .0001$), those who report having read SCT literature in the past 2 years ($P \leq .0001$), and those who work at a facility with machine SCT ($P \leq .0001$) were significantly more likely to initiate conversations with patients about SCT. Financial concerns (58%) were the primary reason for not recommending SCT use; efficacy (31%), staff or facility (24%), and safety (15%) concerns were also noted. Although safety concerns have decreased markedly over time, 14% of providers report patients who continue to express these concerns and 17% of providers see safety issues as barriers to supporting SCT. CONCLUSION: Our findings suggest that oncology provider familiarity and experience with SCT lead to increased support for scalp cooling, which may ultimately result in greater availability and utilization of SCT when indicated.

Dermatology

Pourang A, **Tisack A**, **Ezekwe N**, **Torres AE**, **Kohli I**, **Hamzavi IH**, and **Lim HW**. The Effects of Visible Light on Mechanisms of Skin Photoaging. *Photodermatol Photoimmunol Photomed* 2021; Epub ahead of print. PMID: 34585779. Full Text

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Human skin is not only affected by ultraviolet radiation, but also by visible light wavelengths emitted by sunlight, electronic devices, and light emitting diodes. Similar to ultraviolet radiation, visible light has been implicated in photoaging. In this review, the effects of blue light, yellow light, red light, and broad visible light are discussed in relation to photoaging. Different visible light wavelengths likely contribute beneficial and deleterious effects on photoaging by way of interaction with specific photoreceptors, ROS production, and other photon-mediated reactions. Further in vivo studies are needed to determine the mechanism and action spectrum of photoaging in humans, as well as optimal photoprotection with coverage against visible light wavelengths.

Dermatology

Thompson AM, Fernandez JM, Shih T, **Hamzavi I**, Hsiao JL, and Shi VY. Improving hidradenitis suppurativa patient education using written action plan: a randomized controlled trial. *J Dermatolog Treat* 2021;1-3. Epub ahead of print. PMID: 34579620. Request Article

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The waxing-and-waning nature of hidradenitis suppurativa (HS), complex treatment plans, along with variable responsiveness to therapy, can create management challenges for patients. In this pilot cross-over randomized controlled trial, we aim to evaluate the effectiveness a HS-written action plan (HSWAP) on patient disease understanding and confidence in recognizing flares and adjusting management. Participants were randomized into a pre-crossover control group that received a verbal consultation (VC)-only, and an intervention group which received the VC + HSWAP. The pre-crossover control group then crossed over (post-crossover control) to also receive the VC + HSWAP (ClinicalTrials.gov Identifier: NCT04600375). Patient comprehension of their disease and management steps was high after both a thorough VC and HSWAPs. However, the majority of patients prefer receiving both a VC and a HSWAP. After the addition of the HSWAP, pre-crossover control group patients' understanding and confidence of their disease and management plan increased across all surveyed questions.

Diagnostic Radiology

Gold LS, Marcum ZA, Meier EN, Turner JA, James KT, Kallmes DF, Luetmer PH, **Griffith B**, Sherman KJ, Friedly JL, Suri P, Deyo RA, Johnston SK, Avins AL, Heagerty PJ, and Jarvik JG. Patient, Provider, and Clinic Characteristics Associated with Opioid and Non-Opioid Pain Prescriptions for Patients Receiving Low Back Imaging in Primary Care. *J Am Board Fam Med* 2021; 34(5):950-963. PMID: 34535520. Full Text

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BACKGROUND: To describe characteristics of patients, providers, and clinics associated with opioid or non-opioid pain medication prescribing patterns for patients who received lower spine imaging in primary care clinics. METHODS: In these secondary analyses of the Lumbar Imaging with Reporting of Epidemiology (LIRE) study, a randomized controlled trial conducted in 4 health systems in the United States, we evaluated characteristics associated with receipt of pain medication prescriptions. The outcomes were receipt of prescriptions for opioid or, separately, non-opioid pain medications within 90 days after imaging. Among patients who received opioid or non-opioid prescriptions, we evaluated receipt of multiple prescriptions in the year following imaging. Mixed models were used to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs). RESULTS: Compared with whites, patients identified as Asian (OR, 0.53; 95% CI, 0.51-0.56), Native Hawaiian/Pacific Islander (OR, 0.73; 95% CI, 0.64-0.83), multiracial (OR, 0.84; 95% CI, 0.71-0.98) or Black (OR, 0.92; 95% CI, 0.89-0.96) had significantly reduced odds for receiving prescriptions for opioids within 90 days. Patients identified as Native American/Alaska Native had greater odds for receiving prescriptions for non-opioid pain medications within 90 days (OR, 1.12; 95% CI, 1.01-1.24). Receipt of pain prescriptions 120 days before imaging was strongly predictive of subsequent receipt of pain prescriptions across all categories. CONCLUSIONS: After adjusting for factors that could affect prescribing, the strongest differences observed in pain-medication prescribing were across racial categories and for patients with previous pain prescriptions. Further research is needed to understand these differences and to optimize prescribing.

Diagnostic Radiology

Li K, Li Y, **Qi Z**, Garrett JW, Grist TM, and Chen GH. Quantitative lung perfusion blood volume (PBV) using dual energy CT (DECT)-based effective atomic number (Z_{eff}) imaging. *Med Phys* 2021; Epub ahead of print. PMID: 34520066. Full Text

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BACKGROUND: Iodine material images (aka iodine basis images) generated from dual energy CT (DECT) have been used to assess potential perfusion defects in the pulmonary parenchyma. However, iodine material images do not provide the needed absolute quantification of the pulmonary blood pool, as materials with effective atomic numbers (Z(eff)) different from those of basis materials may also contribute to iodine material images, thus confounding the quantification of perfusion defects. PURPOSE: The purposes of this work were to (i) demonstrate the limitations of iodine material images in pulmonary perfusion defect quantification and (ii) develop and validate a new quantitative biomarker using effective atomic numbers derived from DECT images. METHODS: The quantitative relationship between the

perfusion blood volume (PBV) in pulmonary parenchyma and the effective atomic number (Z(eff)) spatial distribution was studied to show that the desired quantitative PBV maps are determined by the spatial maps of Z(eff) as PBV(Zeff) (x) = a Z(eff) (β) (x) + b, where a, b, and β are three constants. Namely, quantitative PBV(Zeff) is determined by Z(eff) images instead of the iodine basis images. Perfusion maps were generated for four human subjects to demonstrate the differences between conventional iodine material image-based PBV (PBV(iodine)) derived from two-material decompositions and the proposed PBV(Zeff) method. RESULTS: Among patients with pulmonary emboli, the proposed PBV(Zeff) maps clearly show the perfusion defects while the PBV(iodine) maps do not. Additionally, when there are no perfusion defects present in the derived PBV maps, no pulmonary emboli were diagnosed by an experienced thoracic radiologist. CONCLUSION: Effective atomic number based quantitative PBV maps provide the needed sensitive and specific biomarker to quantify pulmonary perfusion defects.

Emergency Medicine

Greene SC, **Folt J**, Wyatt K, and Brandehoff NP. The authors reply: Using lay media for epidemiology of snakebite fatality. *Am J Emerg Med* 2021; 47:289. PMID: 34088502. Full Text

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Emergency Medicine

Khatri SB, Newman C, Hammel JP, Dey T, **Van Laere JJ**, Ross KA, Rose JA, Anderson T, Mukerjee S, Smith L, Landis MS, Holstein A, and Norris GA. Associations of Air Pollution and Pediatric Asthma in Cleveland, Ohio. *ScientificWorldJournal* 2021; 2021:8881390. PMID: 34566522. Full Text

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Air pollution has been associated with poor health outcomes and continues to be a risk factor for respiratory health in children. While higher particulate matter (PM) levels are associated with increased frequency of symptoms, lower lung function, and increase airway inflammation from asthma, the precise composition of the particles that are more highly associated with poor health outcomes or healthcare utilization are not fully elucidated. PM is measured quantifiably by current air pollution monitoring systems. To better determine sources of PM and speciation of such sources, a particulate matter (PM) source apportionment study, the Cleveland Multiple Air Pollutant Study (CMAPS), was conducted in Cleveland, Ohio, in 2009-2010, which allowed more refined assessment of associations with health outcomes. This article presents an evaluation of short-term (daily) and long-term associations between motor vehicle and industrial air pollution components and pediatric asthma emergency department (ED) visits by evaluating two sets of air quality data with healthcare utilization for pediatric asthma. Exposure

estimates were developed using land use regression models for long-term exposures for nitrogen dioxide (NO(2)) and coarse (i.e., with aerodynamic diameters between 2.5 and 10 μm) particulate matter (PM) and the US EPA Positive Matrix Factorization receptor model for short-term exposures to fine (<2.5 μm) and coarse PM components. Exposure metrics from these two approaches were used in asthma ED visit prevalence and time series analyses to investigate seasonal-averaged short- and long-term impacts of both motor vehicles and industry emissions. Increased pediatric asthma ED visits were found for LUR coarse PM and NO(2) estimates, which were primarily contributed by motor vehicles. Consistent, statistically significant associations with pediatric asthma visits were observed, with short-term exposures to components of fine and coarse iron PM associated with steel production. Our study is the first to combine spatial and time series analysis of ED visits for asthma using the same periods and shows that PM related to motor vehicle emissions and iron/steel production are associated with increased pediatric asthma visits.

Emergency Medicine

Lazzara AA, Jr., **Ditmer BI**, **Doughty KW**, and **Reynolds KR**. Tree Stand-Related Injuries in Nonadmitted and Admitted Patients at a Level 2 Trauma Center in Michigan: 2015-2019. *Wilderness Environ Med* 2021; Epub ahead of print. PMID: 34580014. Full Text

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INTRODUCTION: Tree stand-related injuries (TSRI) are more common than firearm-related injuries in hunters. Most previous studies on the topic used trauma databases that only include admitted patients. This study characterizes injury patterns found in nonadmitted and admitted TSRI patients presenting to a level 2 Michigan trauma center. TSRI prevention interventions are also discussed. METHODS: Cases were obtained through a retrospective chart review of the Henry Ford Allegiance Health trauma registry and EPSi cost-accounting database from 2015 to 2019. Keywords searched included fall, hunter, tree, tree stand, treestand, ICD 9 diagnosis (E884.9_Other accidental fall from one level to another), and ICD 10 diagnosis (W14.XXXA_Fall from tree, initial encounter). We analyzed age, sex, body mass index, injury severity score, disposition, alcohol use, injuries sustained, reported height of fall, and narrative of fall. RESULTS: Thirty-three patients were identified. Patient age was 45±13 y (mean±SD). All patients were male. Injury severity score for nonadmitted patients was 2±1 vs 13±11 in admitted patients. Thirty-three percent of cases were nonadmitted; 67% were admitted. The most common injuries sustained were spinal (33%) and lower extremity fractures (15%). The average yearly TSRI case rate was 5.73 per 10,000 hunters in the study area. CONCLUSIONS: Our study found that spinal and lower extremity fractures were the most common injuries sustained. One-third of our patients were nonadmitted and therefore not included in the Henry Ford Allegiance Health trauma registry. Some nonadmitted patients had significant injuries requiring specialist consultation, orthopedic braces, or outpatient surgery.

Emergency Medicine

Mansi ET, Johnson ES, Thorp ML, Go AS, Lee MS, Shen AY, Park KJ, **Budzynska K**, **Markin A**, Sung SH, Thompson JH, Slaughter MT, Luong TQ, An J, Reynolds K, Roblin DW, **Cassidy-Bushrow AE**, Kuntz JL, Schlienger RG, Behr S, and Smith DH. Physician adjudication of angioedema diagnosis codes in a population of patients with heart failure prescribed angiotensin-converting enzyme inhibitor therapy. *Pharmacoepidemiol Drug Saf* 2021; Epub ahead of print. PMID: 34558760. Full Text

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PURPOSE: Our objective was to calculate the positive predictive value (PPV) of the ICD-9 diagnosis code for angioedema when physicians adjudicate the events by electronic health record review. Our secondary objective was to evaluate the inter-rater reliability of physician adjudication. METHODS: Patients from the Cardiovascular Research Network previously diagnosed with heart failure who were started on angiotensin-converting enzyme inhibitors (ACEI) during the study period (July 1, 2006 through September 30, 2015) were included. A team of two physicians per participating site adjudicated possible events using electronic health records for all patients coded for angioedema for a total of five sites. The PPV was calculated as the number of physician-adjudicated cases divided by all cases with the diagnosis code of angioedema (ICD-9-CM code 995.1) meeting the inclusion criteria. The inter-rater reliability of physician teams, or kappa statistic, was also calculated. RESULTS: There were 38 061 adults with heart failure initiating ACEI in the study (21 489 patient-years). Of 114 coded events that were adjudicated by physicians, 98 angioedema events were confirmed for a PPV of 86% (95% CI: 80%, 92%). The kappa statistic based on physician inter-rater reliability was 0.65 (95% CI: 0.47, 0.82). CONCLUSIONS: ICD-9 diagnosis code of 995.1 (angioneurotic edema, not elsewhere classified) is highly predictive of angioedema in adults with heart failure exposed to ACEI.

Emergency Medicine

Ziobrowski HN, Kennedy CJ, Ustun B, House SL, Beaudoin FL, An X, Zeng D, Bollen KA, Petukhova M, Sampson NA, Puac-Polanco V, Lee S, Koenen KC, Ressler KJ, McLean SA, Kessler RC, Stevens JS, Neylan TC, Clifford GD, Jovanovic T, Linnstaedt SD, Germine LT, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Lyons MS, Murty VP, McGrath ME, Pascual JL, Seamon MJ, Datner EM, Chang AM, Pearson C, Peak DA, Jambaulikar G, Merchant RC, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Bruce SE, Pietrzak RH, Joormann J, Barch DM, Pizzagalli DA, Sheridan JF, Harte SE, Elliott JM, and van Rooij SJH. Development and Validation of a Model to Predict Posttraumatic Stress Disorder and Major Depression After a Motor Vehicle Collision. *JAMA Psychiatry* 2021; Epub ahead of print. PMID: 34468741. Full Text

IMPORTANCE: A substantial proportion of the 40 million people in the US who present to emergency departments (EDs) each year after traumatic events develop posttraumatic stress disorder (PTSD) or major depressive episode (MDE). Accurately identifying patients at high risk in the ED would facilitate the targeting of preventive interventions. OBJECTIVES: To develop and validate a prediction tool based on ED reports after a motor vehicle collision to predict PTSD or MDE 3 months later. DESIGN, SETTING, AND PARTICIPANTS: The Advancing Understanding of Recovery After Trauma (AURORA) study is a longitudinal study that examined adverse posttraumatic neuropsychiatric sequalae among patients who presented to 28 US urban EDs in the immediate aftermath of a traumatic experience. Enrollment began on September 25, 2017. The 1003 patients considered in this diagnostic/prognostic report completed 3-month assessments by January 31, 2020. Each patient received a baseline ED assessment along with follow-up self-report surveys 2 weeks, 8 weeks, and 3 months later. An ensemble machine learning method was used to predict 3-month PTSD or MDE from baseline information. Data analysis was performed from November 1, 2020, to May 31, 2021. MAIN OUTCOMES AND MEASURES: The PTSD Checklist for DSM-5 was used to assess PTSD and the Patient Reported Outcomes Measurement Information System Depression Short-Form 8b to assess MDE. RESULTS: A total of 1003 patients (median [interquartile range] age, 34.5 [24-43] years; 715 [weighted 67.9%] female; 100 [weighted 10.7%] Hispanic, 537 [weighted 52.7%] non-Hispanic Black, 324 [weighted 32.2%] non-Hispanic White, and 42 [weighted 4.4%] of non-Hispanic other race or ethnicity were included in this study. A total of 274 patients (weighted 26.6%) met criteria for 3-month PTSD or MDE. An ensemble machine learning model restricted to 30 predictors estimated in a training sample (patients from the Northeast or Midwest) had good prediction accuracy (mean [SE] area under the curve [AUC], 0.815 [0.031]) and calibration (mean [SE] integrated calibration index, 0.040 [0.002]; mean [SE] expected calibration error, 0.039 [0.002]) in an independent test sample (patients from the South). Patients in the top 30% of predicted risk accounted for

65% of all 3-month PTSD or MDE, with a mean (SE) positive predictive value of 58.2% (6.4%) among these patients at high risk. The model had good consistency across regions of the country in terms of both AUC (mean [SE], 0.789 [0.025] using the Northeast as the test sample and 0.809 [0.023] using the Midwest as the test sample) and calibration (mean [SE] integrated calibration index, 0.048 [0.003] using the Northeast as the test sample and 0.024 [0.001] using the Midwest as the test sample; mean [SE] expected calibration error, 0.034 [0.003] using the Northeast as the test sample and 0.025 [0.001] using the Midwest as the test sample). The most important predictors in terms of Shapley Additive Explanations values were symptoms of anxiety sensitivity and depressive disposition, psychological distress in the 30 days before motor vehicle collision, and peritraumatic psychosomatic symptoms. CONCLUSIONS AND RELEVANCE: The results of this study suggest that a short set of questions feasible to administer in an ED can predict 3-month PTSD or MDE with good AUC, calibration, and geographic consistency. Patients at high risk can be identified in the ED for targeting if cost-effective preventive interventions are developed.

Endocrinology and Metabolism

Aleppo G, Beck RW, Bailey R, Ruedy KJ, Calhoun P, Peters AL, Pop-Busui R, Philis-Tsimikas A, Bao S, Umpierrez G, Davis G, **Kruger D**, Bhargava A, Young L, Buse JB, McGill JB, Martens T, Nguyen QT, Orozco I, Biggs W, Lucas KJ, Polonsky WH, Price D, and Bergenstal RM. The Effect of Discontinuing Continuous Glucose Monitoring in Adults With Type 2 Diabetes Treated With Basal Insulin. *Diabetes Care* 2021; Epub ahead of print. PMID: 34588210. Full Text

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University of North Carolina School of Medicine, Chapel Hill, NC.
Washington University School of Medicine, St. Louis, MO.
International Diabetes Center, Park Nicollet Internal Medicine, Minneapolis, MN.
Las Vegas Endocrinology, Henderson, NV.
Carteret Medical Group, Morehead City, NC.
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OBJECTIVE: To explore the effect of discontinuing continuous glucose monitoring (CGM) after 8 months of CGM use in adults with type 2 diabetes treated with basal without bolus insulin. RESEARCH DESIGN AND METHODS: This multicenter trial had an initial randomization to either real-time CGM or blood glucose monitoring (BGM) for 8 months followed by 6 months in which the BGM group continued to use BGM (n = 57) and the CGM group was randomly reassigned either to continue CGM (n = 53) or discontinue CGM with resumption of BGM for glucose monitoring (n = 53). RESULTS: In the group that discontinued CGM, mean time in range (TIR) 70-180 mg/dL, which improved from 38% before initiating CGM to 62% after 8 months of CGM, decreased after discontinuing CGM to 50% at 14 months (mean change from 8 to 14 months -12% [95% CI -21% to -3%], P = 0.01). In the group that continued CGM use, little change was found in TIR from 8 to 14 months (baseline 44%, 8 months 56%, 14 months 57%, mean change from 8 to 14 months 1% [95% CI -11% to 12%], P = 0.89). Comparing the two groups at 14 months, the adjusted treatment group difference in mean TIR was -6% (95% CI -16% to 4%, P = 0.20). CONCLUSIONS: In adults with type 2 diabetes treated with basal insulin who had been using real-time CGM for 8 months, discontinuing CGM resulted in a loss of about one-half of the initial gain in TIR that had been achieved during CGM use.

Endocrinology and Metabolism

Griffin LV, **Warner E**, **Palnitkar S**, **Qiu S**, **Honasoge M**, Griffin SG, **Divine G**, and **Rao SD**. Bone Nanomechanical Properties and Relationship to Bone Turnover and Architecture in Patients With Atypical Femur Fractures: A Prospective Nested Case-Control Study. *JBMR Plus* 2021; 5(9):e10523. PMID: 34532612. Full Text

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Atypical femur fractures (AFFs) are well-established serious complication of long-term bisphosphonate and denosumab therapy in patients with osteopenia or osteoporosis. To elucidate underlying mechanism(s) for the development of AFF, we performed a nested case-control study to investigate bone tissue nanomechanical properties and prevailing bone microstructure and tissue-level remodeling status as assessed by bone histomorphometry. We hypothesized that there would be differences in nanomechanical properties between patients with and without AFF and that bone microstructure and remodeling would be related to nanomechanical properties. Thirty-two full-thickness transiliac bone biopsies were obtained from age- and sex-matched patients on long-term bisphosphonate therapy with (n = 16) and without an AFF (n = 16). Standard histomorphometric measurements were made in each sample on three different bone envelopes (cancellous, intracortical, and endosteal). Iliac bone wall thickness was significantly lower on all three bone surfaces in patients with AFF than in those without AFF. Surface-based bone formation rate was suppressed similarly in both groups in comparison to healthy premenopausal and postmenopausal women, with no significant difference between the two groups. Nanoindentation was used to assess material properties of cortical and cancellous bone separately. Elastic modulus was higher in cortical than in cancellous bone in patients with AFF as well as compared to the elastic modulus of cortical bone from non-AFF patients. However, the elastic modulus of the cancellous bone was not different between AFF and non-AFF groups or between cortical and cancellous bone of non-AFF patients. Resistance to plastic deformation was decreased in cortical bone in both AFF and non-AFF groups compared to cancellous bone, but to a greater extent in AFF patients. We conclude that long-term bisphosphonate therapy is associated with prolonged suppression of bone turnover resulting in altered cortical remodeling and tissue nanomechanical properties leading to AFF.

Endocrinology and Metabolism

Kanwal F, Shubrook JH, Younossi Z, Natarajan Y, Bugianesi E, Rinella ME, Harrison SA, Mantzoros C, Pfotenhauer K, Klein S, Eckel RH, **Kruger D**, El-Serag H, and Cusi K. Preparing for the NASH epidemic: A call to action. *Obesity (Silver Spring)* 2021; 29(9):1401-1412. PMID: 34365735. Full Text

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

Endocrinology and Metabolism
Kanwal F, Shubrook JH, Younossi Z, Natarajan Y, Bugianesi E, Rinella ME, Harrison SA, Mantzoros C, Pfotenhauer K, Klein S, Eckel RH, **Kruger D**, El-Serag H, and Cusi K. Preparing for the NASH Epidemic: A Call to Action. *Diabetes Care* 2021; 44(9):2162-2172. PMID: 34312182. Full Text

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

Endocrinology and Metabolism

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

Endocrinology and Metabolism

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

Endocrinology and Metabolism

Sihota P, Pal R, Yadav RN, Neradi D, Karn S, Goni VG, Sharma S, Mehandia V, Bhadada SK, Kumar N, and **Rao SD**. Can fingernail quality predict bone damage in Type 2 diabetes mellitus? A pilot study. *PLoS One* 2021; 16(9):e0257955. PMID: 34591909. Full Text

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Type 2 diabetes mellitus (T2DM) adversely affects the normal functioning, intrinsic material properties, and structural integrity of many tissues, including bone. It is well known that the clinical utility of areal bone mineral density (aBMD) is limited to assess bone strength in individuals with T2DM. Therefore, there is a need to explore new diagnostic techniques that can better assist and improve the accuracy of assessment of bone tissue quality. The present study investigated the link between bone and fingernail material/compositional properties in type 2 diabetes mellitus (T2DM). For that, femoral head and fingernail samples were obtained from twenty-five adult female patients (with/without T2DM) with fragility femoral neck fractures undergoing hemi/total hip arthroplasty. Cylindrical cores of trabecular bone were subjected to micro-CT, and lower bone volume fraction was observed in the diabetic group than the non-diabetic group due to fewer and thinner trabeculae in individuals with T2DM. The material and compositional properties of bone/fingernail were estimated using nanoindentation and Fourier Transform Infrared Spectroscopy, respectively. Both bone/fingernails in T2DM had lower reduced modulus (Er), hardness (H), lower Amide I and Amide II area ratio (protein content), higher sugar-to-matrix ratio, and relatively high carboxymethyl-lysine (CML) content compared with non-diabetic patients. Sugar-to-matrix ratio and relative CML content were strongly and positively correlated with HbA1c for both bone/fingernail. There was a positive correlation between bone and fingernail glycation content. Our findings provide evidence that the degradation pattern of bone and fingernail properties go hand-in-hand in individuals with T2DM. Hence, the fingernail compositional/material properties might serve as a non-invasive surrogate marker of bone quality in T2DM; however, further large-scale studies need to be undertaken.

Endocrinology and Metabolism

Wysham CH, and **Kruger DF**. Practical Considerations for Initiating and Utilizing Flash Continuous Glucose Monitoring in Clinical Practice. *J Endocr Soc* 2021; 5(9). PMID: 34291180. Full Text

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Use of continuous glucose monitoring (CGM) has been shown to improve clinical outcomes in patients with type 1 diabetes (T1D) and type 2 diabetes (T2D), including improved glycemic control, better treatment adherence, and an increased understanding of their treatment regimens. Retrospective analysis of CGM data allows clinicians and patients to identify glycemic patterns that support and facilitate informed therapy adjustments. There are currently 2 types of CGM systems: real-time CGM (rtCGM) and flash CGM. The FreeStyle Libre 2 (FSL2) is the newest flash CGM system commercially available. Because the FSL2 system was only recently cleared for use in the US, many endocrinologists and diabetes specialists may be unfamiliar with the strengths, limitations, and potential of the FSL2 system. This article focuses on practical approaches and strategies for initiating and using flash CGM in endocrinology and diabetes specialty practices.

Family Medicine

Bryce R, WolfsonBryce JA, CohenBryce A, Milgrom N, Garcia D, Steele A, **Yaphe S**, Pike D, **Valbuena F**, and **Miller-Matero LR**. A pilot randomized controlled trial of a fruit and vegetable prescription program at a federally qualified health center in low income uncontrolled diabetics. *Prev Med Rep* 2021; 23:101410. PMID: 34150472. Full Text

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Eating a healthy diet is important for managing diabetes. Although there are high rates of diabetes in low-income urban areas, these patients often have limited access to fruits and vegetables. The 15-week Fresh Prescription (Fresh Rx) program was designed to improve access and consumption of fruits and vegetables among low-income patients with diabetes in Detroit, MI. The purpose of this study was to evaluate the effects of a fruit and vegetable prescription program on changes in hemoglobin A1C (HbA(1)C), blood pressure (BP), and body mass index (BMI) in patients with diabetes in a randomized controlled trial at a federally qualified health center (FQHC). Patients randomized to the Fresh Rx group (n = 56) were allotted up to $80 ($10 for up to eight weeks) for purchase of produce from a farmers market based at the FQHC. The control group (n = 56) received standard treatment plus information on community resources to improve health. Outcomes were compared at baseline and within three months of program completion. There were no significant between-group differences for any of the outcomes at program completion ($p > .05$); however, there was a small effect size for HbA1c (partial $\eta(2) = 0.02$). Within the Fresh Rx group, HbA1c significantly decreased from 9.64% to 9.14% ($p = 0.006$). However, no changes were noted within the control group (9.38 to 9.41%, $p = 0.89$). BMI and BP did not change from pre- to post-study in either group ($p > .05$). Results from this study offer preliminary evidence that produce prescription programs may reduce HbA(1)C in low-income patients with diabetes.

Family Medicine

Mansi ET, Johnson ES, Thorp ML, Go AS, Lee MS, Shen AY, Park KJ, **Budzynska K**, **Markin A**, Sung SH, Thompson JH, Slaughter MT, Luong TQ, An J, Reynolds K, Roblin DW, **Cassidy-Bushrow AE**, Kuntz JL, Schlienger RG, Behr S, and Smith DH. Physician adjudication of angioedema diagnosis codes in a population of patients with heart failure prescribed angiotensin-converting enzyme inhibitor therapy. *Pharmacoepidemiol Drug Saf* 2021; Epub ahead of print. PMID: 34558760. Full Text

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PURPOSE: Our objective was to calculate the positive predictive value (PPV) of the ICD-9 diagnosis code for angioedema when physicians adjudicate the events by electronic health record review. Our secondary objective was to evaluate the inter-rater reliability of physician adjudication. METHODS: Patients from the Cardiovascular Research Network previously diagnosed with heart failure who were started on angiotensin-converting enzyme inhibitors (ACEI) during the study period (July 1, 2006 through September 30, 2015) were included. A team of two physicians per participating site adjudicated possible events using electronic health records for all patients coded for angioedema for a total of five sites. The PPV was calculated as the number of physician-adjudicated cases divided by all cases with the diagnosis code of angioedema (ICD-9-CM code 995.1) meeting the inclusion criteria. The inter-rater reliability of physician teams, or kappa statistic, was also calculated. RESULTS: There were 38 061 adults with heart failure initiating ACEI in the study (21 489 patient-years). Of 114 coded events that were adjudicated by physicians, 98 angioedema events were confirmed for a PPV of 86% (95% CI: 80%, 92%). The kappa statistic based on physician inter-rater reliability was 0.65 (95% CI: 0.47, 0.82). CONCLUSIONS: ICD-9 diagnosis code of 995.1 (angioneurotic edema, not elsewhere classified) is highly predictive of angioedema in adults with heart failure exposed to ACEI.

Gastroenterology

Ayyash M, **Smith N**, **Keerthy M**, **Singh A**, and **Shaman M**. Benign Recurrent Intrahepatic Cholestasis in Pregnancy: Fetal Death at 36 Weeks of Gestation. *Case Rep Obstet Gynecol* 2021; 2021:5086846. PMID: 34532146. Full Text

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INTRODUCTION: Benign recurrent intrahepatic cholestasis is a rare hepatologic disorder characterized by recurrent, self-limited episodes of severe pruritus, jaundice, and elevated bile acids. While there are guidelines for the management of intrahepatic cholestasis of pregnancy, the literature regarding benign recurrent intrahepatic cholestasis and pregnancy is limited. CASE: A 29-year-old G1P0 woman, with history of liver toxicity, had elevated total serum bile acid levels and liver enzymes documented at 8 weeks of gestation and throughout her pregnancy. She had a reactive nonstress test just 3 days prior to her induction. Fetal demise was noted when she presented at 36 weeks for her induction. CONCLUSION: We recommend that women with elevated total serum bile acid early in pregnancy due to a separate entity relative to intrahepatic cholestasis of pregnancy be managed in a more individualized approach.

Gastroenterology

Ivanics T, **Leonard-Murali S**, **Mouzaihem H**, **Moonka D**, **Kitajima T**, **Yeddula S**, **Shamaa T**, **Rizzari M**, **Collins K**, **Yoshida A**, **Abouljoud M**, and **Nagai S**. Extreme Hyponatremia as a Risk Factor for Early Mortality after Liver Transplantation in the MELD-Sodium Era. *Transpl Int* 2021; Epub ahead of print. PMID: 34580929. Full Text

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BACKGROUND: The impact of hyponatremia on waitlist and post-transplant outcomes following the implementation of MELD-Na-based liver allocation remains unclear. We investigated waitlist and post-liver transplant(LT) outcomes in patients with hyponatremia before and after implementing MELD-Na-based allocation. METHODS: Adult patients registered for a primary LT between 2009 and 2021 were identified in the OPTN/UNOS database. Two eras were defined; pre-MELD-Na and post-MELD-Na. Extreme hyponatremia was defined as a serum sodium concentration≤120mEq/L. 90-day waitlist outcomes and post-LT survival were compared using Fine-Gray proportional hazard and mixed-effects Cox proportional hazard models. RESULTS: 118,487 patients were eligible (n=64,940:pre-MELD-Na;n=53,547:post-MELD-Na). In the pre-MELD-Na era, extreme hyponatremia at listing was associated with an increased risk of 90-day waitlist mortality ([ref:135-145]HR:3.80;95%CI:2.97-4.87;p<0.001) and higher transplant probability (HR: 1.67;95%CI:1.38-2.01;p<0.001). In the post-MELD-Na era, patients with extreme hyponatremia had a proportionally lower relative risk of waitlist mortality (HR:2.27;95%CI1.60-3.23;p<0.001) and proportionally higher transplant probability (HR:2.12;95%CI1.76-2.55;p<0.001) as patients with normal serum sodium levels(135-145). Extreme hyponatremia was associated with a higher risk of 90, 180, and 365-day post-LT survival compared to patients with normal serum sodium levels. CONCLUSION: With the introduction of MELD-Na-based allocation, waitlist outcomes have improved in patients with extreme hyponatremia but continue to have worse short-term post-LT survival.

Gastroenterology
Li J, **Lu M**, **Zhou Y**, Bowlus CL, Lindor K, Rodriguez-Watson C, Romanelli RJ, Haller IV, Anderson H, VanWormer JJ, Boscarino JA, Schmidt MA, Daida YG, Sahota A, Vincent J, **Wu KH**, **Trudeau S**, **Rupp LB**, **Melkonian C**, and **Gordon SC**. Dynamic Risk Prediction of Response to Ursodeoxycholic Acid Among Patients with Primary Biliary Cholangitis in the USA. *Dig Dis Sci* 2021; Epub ahead of print. PMID: 34499271. Full Text

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BACKGROUND: Ursodeoxycholic acid (UDCA) remains the first-line therapy for primary biliary cholangitis (PBC); however, inadequate treatment response (ITR) is common. The UK-PBC Consortium developed the modified UDCA Response Score (m-URS) to predict ITR (using alkaline phosphatase [ALP] > 1.67 times the upper limit of normal [*ULN]) at 12 months post-UDCA initiation). Using data from the US-based Fibrotic Liver Disease Consortium, we assessed the m-URS in our multi-racial cohort. We then used a dynamic modeling approach to improve prediction accuracy. METHODS: Using data collected at the time

of UDCA initiation, we assessed the m-URS using the original formula; then, by calibrating coefficients to our data, we also assessed whether it remained accurate when using Paris II criteria for ITR. Next, we developed and validated a dynamic risk prediction model that included post-UDCA initiation laboratory data. RESULTS: Among 1578 patients (13% men; 8% African American, 9% Asian American/American Indian/Pacific Islander; 25% Hispanic), the rate of ITR was 27% using ALP > 1.67*ULN and 45% using Paris II criteria. M-URS accuracy was "very good" (AUROC = 0.87, sensitivity = 0.62, and specificity = 0.82) for ALP > 1.67*ULN and "moderate" (AUROC = 0.74, sensitivity = 0.57, and specificity = 0.70) for Paris II. Our dynamic model significantly improved accuracy for both definitions of ITR (ALP > 1.67*ULN: AUROC = 0.91; Paris II: AUROC = 0.81); specificity approached 100%. Roughly 9% of patients in our cohort were at the highest risk of ITR. CONCLUSIONS: Early identification of patients who will not respond to UDCA treatment using a dynamic prediction model based on longitudinal, repeated risk factor measurements may facilitate earlier introduction of adjuvant treatment.

Hematology-Oncology

Fleming JL, Pugh SL, Fisher BJ, Lesser GJ, Macdonald DR, Bell EH, McElroy JP, Becker AP, Timmers CD, Aldape KD, Rogers CL, **Doyle TJ**, Werner-Wasik M, Bahary JP, Yu HM, D'Souza DP, Laack NN, Sneed PK, Kwok Y, Won M, Mehta MP, and Chakravarti A. Long-Term Report of a Comprehensive Molecular and Genomic Analysis in NRG Oncology/RTOG 0424: A Phase II Study of Radiation and Temozolomide in High-Risk Grade II Glioma. *JCO Precis Oncol* 2021; 5. PMID: 34589661. Request Article

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Henry Ford Hospital, Detroit, MI.
Thomas Jefferson University Hospital, Philadelphia, PA.
Centre Hospitalier de l`université De Montréal, Montreal, QC, Canada.
Moffitt Cancer Center, Tampa, FL.
Mayo Clinic, Rochester, MN.
UCSF Medical Center-Parnassus, San Francisco, CA.
University of Maryland/Greenebaum Cancer Center, Baltimore, MA.
Miami Cancer Institute, Miami, FL.

PURPOSE: This study sought to determine the prognostic significance of the WHO-defined glioma molecular subgroups along with additional alterations, including MGMT promoter methylation and mutations in ATRX, CIC, FUBP1, TERT, and TP53, in NRG/RTOG 0424 using long-term follow-up data. METHODS: Mutations were determined using an Ion Torrent sequencing panel. 1p/19q co-deletion and MGMT promoter methylation were determined by Affymetrix OncoScan and Illumina 450K arrays. Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method and tested using the log-rank test. Hazard ratios were calculated using the Cox proportional hazard model. Multivariable analyses (MVAs) included patient pretreatment characteristics. RESULTS: We obtained complete molecular data to categorize 80/129 eligible patients within the WHO subgroups. Of these, 26 (32.5%) were IDHmutant/co-deleted, 28 (35%) were IDHmutant/non-co-deleted, and 26 (32.5%) were IDHwild-type. Upon single-marker MVA, both IDHmutant subgroups were associated with significantly better OS and PFS (P values < .001), compared with the IDHwild-type subgroup. MGMT promoter methylation was obtained on 76 patients, where 58 (76%) were methylated and 18 (24%) were unmethylated. Single-marker MVAs demonstrated that MGMT promoter methylation was statistically significant for OS (P value < .001) and PFS (P value = .003). In a multimarker MVA, one WHO subgroup comparison (IDHmutant/co-deleted v IDHwild-type) was significant for OS (P value = .045), whereas MGMT methylation did not retain significance. CONCLUSION: This study reports the long-term prognostic effect of the WHO molecular subgroups, MGMT promoter methylation, and other mutations in NRG/RTOG 0424. These results demonstrate that the WHO molecular classification and MGMT both

serve as strong prognostic indicators, but that MGMT does not appear to add statistically significant prognostic value to the WHO subgrouping, above and beyond IDH and 1p/19q status.

Hematology-Oncology

Geary MK, **Kachalsky E**, and Parnes A. The actual and ideal roles of haemophilia treatment centre social workers in the United States and the barriers to ideal roles. *Haemophilia* 2021; Epub ahead of print. PMID: 34523198. Full Text

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INTRODUCTION: Social Workers (SWs) provide valuable services on multidisciplinary teams of Haemophilia Treatment Centres (HTCs). However, their roles have not been defined and standardized. This paper identifies six major SW roles, including counselling, case management, financial/insurance, outreach/programs, administrative, and grants/research. Roles were further classified as 'actual' roles, those that SWs were actively practicing, and 'ideal' roles, those that SWs felt were most important for their clients. AIM: The goal of this study was to determine the actual and ideal roles of HTC SWs and the barriers to ideal roles. METHODS: An online survey was tested with a focus group and then e-mailed to 147 SWs who were working in the 141 HTCs across the United States. RESULTS: Fifty-five percent of the SWs completed the survey. Data revealed that SWs' most prominent actual role was case management in their work with three client sub-populations: adult patients, paediatric patients and family members. However, SWs identified counselling as the ideal role that was most important for all client groups. Barriers to practicing ideal roles included lack of SW input, insufficient budgeted time and inadequate training. Salaries were found to be stagnant compared to 2010. Twenty-five percent of SWs reported no supervision. CONCLUSIONS: Survey results gave evidence that although HTC SWs were primarily engaged in case management roles, they wanted to take on larger counselling roles. Efforts should be made to eliminate barriers to ideal SW roles so that SWs can provide additional psychosocial services for HTC patients.

Hematology-Oncology

Oyedeji O, **Sheqwara J**, **Onwubiko I**, **Lopez-Plaza I**, **Nagai S**, and **Otrock ZK**. Thrombocytapheresis for acquired von Willebrand syndrome in a patient with essential thrombocythemia and recent multivisceral transplantation. *Transfusion* 2021; Epub ahead of print. PMID: 34569071. Full Text

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BACKGROUND: Essential thrombocythemia (ET) is associated with increased risk of bleeding secondary to acquired von Willebrand syndrome (AVWS). Bleeding in ET requires urgent platelet reduction by cytoreductive therapy such as hydroxyurea or thrombocytapheresis. We report on the efficacy and safety of thrombocytapheresis in managing AVWS in a patient with ET and multivisceral transplantation. CASE REPORT: The patient was a 51-year-old female who underwent multivisceral transplantation. Her postoperative course was complicated by bleeding from oral cavity, IV lines, gastrointestinal and upper respiratory tracts as well as vaginal bleeding, which coincided with ET flare with a platelet count of 1512 × 10(9) /L. Coagulation studies including von Willebrand factor (vWF) antigen and activity, vWF propeptide antigen, and vWF multimer analysis were consistent with AVWS. Hydroxyurea was initiated. However, due to major bleeding, rapidly increasing platelet count, and uncertainty of response to hydroxyurea being given through the enteral tube, thrombocytapheresis was initiated for rapid platelet reduction. The patient tolerated the procedure well. Platelet count was reduced from 1636 × 10(9) /L to 275 × 10(9) /L with rapid cessation of bleeding. The patient's condition stabilized over the next few days; however, bleeding recurred with increasing platelet count, which required a second thrombocytapheresis 8 days after the first one. The patient was maintained on hydroxyurea 500 mg twice/day. At 11-month follow-up, she had a normal platelet count and no recurrence of bleeding. DISCUSSION:

Thrombocytapheresis is safe and efficient in managing postoperative bleeding due to ET/AVWS in solid organ transplant patients. The procedure can be an adjunct to bridging therapy before response to hydroxyurea is achieved.

Hematology-Oncology

Yi Z, Wei S, Jin L, Jeyarajan S, Yang J, Gu Y, Kim HS, Schechter S, Lu S, Paulsen MT, Bedi K, Narayanan IV, Ljungman M, **Crawford HC**, Pasca di Magliano M, Ge K, Dou Y, and Shi J. KDM6A Regulates Cell Plasticity and Pancreatic Cancer Progression by Non-Canonical Activin Pathway. *Cell Mol Gastroenterol Hepatol* 2021; Epub ahead of print. PMID: 34583087. Full Text

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BACKGROUND & AIMS: Inactivating mutations of KDM6A, a histone demethylase, were frequently found in pancreatic ductal adenocarcinoma (PDAC). We investigated the role of KDM6A in PDAC development. METHODS: We performed a pancreatic tissue microarray analysis of KDM6A protein levels. We used human PDAC cell lines for KDM6A knockout and knockdown experiments. We performed Bru-seq analysis to elucidate the effects of KDM6A loss on global transcription. We performed studies with Ptf1a(Cre); LSL-Kras(G12D); Trp53(R172H/+); Kdm6a(fl/fl or fl/Y), Ptf1a(Cre); Kdm6a(fl/fl or fl/Y), and orthotopic xenograft mice to investigate the impacts of Kdm6a deficiency on pancreatic tumorigenesis and pancreatitis. RESULTS: Loss of KDM6A was associated with metastasis in PDAC patients. Bru-seq analysis revealed upregulation of the epithelial-mesenchymal transition pathway in PDAC cells deficient of KDM6A. Loss of KDM6A promoted mesenchymal morphology, migration, and invasion in PDAC cells in vitro. Mechanistically, activin A and subsequent p38 activation likely mediated the role of KDM6A loss. Inhibiting either activin A or p38 reversed the effect. Pancreas-specific Kdm6a-knockout mice pancreata demonstrated accelerated PDAC progression, developed a more aggressive undifferentiated type PDAC, and increased metastases in the background of Kras and p53 mutations. Kdm6a-deficient pancreata in a pancreatitis model had a delayed recovery with increased PDAC precursor lesions compared to wild-type pancreata. CONCLUSIONS: Loss of KDM6A accelerates PDAC progression and metastasis, most likely by a non-canonical p38-dependant activin A pathway. KDM6A also promotes pancreatic tissue recovery from pancreatitis. Activin A might be utilized as a therapeutic target for KDM6A-deficient PDACs.

Hospital Medicine

Raad M, **Gorgis S**, Abshire C, Yost M, **Dabbagh MF**, Chehab O, **Aurora L**, **Patel S**, **Nona P**, **Yan J**, **Singh G**, Syrjamaki J, **Kaatz S**, and **Parikh S**. COVID-19 risk index (CRI): a simple and validated emergency department risk score that predicts mortality and the need for mechanical ventilation. *J Thromb Thrombolysis* 2021;1-9. Epub ahead of print. PMID: 34554359. Full Text

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Although certain risk factors have been associated with morbidity and mortality, validated emergency department (ED) derived risk prediction models specific to coronavirus disease 2019 (COVID-19) are lacking. The objective of this study is to describe and externally validate the COVID-19 risk index (CRI). A large retrospective longitudinal cohort study was performed to analyze consecutively hospitalized patients with COVID-19. Multivariate regression using clinical data elements from the ED was used to create the CRI. The results were validated with an external cohort of 1799 patients from the MI-COVID19 database. The primary outcome was the composite of the need for mechanical ventilation or inpatient mortality, and the secondary outcome was inpatient mortality. A total of 1020 patients were included in the derivation cohort. A total of 236 (23%) patients in the derivation cohort required mechanical ventilation or died. Variables independently associated with the primary outcome were age ≥ 65 years, chronic obstructive pulmonary disease, chronic kidney disease, cerebrovascular disease, initial D-dimer > 1.1 μg/mL, platelet count < 150 K/μL, and severity of SpO2:FiO2 ratio. The derivation cohort had an area under the receiver operator characteristic curve (AUC) of 0.83, and 0.74 in the external validation cohort Calibration shows close adherence between the observed and expected primary outcomes within the validation cohort. The CRI is a novel disease-specific tool that assesses the risk for mechanical ventilation or death in hospitalized patients with COVID-19. Discrimination of the score may change given continuous updates in contemporary COVID-19 management and outcomes.

Hypertension and Vascular Research

Pan G, **Roy B**, and **Palaniyandi SS**. Diabetic Aldehyde Dehydrogenase 2 Mutant (ALDH2*2) Mice Are More Susceptible to Cardiac Ischemic-Reperfusion Injury Due to 4-Hydroxy-2-Nonenal Induced Coronary Endothelial Cell Damage. *J Am Heart Assoc* 2021; 10(18):e021140. PMID: 34482710. Full Text

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Background Aldehyde dehydrogenase-2 (ALDH2), a mitochondrial enzyme, detoxifies reactive aldehydes such as 4-hydroxy-2-nonenal (4HNE). A highly prevalent E487K mutation in ALDH2 (ALDH2*2) in East Asian people with intrinsic low ALDH2 activity is implicated in diabetic complications. 4HNE-induced cardiomyocyte dysfunction was studied in diabetic cardiac damage; however, coronary endothelial cell (CEC) injury in myocardial ischemia-reperfusion injury (IRI) in diabetic mice has not been studied. Therefore, we hypothesize that the lack of ALDH2 activity exacerbates 4HNE-induced CEC dysfunction which leads to cardiac damage in ALDH2*2 mutant diabetic mice subjected to myocardial IRI. Methods and Results Three weeks after diabetes mellitus (DM) induction, hearts were subjected to IRI either in vivo via left anterior descending artery occlusion and release or ex vivo IRI by using the Langendorff system. The cardiac performance was assessed by conscious echocardiography in mice or by inserting a balloon catheter in the left ventricle in the ex vivo model. Just 3 weeks of DM led to an increase in cardiac 4HNE protein adducts and, cardiac dysfunction, and a decrease in the number of CECs along with reduced myocardial ALDH2 activity in ALDH2*2 mutant diabetic mice compared with their wild-type counterparts. Systemic pretreatment with Alda-1 (10 mg/kg per day), an activator of both ALDH2 and ALDH2*2, led to a reduction in myocardial infarct size and dysfunction, and coronary perfusion pressure upon cardiac IRI by increasing CEC population and coronary arteriole opening. Conclusions Low ALDH2 activity exacerbates 4HNE-mediated CEC injury and thereby cardiac dysfunction in diabetic mouse hearts subjected to IRI, which can be reversed by ALDH2 activation.

Infectious Diseases

Bakthavatchalam YD, Vasudevan K, Rao S, Varughese S, Rupali P, **Gina M**, **Zervos M**, Peter JV, and Veeraraghavan B. Genomic portrait of community-associated methicillin-resistant Staphylococcus aureus ST772-SCCmec V lineage from India. *Gene Reports* 2021; 24. PMID: Not assigned. Full Text

Background: Significant changes in the epidemiology of methicillin-resistant Staphylococcus aureus (MRSA) were recognised with the emergence of community-associated methicillin-resistant Staphylococcus aureus. However, studies on the molecular epidemiology and the genomic investigation

of MRSA are limited in India. Aim: The study was aims to understand the molecular epidemiology of MRSA causing bloodstream infection and also to investigate the origin and evolution of ST772 S. aureus isolated from India. Methods: A total of 233 non-repetitive MRSA isolates were screened for the presence staphylococcal cassette chromosome (SCCmec) types, multi-locus sequence types (MLST) and staphylococcal protein A (spa) types. Whole genome sequence data of ST772-SCCmec V (n = 32) isolates were generated and comparative analysis was performed. Results: MLST analysis revealed ten different clonal complexes and three singletons. ST772 (27%), ST22 (19%) and ST239 (16%) were the predominant MRSA genotypes in causing bloodstream infection. The spa types were highly diverse. Phylogenetic analysis revealed that nearly three-fourth of the Indian STT72-SCCmec V isolates belongs to dominant (ST772-A2) and emerging subgroups (ST772-A3). A pattern of increasing antimicrobial resistance was noticed in the dominant and emerging subgroups. An integrated resistance plasmid encoding resistance clusters for beta-lactam (blaZ), macrolides (mphC, msrA), and aminoglycoside resistance (aphA-III, sat-4, aadE) was identified in all isolates, except four basal strains. ST772-SCCmec V was emerged on the Indian subcontinent in 1964 and diverged into a dominant subgroup in 1991. Furthermore, the expansion is likely to be associated with the acqusition of mobile genetic elements such as integrated resistance plasmid and SCCmec V (5C2) as well as the fixation of double serine mutation (S84L, S80Y) in the quinolone resistance determining region. Conclusions: ST772 S. aureus have consistent virulence and resistance determinants which may results in successful survival in both community and hospital settings.

Infectious Diseases

Bhargava P. Response to "Tocilizumab therapy and COVID-19". *J Osteopath Med* 2021; Epub ahead of print. PMID: 34492174. Full Text

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Infectious Diseases

El Sahly HM, Baden LR, Essink B, Doblecki-Lewis S, Martin JM, Anderson EJ, Campbell TB, Clark J, Jackson LA, Fichtenbaum CJ, **Zervos M**, Rankin B, Eder F, Feldman G, Kennelly C, Han-Conrad L, Levin M, Neuzil KM, Corey L, Gilbert P, Janes H, Follmann D, Marovich M, Polakowski L, Mascola JR, Ledgerwood JE, Graham BS, August A, Clouting H, Deng W, Han S, Leav B, Manzo D, Pajon R, Schödel F, Tomassini JE, Zhou H, and Miller J. Efficacy of the mRNA-1273 SARS-CoV-2 Vaccine at Completion of Blinded Phase. *N Engl J Med* 2021; Epub ahead of print. PMID: 34551225. Full Text

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BACKGROUND: At interim analysis in a phase 3, observer-blinded, placebo-controlled clinical trial, the mRNA-1273 vaccine showed 94.1% efficacy in preventing coronavirus disease 2019 (Covid-19). After emergency use of the vaccine was authorized, the protocol was amended to include an open-label phase. Final analyses of efficacy and safety data from the blinded phase of the trial are reported. METHODS: We enrolled volunteers who were at high risk for Covid-19 or its complications; participants were randomly assigned in a 1:1 ratio to receive two intramuscular injections of mRNA-1273 (100 μg) or placebo, 28

days apart, at 99 centers across the United States. The primary end point was prevention of Covid-19 illness with onset at least 14 days after the second injection in participants who had not previously been infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The data cutoff date was March 26, 2021. RESULTS: The trial enrolled 30,415 participants; 15,209 were assigned to receive the mRNA-1273 vaccine, and 15,206 to receive placebo. More than 96% of participants received both injections, 2.3% had evidence of SARS-CoV-2 infection at baseline, and the median follow-up was 5.3 months in the blinded phase. Vaccine efficacy in preventing Covid-19 illness was 93.2% (95% confidence interval [CI], 91.0 to 94.8), with 55 confirmed cases in the mRNA-1273 group (9.6 per 1000 person-years; 95% CI, 7.2 to 12.5) and 744 in the placebo group (136.6 per 1000 person-years; 95% CI, 127.0 to 146.8). The efficacy in preventing severe disease was 98.2% (95% CI, 92.8 to 99.6), with 2 cases in the mRNA-1273 group and 106 in the placebo group, and the efficacy in preventing asymptomatic infection starting 14 days after the second injection was 63.0% (95% CI, 56.6 to 68.5), with 214 cases in the mRNA-1273 group and 498 in the placebo group. Vaccine efficacy was consistent across ethnic and racial groups, age groups, and participants with coexisting conditions. No safety concerns were identified. CONCLUSIONS: The mRNA-1273 vaccine continued to be efficacious in preventing Covid-19 illness and severe disease at more than 5 months, with an acceptable safety profile, and protection against asymptomatic infection was observed. (Funded by the Biomedical Advanced Research and Development Authority and the National Institute of Allergy and Infectious Diseases; COVE ClinicalTrials.gov number, NCT04470427.).

Infectious Diseases

Hagins D, Kumar P, Saag M, Wurapa AK, **Brar I**, Berger D, Osiyemi O, Hileman CO, Ramgopal MN, McDonald C, Blair C, Andreatta K, Collins SE, Brainard DM, and Martin H. Switching to Bictegravir/Emtricitabine/Tenofovir Alafenamide in Black Americans With HIV-1: A Randomized Phase 3b, Multicenter, Open-Label Study. *J Acquir Immune Defic Syndr* 2021; 88(1):86-95. PMID: 34397746. Full Text

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BACKGROUND: With the highest rates of HIV/AIDS in the United States, Black Americans are still underrepresented in HIV medical research. SETTING: BRAAVE (NCT03631732) is a randomized, phase 3b, multicenter, open-label US study. METHODS: Adults identifying as Black or African American and virologically suppressed on 2 nucleoside reverse transcriptase inhibitors (NRTIs) plus third agent were randomized (2:1) to switch to open-label bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) once daily or stay on baseline regimen (SBR) for 24 weeks, after which SBR had delayed switch to B/F/TAF. Resistance to non-NRTIs, protease inhibitors, and/or NRTIs was permitted; integrase strand transfer inhibitor resistance was exclusionary. Primary endpoint was proportion of participants with HIV-1 RNA ≥50 copies/mL at week 24 (snapshot algorithm; noninferiority margin of 6%). RESULTS: Of 558 screened, 495 were randomized/treated (B/F/TAF n = 330; SBR n = 165). Overall, 32% were ciswomen, 2% transwomen, and 10% had an M184V/I mutation. At week 24, 0.6% on B/F/TAF vs 1.8% on SBR had HIV-1 RNA ≥50 copies/mL (difference -1.2%; 95% confidence interval -4.8% to 0.9%), demonstrating noninferiority of B/F/TAF vs SBR. Proportions with HIV-1 RNA <50 copies/mL at week 24 were 96% B/F/TAF and 95% SBR and remained high at week 48. No participant had treatment-emergent resistance to study drug. Treatments were well tolerated. Study drug-related adverse events, mostly grade 1, occurred in 10% of participants on B/F/TAF through week 48 and led to discontinuation in 9 participants

through week 48. CONCLUSIONS: For Black Americans with HIV, switching to B/F/TAF was noninferior to continuing a variety of regimens, including those with pre-existing NRTI mutations.

Infectious Diseases

Heldman MR, Kates OS, Safa K, Kotton CN, Georgia SJ, Steinbrink JM, Alexander BD, Hemmersbach-Miller M, Blumberg EA, Multani A, 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 PP, Hughes Kramer K, Velioglu A, Yabu JM, Morillis JA, Mehta SA, Tanna SD, Ison MG, Derenge AC, van Duin D, Maximin A, Gilbert C, Goldman JD, Lease ED, Fisher CE, and Limaye AP. Changing Trends in Mortality Among Solid Organ Transplant Recipients Hospitalized for Covid-19 During the Course of the Pandemic. *Am J Transplant* 2021; Epub ahead of print. PMID: 34514710. Full Text

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Mortality among patients hospitalized for Covid-19 has declined over the course of the pandemic. Mortality trends specifically in solid organ transplant recipients (SOTR) are unknown. Using data from a multicenter registry of SOTR hospitalized for Covid-19, we compared 28-day mortality between early 2020 (3/1/20-6/19/20) and late 2020 (6/20/20-12/31/20). Multivariable logistic regression was used to assess comorbidity-adjusted mortality. Time period of diagnosis was available for 1,435/1,616 (88.8%) SOTR and 971/1,435 (67.7%) were hospitalized: 571/753 (75.8%) in early 2020 and 402/682 (58.9%) in late 2020 (P<0.001). Crude 28-day mortality decreased between the early and late periods (112/571 [19.6%] vs. 55/402 [13.7%] and remained lower in the late period even after adjusting for baseline

comorbidities (aOR 0.67, 95% CI 0.46-0.98, P=0.016). Between the early and late periods, corticosteroids (≥ 6mg dexamethasone/day) and remdesivir use increased (62/571 [10.9%] vs. 243/402 [61.5%], P <0.001 and 50/571 [8.8%] vs. 213/402 [52.2%], P<0.001, respectively) and hydroxychloroquine and IL-6/IL-6 receptor inhibitor use decreased (329/571 [60.0%] vs. 4/492 [1.0 %], P <0.001 and 73/571 [12.8%] vs. 5/402 [1.2%], P <0.001, respectively). Mortality among SOTR hospitalized for Covid-19 declined between early and late 2020, consistent with trends reported in the general population. The mechanism(s) underlying improved survival require further study.

Infectious Diseases

Maki G, and **Zervos M**. Health Care-Acquired Infections in Low- and Middle-Income Countries and the Role of Infection Prevention and Control. *Infect Dis Clin North Am* 2021; 35(3):827-839. PMID: 34362546. Full Text

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Health care-associated infections (HAIs) account for many morbidity and mortality worldwide, with disproportionate adverse effects in low- and middle-income countries (LMIC). Many factors contribute to the impact in LMIC, including lack of infrastructure, inconsistent surveillance, deficiency in trained personnel and infection control programs, and poverty-related factors. Therefore, optimal approaches must be tailored for LMIC and balance effectiveness and cost in the control of HAIs.

Infectious Diseases

Wu T, Davis SL, Church B, Alangaden GJ, and **Kenney RM**. Outcomes of clinical decision support for outpatient management of Clostridioides difficile infection. *Infect Control Hosp Epidemiol* 2021;1-4. Epub ahead of print. PMID: 34583800. Full Text

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OBJECTIVE: To determine the impact of clinical decision support on guideline-concordant Clostridioides difficile infection (CDI) treatment. DESIGN: Quasi-experimental study in >50 ambulatory clinics. SETTING: Primary, specialty, and urgent-care clinics. PATIENTS: Adult patients were eligible for inclusion if they were diagnosed with and treated for a first episode of symptomatic CDI at an ambulatory clinic between November 1, 2019, and November 30, 2020. INTERVENTIONS: An outpatient best practice advisory (BPA) was implemented to notify prescribers that "vancomycin or fidaxomicin are preferred over metronidazole for C.difficile infection" when metronidazole was prescribed to a patient with CDI. RESULTS: In total, 189 patients were included in the study: 92 before the BPA and 97 after the BPA. Their median age was 59 years; 31% were male; 75% were white; 30% had CDI-related comorbidities; 35% had healthcare exposure; 65% had antibiotic exposure; 44% had gastric acid suppression therapy within 90 days of CDI diagnosis. The BPA was accepted 23 of 26 times and was used to optimize the therapy of 16 patients in 6 months. Guideline-concordant therapy increased after implementation of the BPA (72% vs 91%; P = .001). Vancomycin prescribing increased and metronidazole prescribing decreased after the BPA. There was no difference in clinical response or unplanned encounter within 14 days after treatment initiation. Fewer patients after the BPA had CDI recurrence within 14-56 days of the initial episode (27% vs 7%; P < .001). CONCLUSIONS: Clinical decision support increased prescribing of guideline-concordant CDI therapy in the outpatient setting. A targeted BPA is an effective stewardship intervention and may be especially useful in settings with limited antimicrobial stewardship resources.

Internal Medicine

Mahmood S, **Nona P**, **Villablanca P**, Nunez-Gil I, and Ramakrishna H. The Meta-Analysis in Evidence-Based Medicine: High-Quality Research When Properly Performed. *J Cardiothorac Vasc Anesth* 2021; 35(9):2556-2558. PMID: 34127359. Full Text

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Internal Medicine

Muhanna A, **Nimri F**, Almomani ZA, Al Momani L, Likhitsup A, and Hamid F. Small Bowel Metastasis as a Presentation of Testicular Seminoma. *Cureus* 2021; 13(9):e17962. PMID: 34548993. Full Text

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Testicular germ cell tumors account for 95% of testicular cancers in men with approximately 71,000 patients being diagnosed with testicular cancer every year. The overall survival of testicular germ cell tumors is approximately 95%. However, the prognosis becomes less favorable when distant metastasis is present. Gastrointestinal (GI) tract metastasis occurs in less than 5% of patients with non-seminomatous tumors, and in less than 1% in patients with pure seminomas. GI metastasis usually involves the colon, esophagus, and stomach with the most common symptoms of GI metastasis being diarrhea, nausea, vomiting, and obstruction. We discuss the case of a 42-year-old male patient with GI manifestations as the first presentation of testicular seminoma with metastasis to the small bowel. Computed tomography of the abdomen and pelvis revealed a small bowel mass, and the diagnosis was confirmed with histopathologic examination of endoscopic biopsy samples. The patient subsequently underwent chemotherapy treatment with close surveillance. Clinicians should maintain a high index of suspicion in the differential diagnosis of abdominal pain in young male patients, especially when associated with symptoms like unexplained weight loss, constitutional symptoms, and testicular pain or swelling. Metastasis to the GI tract from the testis should be promptly diagnosed and managed, as the overall survival rates can significantly decrease with the delay of diagnosis.

Internal Medicine

Muhanna A, **Nimri FM**, Almomani ZA, Al Momani L, and Likhitsup A. Granulomatous Hepatitis Secondary to Histoplasmosis in an Immunocompetent Patient. *Cureus* 2021; 13(9):e17631. PMID: 34513533. Full Text

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Histoplasma capsulatum is the most common endemic mycosis in the United States and usually occurs in certain geographic areas, such as the Mississippi or Ohio River valleys. Histoplasmosis usually causes a mild disease in the immunocompetent but can progress to disseminated disease in patients with impaired immunity. Granulomatous hepatitis as a manifestation of disseminated histoplasmosis in immunocompetent patients is extremely rare. We report the case of a 62-year-old immunocompetent

gentleman with a history of histoplasmosis who presented with abdominal pain, elevated liver enzymes, who was diagnosed with granulomatous hepatitis secondary to histoplasmosis.

Nephrology

Swaminathan M, Kopyt N, Atta MG, Radhakrishnan J, **Umanath K**, Nguyen S, O'Rourke B, Allen A, Vaninov N, Tilles A, LaPointe E, Blair A, Gemmiti C, Miller B, Parekkadan B, and Barcia RN. Pharmacological effects of ex vivo mesenchymal stem cell immunotherapy in patients with acute kidney injury and underlying systemic inflammation. *Stem Cells Transl Med* 2021; Epub ahead of print. PMID: 34581517. Full Text

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Mesenchymal stem cells (MSCs) have natural immunoregulatory functions that have been explored for medicinal use as a cell therapy with limited success. A phase Ib study was conducted to evaluate the safety and immunoregulatory mechanism of action of MSCs using a novel ex vivo product (SBI-101) to preserve cell activity in patients with severe acute kidney injury. Pharmacological data demonstrated MSC-secreted factor activity that was associated with anti-inflammatory signatures in the molecular and cellular profiling of patient blood. Systems biology analysis captured multicompartment effects consistent with immune reprogramming and kidney tissue repair. Although the study was not powered for clinical efficacy, these results are supportive of the therapeutic hypothesis, namely, that treatment with SBI-101 elicits an immunotherapeutic response that triggers an accelerated phenotypic switch from tissue injury to tissue repair. Ex vivo administration of MSCs, with increased power of testing, is a potential new biological delivery paradigm that assures sustained MSC activity and immunomodulation.

Neurology

Arandela K, Samudrala S, Abdalkader M, Anand P, Daneshmand A, Dasenbrock H, Nguyen T, Ong C, Takahashi C, Shulman J, Babi MA, Sivakumar S, Shah N, Jain S, Anand S, Nobleza COS, Shekhar S, Venkatasubramanian C, Salahuddin H, Taqi MA, **Nour HA**, **Nofar JB**, and Cervantes-Arslanian AM. Reversible Cerebral Vasoconstriction Syndrome in Patients with Coronavirus Disease: A Multicenter Case Series. *J Stroke Cerebrovasc Dis* 2021; 30(12):106118. PMID: 34560378. Full Text

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BACKGROUND AND OBJECTIVES: RCVS (Reversible Cerebral Vasoconstrictive Syndrome) is a condition associated with vasoactive agents that alter endothelial function. There is growing evidence that endothelial inflammation contributes to cerebrovascular disease in patients with coronavirus disease 2019 (COVID-19). In our study, we describe the clinical features, risk factors, and outcomes of RCVS in a multicenter case series of patients with COVID-19. MATERIALS AND METHODS: Multicenter retrospective case series. We collected clinical characteristics, imaging, and outcomes of patients with RCVS and COVID-19 identified at each participating site. RESULTS: Ten patients were identified, 7 women, ages 21 - 62 years. Risk factors included use of vasoconstrictive agents in 7 and history of migraine in 2. Presenting symptoms included thunderclap headache in 5 patients with recurrent headaches in 4. Eight were hypertensive on arrival to the hospital. Symptoms of COVID-19 included fever in 2, respiratory symptoms in 8, and gastrointestinal symptoms in 1. One patient did not have systemic COVID-19 symptoms. MRI showed subarachnoid hemorrhage in 3 cases, intraparenchymal hemorrhage in 2, acute ischemic stroke in 4, FLAIR hyperintensities in 2, and no abnormalities in 1 case. Neurovascular imaging showed focal segment irregularity and narrowing concerning for vasospasm of the left MCA in 4 cases and diffuse, multifocal narrowing of the intracranial vasculature in 6 cases. Outcomes varied, with 2 deaths, 2 remaining in the ICU, and 6 surviving to discharge with modified Rankin scale (mRS) scores of 0 (n=3), 2 (n=2), and 3 (n=1). CONCLUSIONS: Our series suggests that patients with COVID-19 may be at risk for RCVS, particularly in the setting of additional risk factors such as exposure to vasoactive agents. There was variability in the symptoms and severity of COVID-19, clinical characteristics, abnormalities on imaging, and mRS scores. However, a larger study is needed to validate a causal relationship between RCVS and COVID-19.

Neurology

Ganesan K, Plass J, Beltz AM, Liu Z, Grabowecky M, Suzuki S, Stacey WC, **Wasade VS**, Towle VL, Tao JX, Wu S, Issa NP, and Brang D. Visual speech differentially modulates beta, theta, and high gamma bands in auditory cortex. *Eur J Neurosci* 2021; Epub ahead of print. PMID: 34587350. Full Text

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Speech perception is a central component of social communication. Although principally an auditory process, accurate speech perception in everyday settings is supported by meaningful information extracted from visual cues. Visual speech modulates activity in cortical areas subserving auditory speech perception including the superior temporal gyrus (STG). However, it is unknown whether visual modulation of auditory processing is a unitary phenomenon or, rather, consists of multiple functionally distinct processes. To explore this question, we examined neural responses to audiovisual speech measured from intracranially implanted electrodes in 21 patients with epilepsy. We found that visual speech modulated auditory processes in the STG in multiple ways, eliciting temporally and spatially distinct patterns of activity that differed across frequency bands. In the theta band, visual speech suppressed the auditory response from before auditory speech onset to after auditory speech onset (-93 ms to 500 ms) most strongly in the posterior STG. In the beta band, suppression was seen in the anterior

STG from -311 to -195 ms before auditory speech onset and in the middle STG from -195 ms to 235 ms after speech onset. In high gamma, visual speech enhanced the auditory response from -45 ms to 24 ms only in the posterior STG. We interpret the visual-induced changes prior to speech onset as reflecting crossmodal prediction of speech signals. In contrast, modulations after sound onset may reflect a decrease in sustained feedforward auditory activity. These results are consistent with models that posit multiple distinct mechanisms supporting audiovisual speech perception.

Neurology

Hauser RA, Hattori N, Fernandez H, Isaacson SH, Mochizuki H, Rascol O, Stocchi F, Li J, Mori A, Nakajima Y, Ristuccia R, and **LeWitt P**. Efficacy of Istradefylline, an Adenosine A2A Receptor Antagonist, as Adjunctive Therapy to Levodopa in Parkinson's Disease: A Pooled Analysis of 8 Phase 2b/3 Trials. *J Parkinsons Dis* 2021; Epub ahead of print. PMID: 34486986. Request Article

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BACKGROUND: Istradefylline is a selective adenosine A2A receptor antagonist for the treatment of patients with Parkinson's disease (PD) experiencing OFF episodes while on levodopa/decarboxylase inhibitor. OBJECTIVE: This pooled analysis of eight randomized, placebo-controlled, double-blind phase 2b/3 studies evaluated the efficacy and safety of istradefylline. METHODS: Istradefylline was evaluated in PD patients receiving levodopa with carbidopa/benserazide and experiencing motor fluctuations. Eight 12- or 16-week trials were conducted (n=3,245); four of these studies were the basis for istradefylline's FDA approval. Change in OFF time as assessed in patient-completed 24-h PD diaries at Week 12 was the primary endpoint. All studies were designed with common methodology, thereby permitting pooling of data. Pooled analysis results from once-daily oral istradefylline (20 and 40 mg/day) and placebo were evaluated using a mixed-model repeated-measures approach including study as a factor. RESULTS: Among 2,719 patients (placebo, n=992; 20 mg/day, n=848; 40 mg/day, n=879), OFF hours/day were reduced at Week 12 at istradefylline dosages of 20 mg/day (least-squares mean difference [LSMD] from placebo in reduction from baseline [95%CI], -0.38 h [-0.61, -0.15]) and 40 mg/day (-0.45 h [-0.68, -0.22], p< 0.0001); ON time without troublesome dyskinesia (ON-WoTD) significantly increased. Similar results were found in the four-study pool (OFF hours/day, 20 mg/day, -0.75 h [-1.10, -0.40]; 40 mg/day, -0.82 h [-1.17, -0.47]). Istradefylline was generally well-tolerated; the average study completion rate among istradefylline-treated patients across all studies was 89.2%. Dyskinesia was the most frequent adverse event (placebo, 9.6%; 20 mg/day, 16.1%; 40 mg/day, 17.7%). CONCLUSION: In this pooled analysis, istradefylline significantly improved OFF time and ON-WoTD relative to placebo and was well-tolerated.

Neurology

Nagaraja TN, **Bartlett S**, **Farmer KG**, **Cabral G**, **Knight RA**, **Valadie OG**, **Brown SL**, **Ewing JR**, and **Lee IY**. Adaptation of laser interstitial thermal therapy for tumor ablation under MRI monitoring in a rat orthotopic model of glioblastoma. *Acta Neurochir (Wien)* 2021; Epub ahead of print. PMID: 34554269. Full Text

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BACKGROUND: Laser interstitial thermal therapy (LITT) under magnetic resonance imaging (MRI) monitoring is being increasingly used in cytoreductive surgery of recurrent brain tumors and tumors located in eloquent brain areas. The objective of this study was to adapt this technique to an animal glioma model. METHODS: A rat model of U251 glioblastoma (GBM) was employed. Tumor location and extent were determined by MRI and dynamic contrast-enhanced (DCE) MRI. A day after assessing tumor appearance, tumors were ablated during diffusion-weighted imaging (DWI)-MRI using a Visualase LITT system (n = 5). Brain images were obtained immediately after ablation and again at 24 h post-ablation to confirm the efficacy of tumor cytoablation. Untreated tumors served as controls (n = 3). Rats were injected with fluorescent isothiocyanate (FITC) dextran and Evans blue that circulated for 10 min after post-LITT MRI. The brains were then removed for fluorescence microscopy and histopathology evaluations using hematoxylin and eosin (H&E) and major histocompatibility complex (MHC) staining. RESULTS: All rats showed a space-occupying tumor with T2 and T1 contrast-enhancement at pre-LITT imaging. The rats that underwent the LITT procedure showed a well-demarcated ablation zone with near-complete ablation of tumor tissue and with peri-ablation contrast enhancement at 24 h post-ablation. Tumor cytoreduction by ablation as seen on MRI was confirmed by H&E and MHC staining. CONCLUSIONS: Data showed that tumor cytoablation using MRI-monitored LITT was possible in preclinical glioma models. Real-time MRI monitoring facilitated visualizing and controlling the area of ablation as it is otherwise performed in clinical applications.

Neurology
Poewe W, Stocchi F, Arkadir D, Ebersbach G, Ellenbogen AL, Giladi N, Isaacson SH, **Kieburtz K**, LeWitt P, **Olanow CW**, Simuni T, Thomas A, Zlotogorski A, Adar L, Case R, Oren S, Fuchs Orenbach S, Rosenfeld O, Sasson N, Yardeni T, and Espay AJ. Subcutaneous Levodopa Infusion for Parkinson's Disease: 1-Year Data from the Open-Label BeyoND Study. *Mov Disord* 2021; Epub ahead of print. PMID: 34496081. Full Text

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BACKGROUND: Continuous, subcutaneous (SC) levodopa/carbidopa infusion with ND0612 is under development as a treatment for patients with Parkinson's disease (PD) and motor fluctuations. OBJECTIVE: Evaluate 1-year safety data. METHODS: BeyoND is an open-label study evaluating the long-term safety of two ND0612 dosing regimens. RESULTS: Of the 214 enrolled patients (24-hour SC infusion: n = 90; 16-hour SC infusion: n = 124), 120 (56%) completed 12 months of treatment. Leading causes for study discontinuation were consent withdrawal (19.6%) and adverse events (17.3%). Rates of discontinuation were reduced from 49% to 29% after a protocol revision and retraining. Systemic safety was typical for PD patients treated with levodopa/carbidopa. Most patients experienced infusion site reactions, particularly nodules (30.8%) and hematoma (25.2%), which were judged mostly mild to moderate and led to discontinuation in only 10.3% of the participants. CONCLUSIONS: Subcutaneous levodopa/carbidopa continuous infusion with ND0612 is generally safe, with typical infusion site reactions for SC delivery as the main adverse event. © 2021 The Authors. Movement Disorders published by Wiley Periodicals LLC on behalf of International Parkinson and Movement Disorder Society.

Neurology

Schwarzschild MA, Ascherio A, Casaceli C, Curhan GC, Fitzgerald R, Kamp C, Lungu C, Macklin EA, Marek K, Mozaffarian D, Oakes D, Rudolph A, Shoulson I, Videnovic A, Scott B, Gauger L, Aldred J, Bixby M, Ciccarello J, Gunzler SA, Henchcliffe C, Brodsky M, Keith K, Hauser RA, Goetz C, LeDoux MS, Hinson V, Kumar R, Espay AJ, Jimenez-Shahed J, Hunter C, Christine C, Daley A, Leehey M, de Marcaida JA, Friedman JH, Hung A, Bwala G, Litvan I, Simon DK, Simuni T, Poon C, Schiess MC, Chou K, Park A, Bhatti D, Peterson C, Criswell SR, Rosenthal L, Durphy J, Shill HA, Mehta SH, Ahmed A, Deik AF, Fang JY, Stover N, Zhang L, Dewey RB, Jr., Gerald A, Boyd JT, Houston E, Suski V, Mosovsky S, Cloud L, Shah BB, Saint-Hilaire M, James R, Zauber SE, Reich S, Shprecher D, Pahwa R, Langhammer A, LaFaver K, **LeWitt PA**, **Kaminski P**, Goudreau J, Russell D, Houghton DJ, Laroche A, Thomas K, McGraw M, Mari Z, Serrano C, Blindauer K, Rabin M, Kurlan R, Morgan JC, Soileau M, Ainslie M, Bodis-Wollner I, Schneider RB, Waters C, Ratel AS, Beck CA, Bolger P, Callahan KF, Crotty GF, Klements D, Kostrzebski M, McMahon GM, Pothier L, Waikar SS, Lang A, and Mestre T. Effect of Urate-Elevating Inosine on Early Parkinson Disease Progression: The SURE-PD3 Randomized Clinical Trial. *Jama* 2021; 326(10):926-939. PMID: 34519802. Full Text

IMPORTANCE: Urate elevation, despite associations with crystallopathic, cardiovascular, and metabolic disorders, has been pursued as a potential disease-modifying strategy for Parkinson disease (PD) based on convergent biological, epidemiological, and clinical data. OBJECTIVE: To determine whether sustained urate-elevating treatment with the urate precursor inosine slows early PD progression. DESIGN, PARTICIPANTS, AND SETTING: Randomized, double-blind, placebo-controlled, phase 3 trial of oral inosine treatment in early PD. A total of 587 individuals consented, and 298 with PD not yet requiring dopaminergic medication, striatal dopamine transporter deficiency, and serum urate below the population median concentration (<5.8 mg/dL) were randomized between August 2016 and December 2017 at 58 US sites, and were followed up through June 2019. INTERVENTIONS: Inosine, dosed by blinded titration to increase serum urate concentrations to 7.1-8.0 mg/dL (n = 149) or matching placebo (n = 149) for up to 2 years. MAIN OUTCOMES AND MEASURES: The primary outcome was rate of change in the Movement Disorder Society Unified Parkinson Disease Rating Scale (MDS-UPDRS; parts I-III) total score (range, 0-236; higher scores indicate greater disability; minimum clinically important difference of 6.3 points) prior to dopaminergic drug therapy initiation. Secondary outcomes included serum urate to measure target engagement, adverse events to measure safety, and 29 efficacy measures of disability, quality of life, cognition, mood, autonomic function, and striatal dopamine transporter binding as a biomarker of neuronal integrity. RESULTS: Based on a prespecified interim futility analysis, the study closed early, with 273 (92%) of the randomized participants (49% women; mean age, 63 years) completing the study. Clinical progression rates were not significantly different between participants randomized to inosine (MDS-UPDRS score, 11.1 [95% CI, 9.7-12.6] points per year) and placebo (MDS-UPDRS score, 9.9 [95% CI, 8.4-11.3] points per year; difference, 1.26 [95% CI, -0.59 to 3.11] points per year; P = .18). Sustained elevation of serum urate by 2.03 mg/dL (from a baseline level of 4.6 mg/dL; 44% increase) occurred in the inosine group vs a 0.01-mg/dL change in serum urate in the

placebo group (difference, 2.02 mg/dL [95% CI, 1.85-2.19 mg/dL]; P<.001). There were no significant differences for secondary efficacy outcomes including dopamine transporter binding loss. Participants randomized to inosine, compared with placebo, experienced fewer serious adverse events (7.4 vs 13.1 per 100 patient-years) but more kidney stones (7.0 vs 1.4 stones per 100 patient-years). CONCLUSIONS AND RELEVANCE: Among patients recently diagnosed as having PD, treatment with inosine, compared with placebo, did not result in a significant difference in the rate of clinical disease progression. The findings do not support the use of inosine as a treatment for early PD. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT02642393.

Neurosurgery
Lim S, and **Chang V**. Commentary: Complications Associated with Oblique Lumbar Interbody Fusion at L5-S1: A Systematic Review of the Literature. *Neurosurgery Open* 2021; 2(3). PMID: Not assigned. Full Text

V. Chang, Department of Neurosurgery, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI, United States

Neurosurgery
Lim S, **Zervos TM**, **Hamilton T**, and **Chang V**. Minimally Invasive Posterior Cervical Discectomy: 2-Dimensional Operative Video. *Oper Neurosurg (Hagerstown)* 2021; Epub ahead of print. PMID: 34498688. Full Text

Department of Neurosurgery, Henry Ford Hospital, Detroit, Michigan, USA.

Minimally invasive posterior cervical microdiscectomy is an appropriate surgical approach for patients with foraminal stenosis from herniated disc with radicular symptoms that is not responsive to conservative management. While anterior cervical discectomy and fusion (ACDF) or arthroplasty is increasingly utilized to treat herniated disc, a posterior approach eliminates the risk of potential approach related injuries to the esophagus, carotid artery, or recurrent laryngeal nerve. Additional benefits of posterior decompression include avoidance of instrumentation, which represents an increased healthcare cost, as well as potential long-term risks of adjacent-level pathologies or device failures. A traditional open posterior cervical approach has the potential to cause significant postoperative pain due to dissection of the paraspinal musculature and the potential for disrupting the posterior tension band with inadvertent injury to the interspinous ligaments. Such disadvantages are reduced by utilizing the minimally invasive technique where a small tubular working channel is placed through a muscle splitting technique via a paramedian approach. This technique minimizes the need for muscle stripping, and thus decreases postoperative functional and structural disturbance. Discectomy in this case can also be safely performed with minimal retraction at the axilla of the nerve root. Additionally, this approach can be utilized in an ambulatory setting, which coupled with the lack of any additional instrumentation helps contribute to the overall healthcare cost savings of such a procedure. This video describes how the minimally invasive posterior cervical discectomy can be effectively and safely performed in this illustrative case. The patient consented to the procedure and publication.

Neurosurgery
Macki M, **Hamilton T**, **Lim S**, **Mansour TR**, **Telemi E**, **Bazydlo M**, **Schultz L**, **Nerenz DR**, Park P, **Chang V**, **Schwalb J**, and **Abdulhak MM**. The role of postoperative antibiotic duration on surgical site infection after lumbar surgery. *J Neurosurg Spine* 2021;1-7. Epub ahead of print. PMID: 34534952. Full Text

Departments of1Neurosurgery.
2Public Health Sciences, and.
3Center for Health Policy and Health Services Research, Henry Ford Hospital, Detroit, Michigan; and.
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OBJECTIVE: Despite a general consensus regarding the administration of preoperative antibiotics, poorly defined comparison groups and underpowered studies prevent clear guidelines for postoperative

antibiotics. Utilizing a data set tailored specifically to spine surgery outcomes, in this clinical study the authors aimed to determine whether there is a role for postoperative antibiotics in the prevention of surgical site infection (SSI). METHODS: The Michigan Spine Surgery Improvement Collaborative registry was queried for all lumbar operations performed for degenerative spinal pathologies over a 5-year period from 2014 to 2019. Preoperative prophylactic antibiotics were administered for all surgical procedures. The study population was divided into three cohorts: no postoperative antibiotics, postoperative antibiotics ≤ 24 hours, and postoperative antibiotics > 24 hours. This categorization was intended to determine 1) whether postoperative antibiotics are helpful and 2) the appropriate duration of postoperative antibiotics. First, multivariable analysis with generalized estimating equations (GEEs) was used to determine the association between antibiotic duration and all-type SSI with adjusted odds ratios; second, a three-tiered outcome-no SSI, superficial SSI, and deep SSI-was calculated with multivariable multinomial logistical GEE analysis. RESULTS: Among 37,161 patients, the postoperative antibiotics > 24 hours cohort had more men with older average age, greater body mass index, and greater comorbidity burden. The postoperative antibiotics > 24 hours cohort had a 3% rate of SSI, which was significantly higher than the 2% rate of SSI of the other two cohorts (p = 0.004). On multivariable GEE analysis, neither postoperative antibiotics > 24 hours nor postoperative antibiotics ≤ 24 hours, as compared with no postoperative antibiotics, was associated with a lower rate of all-type postoperative SSIs. On multivariable multinomial logistical GEE analysis, neither postoperative antibiotics ≤ 24 hours nor postoperative antibiotics > 24 hours was associated with rate of superficial SSI, as compared with no antibiotic use at all. The odds of deep SSI decreased by 45% with postoperative antibiotics ≤ 24 hours (p = 0.002) and by 40% with postoperative antibiotics > 24 hours (p = 0.008). CONCLUSIONS: Although the incidence of all-type SSI was highest in the antibiotics > 24 hours cohort, which also had the highest proportions of risk factors, duration of antibiotics failed to predict all-type SSI. On multinomial subanalysis, administration of postoperative antibiotics for both ≤ 24 hours and > 24 hours was associated with decreased risk of only deep SSI but not superficial SSI. Spine surgeons can safely consider antibiotics for 24 hours, which is equally as effective as long-term administration for prophylaxis against deep SSI.

Neurosurgery

Mariano ER, Dickerson DM, Szokol JW, Harned M, Mueller JT, Philip BK, Baratta JL, Gulur P, Robles J, Schroeder KM, Wyatt KEK, **Schwalb JM**, Schwenk ES, Wardhan R, Kim TS, Higdon KK, Krishnan DG, Shilling AM, Schwartz G, Wiechmann L, Doan LV, Elkassabany NM, Yang SC, Muse IO, Eloy JD, Mehta V, Shah S, Johnson RL, Englesbe MJ, Kallen A, Mukkamala SB, Walton A, and Buvanendran A. A multisociety organizational consensus process to define guiding principles for acute perioperative pain management. *Reg Anesth Pain Med* 2021; Epub ahead of print. PMID: 34552003. Full Text

The US Health and Human Services Pain Management Best Practices Inter-Agency Task Force initiated a public-private partnership which led to the publication of its report in 2019. The report emphasized the need for individualized, multimodal, and multidisciplinary approaches to pain management that decrease the over-reliance on opioids, increase access to care, and promote widespread education on pain and substance use disorders. The Task Force specifically called on specialty organizations to work together to develop evidence-based guidelines. In response to this report's recommendations, a consortium of 14 professional healthcare societies committed to a 2-year project to advance pain management for the surgical patient and improve opioid safety. The modified Delphi process included two rounds of electronic voting and culminated in a live virtual event in February 2021, during which seven common guiding principles were established for acute perioperative pain management. These principles should help to inform local action and future development of clinical practice recommendations.

Neurosurgery

Nagahama Y, **Zervos TM**, Murata KK, Holman L, Karsonovich T, Parker JJ, Chen JS, Phillips HW, Fajardo M, Nariai H, Hussain SA, Porter BE, Grant GA, Ragheb J, Wang S, O'Neill BR, Alexander AL, Bollo RJ, and Fallah A. Real-World Preliminary Experience With Responsive Neurostimulation in Pediatric Epilepsy: A Multicenter Retrospective Observational Study. *Neurosurgery* 2021; Epub ahead of print. PMID: 34528103. Full Text

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Warren Alpert Medical School of Brown University, Providence, Rhode Island, USA.
Division of Neurology, Brain Institute, Nicklaus Children's Hospital, Miami, Florida, USA.
Division of Pediatric Neurology, Lucile Packard Children's Hospital, Stanford University, Palo Alto, California, USA.
Division of Neurosurgery, Brain Institute, Nicklaus Children's Hospital, Miami, Florida, USA.

BACKGROUND: Despite the well-documented utility of responsive neurostimulation (RNS, NeuroPace) in adult epilepsy patients, literature on the use of RNS in children is limited. OBJECTIVE: To determine the real-world efficacy and safety of RNS in pediatric epilepsy patients. METHODS: Patients with childhood-onset drug-resistant epilepsy treated with RNS were retrospectively identified at 5 pediatric centers. Reduction of disabling seizures and complications were evaluated for children (<18 yr) and young adults (>18 yr) and compared with prior literature pertaining to adult patients. RESULTS: Of 35 patients identified, 17 were <18 yr at the time of RNS implantation, including a 3-yr-old patient. Four patients (11%) had concurrent resection. Three complications, requiring additional surgical interventions, were noted in young adults (2 infections [6%] and 1 lead fracture [3%]). No complications were noted in children. Among the 32 patients with continued therapy, 2 (6%) achieved seizure freedom, 4 (13%) achieved ≥90% seizure reduction, 13 (41%) had ≥50% reduction, 8 (25%) had <50% reduction, and 5 (16%) experienced no improvement. The average follow-up duration was 1.7 yr (median 1.8 yr, range 0.3-4.8 yr). There was no statistically significant difference for seizure reduction and complications between children and young adults in our cohort or between our cohort and the adult literature. CONCLUSION: These preliminary data suggest that RNS is well tolerated and an effective off-label surgical treatment of drug-resistant epilepsy in carefully selected pediatric patients as young as 3 yr of age. Data regarding long-term efficacy and safety in children will be critical to optimize patient selection.

Neurosurgery

Nagaraja TN, **Bartlett S**, **Farmer KG**, **Cabral G**, **Knight RA**, **Valadie OG**, **Brown SL**, **Ewing JR**, and **Lee IY**. Adaptation of laser interstitial thermal therapy for tumor ablation under MRI monitoring in a rat orthotopic model of glioblastoma. *Acta Neurochir (Wien)* 2021; Epub ahead of print. PMID: 34554269.
Full Text

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BACKGROUND: Laser interstitial thermal therapy (LITT) under magnetic resonance imaging (MRI) monitoring is being increasingly used in cytoreductive surgery of recurrent brain tumors and tumors located in eloquent brain areas. The objective of this study was to adapt this technique to an animal glioma model. METHODS: A rat model of U251 glioblastoma (GBM) was employed. Tumor location and

extent were determined by MRI and dynamic contrast-enhanced (DCE) MRI. A day after assessing tumor appearance, tumors were ablated during diffusion-weighted imaging (DWI)-MRI using a Visualase LITT system (n = 5). Brain images were obtained immediately after ablation and again at 24 h post-ablation to confirm the efficacy of tumor cytoablation. Untreated tumors served as controls (n = 3). Rats were injected with fluorescent isothiocyanate (FITC) dextran and Evans blue that circulated for 10 min after post-LITT MRI. The brains were then removed for fluorescence microscopy and histopathology evaluations using hematoxylin and eosin (H&E) and major histocompatibility complex (MHC) staining. RESULTS: All rats showed a space-occupying tumor with T2 and T1 contrast-enhancement at pre-LITT imaging. The rats that underwent the LITT procedure showed a well-demarcated ablation zone with near-complete ablation of tumor tissue and with peri-ablation contrast enhancement at 24 h post-ablation. Tumor cytoreduction by ablation as seen on MRI was confirmed by H&E and MHC staining. CONCLUSIONS: Data showed that tumor cytoablation using MRI-monitored LITT was possible in preclinical glioma models. Real-time MRI monitoring facilitated visualizing and controlling the area of ablation as it is otherwise performed in clinical applications.

Neurosurgery

Testini P, Sarva H, **Schwalb J**, Barkan S, and Cabrera LY. Neurosurgeons perspective on the shift towards earlier use of deep brain stimulation for Parkinson disease. *Interdisciplinary Neurosurgery: Advanced Techniques and Case Management* 2021; 25. PMID: Not assigned. Full Text

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Background: The US Food and Drug Administration approved in 2015 the use of deep brain stimulation for Parkinson disease after “four years duration and with recent onset of motor complications”. The aim of this study was to identify neurosurgeons’ attitudes and perspectives around the use of deep brain stimulation for Parkinson disease earlier in the disease course. Methods: An anonymous survey examining attitudes and perceptions towards deep brain stimulation practice and timing in Parkinson disease was developed by the study team and distributed by the American Society for Stereotactic and Functional Neurosurgeons to its members. Results from 32 subjects with answers to at least 50% of the survey were included. Data were analyzed with descriptive statistics and chi-square test. Results: Motor fluctuations, dyskinesia, quality of life impairment, and medically refractory tremor were the most important reasons to proceed with deep brain stimulation, which was overall considered more useful after the onset of motor symptoms. Unresponsiveness to levodopa, cognitive impairment, and unclear diagnosis were important reasons not to consider deep brain stimulation. Earlier surgery was considered to be less risky compared to later in the disease progression. Ten out of 25 neurosurgeons reported considering deep brain stimulation as a therapeutic option after a minimum disease duration of three to four years. Conclusions: We conclude that neurosurgeons support the use of earlier deep brain stimulation, but not preceding motor complications. Further research surrounding the benefits and adverse effects of earlier deep brain stimulation is needed to guide practice and better inform potential candidates.

Obstetrics, Gynecology and Women’s Health Services

Ayyash M, **Smith N**, **Keerthy M**, **Singh A**, and **Shaman M**. Benign Recurrent Intrahepatic Cholestasis in Pregnancy: Fetal Death at 36 Weeks of Gestation. *Case Rep Obstet Gynecol* 2021; 2021:5086846. PMID: 34532146. Full Text

Department of Obstetrics and Gynecology, Henry Ford Health System, Detroit, Michigan, USA. Department of Gastroenterology and Hepatology, Henry Ford Health System, Detroit, Michigan, USA. Division of Maternal and Fetal Medicine, Department of Obstetrics and Gynecology, Henry Ford Health System, Detroit, Michigan, USA.

INTRODUCTION: Benign recurrent intrahepatic cholestasis is a rare hepatologic disorder characterized by recurrent, self-limited episodes of severe pruritus, jaundice, and elevated bile acids. While there are guidelines for the management of intrahepatic cholestasis of pregnancy, the literature regarding benign recurrent intrahepatic cholestasis and pregnancy is limited. CASE: A 29-year-old G1P0 woman, with

history of liver toxicity, had elevated total serum bile acid levels and liver enzymes documented at 8 weeks of gestation and throughout her pregnancy. She had a reactive nonstress test just 3 days prior to her induction. Fetal demise was noted when she presented at 36 weeks for her induction. CONCLUSION: We recommend that women with elevated total serum bile acid early in pregnancy due to a separate entity relative to intrahepatic cholestasis of pregnancy be managed in a more individualized approach.

Orthopedics/Bone and Joint Center
Ali SA, Peffers MJ, Ormseth MJ, Jurisica I, and Kapoor M. The non-coding RNA interactome in joint health and disease. *Nat Rev Rheumatol* 2021; Epub ahead of print. PMID: 34588660. Request Article

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Non-coding RNAs have distinct regulatory roles in the pathogenesis of joint diseases including osteoarthritis (OA) and rheumatoid arthritis (RA). As the amount of high-throughput profiling studies and mechanistic investigations of microRNAs, long non-coding RNAs and circular RNAs in joint tissues and biofluids has increased, data have emerged that suggest complex interactions among non-coding RNAs that are often overlooked as critical regulators of gene expression. Identifying these non-coding RNAs and their interactions is useful for understanding both joint health and disease. Non-coding RNAs regulate signalling pathways and biological processes that are important for normal joint development but, when dysregulated, can contribute to disease. The specific expression profiles of non-coding RNAs in various disease states support their roles as promising candidate biomarkers, mediators of pathogenic mechanisms and potential therapeutic targets. This Review synthesizes literature published in the past 2 years on the role of non-coding RNAs in OA and RA with a focus on inflammation, cell death, cell proliferation and extracellular matrix dysregulation. Research to date makes it apparent that 'non-coding' does not mean 'non-essential' and that non-coding RNAs are important parts of a complex interactome that underlies OA and RA.

Orthopedics/Bone and Joint Center
Jildeh TR, **Buckley P**, **Abbas MJ**, Page B, Young J, Mehran N, and **Okoroha KR**. Impact of Patellar Tendinopathy on Player Performance in the National Basketball Association. *Orthop J Sports Med* 2021; 9(9):23259671211025305. PMID: 34504899. Full Text

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BACKGROUND: The extent to which patellar tendinopathy affects National Basketball Association (NBA) athletes has not been thoroughly elucidated. PURPOSE: To assess the impact patellar tendinopathy has on workload, player performance, and career longevity in NBA athletes. STUDY DESIGN: Cohort study; Level of evidence, 3. METHODS: NBA players diagnosed with patellar tendinopathy between the 2000-2001 and 2018-2019 seasons were identified through publicly available data. Characteristics, return to

play (RTP), player statistics, and workload data were compiled. The season of diagnosis was set as the index year, and the statistical analysis compared post- versus preindex data acutely and in the long term, both within the injured cohort and with a matched healthy NBA control cohort. RESULTS: A total of 46 NBA athletes were included in the tendinopathy group; all 46 players returned to the NBA after their diagnosis. Compared with controls, the tendinopathy cohort had longer careers (10.50 ± 4.32 vs 7.18 ± 5.28 seasons; P < .001) and played more seasons after return from injury (4.26 ± 2.46 vs 2.58 ± 3.07 seasons; P = .001). Risk factors for patellar tendinopathy included increased workload before injury (games started, 45.83 ± 28.67 vs 25.01 ± 29.77; P < .001) and time played during the season (1951.21 ± 702.09 vs 1153.54 ± 851.05 minutes; P < .001) and during games (28.71 ± 6.81 vs 19.88 ± 9.36 minutes per game; P < .001). Players with increased productivity as measured by player efficiency rating (PER) were more likely to develop patellar tendinopathy compared with healthy controls (15.65 ± 4.30 vs 12.76 ± 5.27; P = .003). When comparing metrics from 1 year preinjury, there was a decrease in games started at 1 year postinjury (-12.42 ± 32.38 starts; P = .028) and total time played (-461.53 ± 751.42 minutes; P = .001); however, PER at 1 and 3 years after injury was unaffected compared with corresponding preinjury statistics. CONCLUSION: NBA players with a higher PER and significantly more playing time were more likely to be diagnosed with patellar tendinopathy. Player performance was not affected by the diagnosis of patellar tendinopathy, and athletes were able to RTP without any impact on career longevity.

Orthopedics/Bone and Joint Center

Tramer JS, **Jildeh TR**, **Castle JP**, **Buckley P**, Nowak C, and Okoroha KR. The impact of nonoperative hip and core injuries on National Football League athlete performance. *Phys Sportsmed* 2021;1-6. Epub ahead of print. PMID: 34488522. Request Article

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OBJECTIVES: Hip and core injuries are common in National Football League (NFL) athletes; however, the impact following injury remains unclear. The goal of this manuscript was to determine the impact of nonoperative hip and core injuries on return to play and performance. METHODS: NFL athletes who sustained a hip or core injury treated nonoperatively between 2010 and 2016 were identified. Offensive and defensive power ratings were calculated for each player's injury season and two seasons before and after to assess longitudinal impact. A matched control group without an identified hip and/or core injury was assembled for comparison. RESULTS: A total of 41 offensive and 71 defensive players with nonoperative hip or core injury were analyzed. All athletes returned to play; offensive and defensive players missed 4.0 ± 5.2 and 3.1 ± 2.6 games after injury, respectively. Offensive players played fewer cumulative career games returning from core injury versus hip (23.5 ± 20.6 vs 41.0 ± 26.4). Defensive players played fewer games (58.1 ± 41.1 versus 37.4 ± 27.1, p < 0.05) with lower defensive power rating (133.9 ± 128.5 versus 219.8 ± 212.2, p < 0.05) cumulatively after hip or core injury. Additionally, 2 years following injury, defensive players played fewer games compared to controls (9.5 ± 7.0 versus 10.9 ± 6.8, p < 0.05). Following hip injury specifically, NFL defenders played fewer games (39.8 ± 27.9 vs 61.9 ± 38.8; p < 0.05) and had a lower defensive power rating (145.9 ± 131.7 vs 239.0 ± 205.9; p < 0.05) compared to before injury. CONCLUSION: Overall, NFL players return to play following nonoperative hip and core injuries. Defensive players played in fewer games following hip or core injury compared to controls; offensive players were unaffected. Hip injuries have a greater impact on performance compared to core injuries in defensive athletes; offensive players played fewer games upon return from core injury.

Otolaryngology – Head and Neck Surgery

Chang SS, and **Movsas B**. How Vital are Patient Reported Outcomes? *J Natl Cancer Inst* 2021; Epub ahead of print. PMID: 34508599. Full Text

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Otolaryngology – Head and Neck Surgery

Garcia-Rodriguez L, **Williams A**, and Spiegel JH. Surgeon Opinion of Beauty Devices and Gadgets That Patients May Find Online. *Facial Plast Surg Aesthet Med* 2021; Epub ahead of print. PMID: 34591709. Full Text

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Otolaryngology – Head and Neck Surgery

Mansour Y, and Kulesza RJ. Premature termination of the sympathetic chain. *Folia Morphol (Warsz)* 2021; Epub ahead of print. PMID: 34545560. Full Text

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The sympathetic chain serves to distribute visceral efferents and afferents over the entire body. The sympathetic chain courses from the base of the skull to the coccyx and sends branches to distribute along spinal nerves and a number of visceral nerves that distribute to cardiac muscle, smooth muscle and glands. During dissection of the posterior abdominal wall, we identified a rare variation of the sympathetic chain. In this subject, the sympathetic chain failed to send gray rami to the L2-4 spinal nerves and terminated by joining the S1 anterior ramus. Such a variation has only been reported once in the literature in 1895. We provide both schematic and photographic documentation of this variation and propose a number of possible circuits whereby visceral axons can reach their target despite these anatomical barriers.

Otolaryngology – Head and Neck Surgery

Shama M, Al-Qurayshi Z, Dahl M, Amdur RJ, Bates J, Mendenhall W, Hitchcock K, Festa BM, **Ghanem T**, and Dziegielewski PT. Human Papillomavirus-Negative Oropharyngeal Cancer Survival Outcomes Based on Primary Treatment: National Cancer Database Analysis. *Otolaryngol Head Neck Surg* 2021; Epub ahead of print. PMID: 34546828. Full Text

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OBJECTIVE: To compare survival outcomes between primary surgery and primary radiation therapy (RT) in patients with human papillomavirus (HPV)-negative oropharyngeal squamous cell carcinoma (OPSCC). STUDY DESIGN: A retrospective observational cohort study. SETTING: National Cancer Database. METHODS: A National Cancer Database review was conducted of 2635 patients with HPV-negative OPSCC who underwent surgery or RT ± chemotherapy between 2010 and 2014. Univariate analysis was performed on all variables and entered into a multivariate model. The main outcome was overall survival (OS). RESULTS: A total of 2635 patients with HPV-negative OPSCC were organized into 4 groups based on cancer staging. In group 1 (T1-2 N0-1; n = 774), up-front surgery had significantly better 5-year OS (76.2%) than RT (56.8%; adjusted hazard ratio [aHR], 1.76; P = .009; 95% CI, 1.15-2.69) and chemoradiation therapy (CRT; 69.5%; aHR, 1.56; P = .019; 95% CI, 1.08-2.26). In group 2 (T3-4 N0-1; n = 327), no significant difference existed between surgery and CRT (5-year OS, 51.3% vs 52.4%; aHR, 0.96; P = .88; 95% CI, 0.54-1.69). In group 3a (T1-2 N2-3; n = 807), surgery with adjuvant treatment showed significantly better 5-year OS than CRT (78.6% vs 68.8%; aHR, 1.51; P = .027; 95% CI, 1.05-

2.18). In group 3b (T3-4 N2-3; n = 737), surgery with adjuvant treatment was not statistically associated with better 5-year OS as compared with CRT (61.0% vs 43.7%; aHR, 1.53; P = .06; 95% CI, 0.98-2.39). CONCLUSION: Primary surgery may provide improved survival outcomes in many cases of HPV-negative OPSCCs. These data should be used in weighing treatment options and may serve as a basis to better delineate treatment algorithms for HPV-negative disease.

Pathology and Laboratory Medicine

Goel S, Bhatia V, Kundu S, Biswas T, **Carskadon S**, **Gupta N**, Asim M, Morrissey C, **Palanisamy N**, and Ateeq B. Transcriptional network involving ERG and AR orchestrates Distal-less homeobox-1 mediated prostate cancer progression. *Nat Commun* 2021; 12(1):5325. PMID: 34493733. Full Text

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Distal-less homeobox-1 (DLX1) is a well-established non-invasive biomarker for prostate cancer (PCa) diagnosis, however, its mechanistic underpinnings in disease pathobiology are not known. Here, we reveal the oncogenic role of DLX1 and show that abrogating its function leads to reduced tumorigenesis and metastases. We observed that ~60% of advanced-stage and metastatic patients display higher DLX1 levels. Moreover, ~96% of TMPRSS2-ERG fusion-positive and ~70% of androgen receptor (AR)-positive patients show elevated DLX1, associated with aggressive disease and poor survival. Mechanistically, ERG coordinates with enhancer-bound AR and FOXA1 to drive transcriptional upregulation of DLX1 in ERG-positive background. However, in ERG-negative context, AR/AR-V7 and FOXA1 suffice to upregulate DLX1. Notably, inhibiting ERG/AR-mediated DLX1 transcription using BET inhibitor (BETi) or/and anti-androgen drugs reduce its expression and downstream oncogenic effects. Conclusively, this study establishes DLX1 as a direct-target of ERG/AR with an oncogenic role and demonstrates the clinical significance of BETi and anti-androgens for DLX1-positive patients.

Pathology and Laboratory Medicine

Oyedeji O, **Sheqwara J**, **Onwubiko I**, **Lopez-Plaza I**, **Nagai S**, and **Otrock ZK**. Thrombocytapheresis for acquired von Willebrand syndrome in a patient with essential thrombocythemia and recent multivisceral transplantation. *Transfusion* 2021; Epub ahead of print. PMID: 34569071. Full Text

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BACKGROUND: Essential thrombocythemia (ET) is associated with increased risk of bleeding secondary to acquired von Willebrand syndrome (AVWS). Bleeding in ET requires urgent platelet reduction by cytoreductive therapy such as hydroxyurea or thrombocytapheresis. We report on the efficacy and safety of thrombocytapheresis in managing AVWS in a patient with ET and multivisceral transplantation. CASE REPORT: The patient was a 51-year-old female who underwent multivisceral transplantation. Her postoperative course was complicated by bleeding from oral cavity, IV lines, gastrointestinal and upper respiratory tracts as well as vaginal bleeding, which coincided with ET flare with a platelet count of 1512 × 10(9) /L. Coagulation studies including von Willebrand factor (vWF) antigen and activity, vWF propeptide antigen, and vWF multimer analysis were consistent with AVWS. Hydroxyurea was initiated.

However, due to major bleeding, rapidly increasing platelet count, and uncertainty of response to hydroxyurea being given through the enteral tube, thrombocytapheresis was initiated for rapid platelet reduction. The patient tolerated the procedure well. Platelet count was reduced from 1636 × 10(9) /L to 275 × 10(9) /L with rapid cessation of bleeding. The patient's condition stabilized over the next few days; however, bleeding recurred with increasing platelet count, which required a second thrombocytapheresis 8 days after the first one. The patient was maintained on hydroxyurea 500 mg twice/day. At 11-month follow-up, she had a normal platelet count and no recurrence of bleeding. DISCUSSION: Thrombocytapheresis is safe and efficient in managing postoperative bleeding due to ET/AVWS in solid organ transplant patients. The procedure can be an adjunct to bridging therapy before response to hydroxyurea is achieved.

Pediatrics

Beidas RS, **Ahmedani BK**, Linn KA, Marcus SC, Johnson C, **Maye M**, **Westphal J**, Wright L, Beck AL, Buttenheim AM, Daley MF, Davis M, **Elias ME**, Jager-Hyman S, Hoskins K, Lieberman A, **McArdle B**, Ritzwoller DP, Small DS, Wolk CB, Williams NJ, and Boggs JM. Study protocol for a type III hybrid effectiveness-implementation trial of strategies to implement firearm safety promotion as a universal suicide prevention strategy in pediatric primary care. *Implement Sci* 2021; 16(1):89. PMID: 34551811. Full Text

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BACKGROUND: Insights from behavioral economics, or how individuals' decisions and behaviors are shaped by finite cognitive resources (e.g., time, attention) and mental heuristics, have been underutilized in efforts to increase the use of evidence-based practices in implementation science. Using the example of firearm safety promotion in pediatric primary care, which addresses an evidence-to-practice gap in universal suicide prevention, we aim to determine: is a less costly and more scalable behavioral economic-informed implementation strategy (i.e., "Nudge") powerful enough to change clinician behavior or is a more intensive and expensive facilitation strategy needed to overcome implementation barriers? METHODS: The Adolescent and child Suicide Prevention in Routine clinical Encounters (ASPIRE) hybrid type III effectiveness-implementation trial uses a longitudinal cluster randomized design. We will test the comparative effectiveness of two implementation strategies to support clinicians' use of an evidence-based firearm safety practice, S.A.F.E. Firearm, in 32 pediatric practices across two health systems. All pediatric practices in the two health systems will receive S.A.F.E. Firearm materials, including training and cable locks. Half of the practices (k = 16) will be randomized to receive Nudge; the other half (k = 16) will be randomized to receive Nudge plus 1 year of facilitation to target additional practice and clinician implementation barriers (Nudge+). The primary implementation outcome is parent-reported clinician fidelity to the S.A.F.E Firearm program. Secondary implementation outcomes include reach and cost. To understand how the implementation strategies work, the primary mechanism to be tested is practice adaptive reserve, a self-report practice-level measure that includes relationship infrastructure, facilitative leadership, sense-making, teamwork, work environment, and culture of learning. DISCUSSION: The ASPIRE trial will integrate implementation science and behavioral economic approaches to advance our understanding of methods for implementing evidence-based firearm safety promotion practices in pediatric primary care. The study answers a question at the heart of many practice change efforts: which strategies are sufficient to support change, and why? Results of the trial will offer valuable insights into how best to implement evidence-based practices that address sensitive health matters in pediatric primary care. TRIAL REGISTRATION: ClinicalTrials.gov, NCT04844021 . Registered 14 April 2021.

Public Health Sciences

Burnett-Hartman AN, Carroll NM, Honda SA, Joyce C, Mitra N, **Neslund-Dudas C**, Olaiya O, Rendle KA, Schnall MD, Vachani A, and Ritzwoller DP. Community-based Lung Cancer Screening Results in Relation to Patient and Radiologist Characteristics: the PROSPR Consortium. *Ann Am Thorac Soc* 2021; Epub ahead of print. PMID: 34543590. Full Text

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RATIONALE: Lung-RADS classification was developed to standardize reporting and management of lung cancer screening using low-dose computed tomography (LDCT). While variation in Lung-RADS distribution between healthcare systems has been reported, it is unclear if this is explained by patient characteristics, radiologist experience with lung cancer screening, or other factors. OBJECTIVE: Our objective was to determine if patient or radiologist factors are associated with Lung-RADS score. METHODS: In the Population-based Research to Optimize the Screening Process (PROSPR) Lung consortium, we conducted a study of patients who received their first screening LDCT at one of the five healthcare systems in the PROSPR Lung Research Center from 5/1/2014 through 12/31/2017. Data on LDCTs, patient factors, and radiologist characteristics were obtained via electronic health records. LDCT findings were categorized using Lung-RADS [negative (1), benign (2), probably benign (3), or suspicious (4)]. We used generalized estimating equations with a multinomial distribution to compare the odds of Lung-RADS 3, and separately Lung-RADS 4, vs. Lung-RADS 1 or 2 and estimated adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the associations between Lung-RADS assignment and patient and radiologist characteristics. RESULTS: Analyses included 8,556 patients; 24% were assigned Lung-RADS 1, 60% Lung-RADS 2,10% Lung-RADS 3, and 5% Lung-RADS 4. Age was positively associated with Lung-RADS 3 (OR=1.02; CI: 1.01-1.03) and 4 (OR=1.03; CI: 1.01-1.05); chronic obstructive pulmonary disease (COPD) was positively associated with Lung-RADS 4 (OR=1.78; 95% CI: 1.45-2.20); obesity was inversely associated with Lung-RADS 3 (OR=0.70; CI: 0.58-0.84) and 4 (OR=0.58; 95% CI: 0.45-0.75). There was no association between sex, race, ethnicity, education, or smoking status and Lung-RADS assignment. Radiologist volume of interpreting screening LDCTs, years in practice, and thoracic specialty were also not associated with Lung-RADS assignment. CONCLUSIONS: Healthcare systems that are comprised of patients with an older age distribution or higher levels of COPD will have a greater proportion of screening LDCTs with Lung-RADS 3 or 4 findings and should plan for additional resources to support appropriate and timely management of noted positive findings.

Public Health Sciences

Griffin LV, **Warner E**, **Palnitkar S**, **Qiu S**, **Honasoge M**, Griffin SG, **Divine G**, and **Rao SD**. Bone Nanomechanical Properties and Relationship to Bone Turnover and Architecture in Patients With Atypical Femur Fractures: A Prospective Nested Case-Control Study. *JBMR Plus* 2021; 5(9):e10523. PMID: 34532612. Full Text

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Atypical femur fractures (AFFs) are well-established serious complication of long-term bisphosphonate and denosumab therapy in patients with osteopenia or osteoporosis. To elucidate underlying mechanism(s) for the development of AFF, we performed a nested case-control study to investigate bone tissue nanomechanical properties and prevailing bone microstructure and tissue-level remodeling status as assessed by bone histomorphometry. We hypothesized that there would be differences in nanomechanical properties between patients with and without AFF and that bone microstructure and remodeling would be related to nanomechanical properties. Thirty-two full-thickness transiliac bone biopsies were obtained from age- and sex-matched patients on long-term bisphosphonate therapy with (n = 16) and without an AFF (n = 16). Standard histomorphometric measurements were made in each sample on three different bone envelopes (cancellous, intracortical, and endosteal). Iliac bone wall thickness was significantly lower on all three bone surfaces in patients with AFF than in those without AFF. Surface-based bone formation rate was suppressed similarly in both groups in comparison to healthy premenopausal and postmenopausal women, with no significant difference between the two groups. Nanoindentation was used to assess material properties of cortical and cancellous bone separately. Elastic modulus was higher in cortical than in cancellous bone in patients with AFF as well as compared to the elastic modulus of cortical bone from non-AFF patients. However, the elastic modulus of the cancellous bone was not different between AFF and non-AFF groups or between cortical and cancellous bone of non-AFF patients. Resistance to plastic deformation was decreased in cortical bone in both AFF and non-AFF groups compared to cancellous bone, but to a greater extent in AFF patients. We conclude that long-term bisphosphonate therapy is associated with prolonged suppression of bone turnover resulting in altered cortical remodeling and tissue nanomechanical properties leading to AFF.

Public Health Sciences

Kim SS, Chung JR, Belongia EA, McLean HQ, King JP, Nowalk MP, Zimmerman RK, Balasubramani GK, Martin ET, Monto AS, **Lamerato LE**, Gaglani M, Smith ME, Dunnigan KM, Jackson ML, Jackson LA, Tenforde MW, Verani JR, Kobayashi M, Schrag S, Patel MM, and Flannery B. mRNA Vaccine Effectiveness against COVID-19 among Symptomatic Outpatients Aged ≥16 Years in the United States, February - May 2021. *J Infect Dis* 2021; Epub ahead of print. PMID: 34498052. Full Text

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Evaluations of vaccine effectiveness (VE) are important to monitor as COVID-19 vaccines are introduced in the general population. Research staff enrolled symptomatic participants seeking outpatient medical care for COVID-19-like illness or SARS-CoV-2 testing from a multisite network. VE was evaluated using the test-negative design. Among 236 SARS-CoV-2 nucleic acid amplification test-positive and 576 test-negative participants aged ≥16 years, VE of mRNA vaccines against COVID-19 was 91% (95% CI: 83-95) for full vaccination and 75% (95% CI: 55-87) for partial vaccination. Vaccination was associated with prevention of most COVID-19 cases among people seeking outpatient medical care.

Public Health Sciences

Li J, **Lu M**, **Zhou Y**, Bowlus CL, Lindor K, Rodriguez-Watson C, Romanelli RJ, Haller IV, Anderson H, VanWormer JJ, Boscarino JA, Schmidt MA, Daida YG, Sahota A, Vincent J, **Wu KH**, **Trudeau S**, **Rupp LB**, **Melkonian C**, and **Gordon SC**. Dynamic Risk Prediction of Response to Ursodeoxycholic Acid Among Patients with Primary Biliary Cholangitis in the USA. *Dig Dis Sci* 2021; Epub ahead of print. PMID: 34499271. Full Text

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BACKGROUND: Ursodeoxycholic acid (UDCA) remains the first-line therapy for primary biliary cholangitis (PBC); however, inadequate treatment response (ITR) is common. The UK-PBC Consortium developed the modified UDCA Response Score (m-URS) to predict ITR (using alkaline phosphatase [ALP] > 1.67 times the upper limit of normal [*ULN]) at 12 months post-UDCA initiation). Using data from the US-based Fibrotic Liver Disease Consortium, we assessed the m-URS in our multi-racial cohort. We then used a dynamic modeling approach to improve prediction accuracy. METHODS: Using data collected at the time of UDCA initiation, we assessed the m-URS using the original formula; then, by calibrating coefficients to our data, we also assessed whether it remained accurate when using Paris II criteria for ITR. Next, we developed and validated a dynamic risk prediction model that included post-UDCA initiation laboratory data. RESULTS: Among 1578 patients (13% men; 8% African American, 9% Asian American/American Indian/Pacific Islander; 25% Hispanic), the rate of ITR was 27% using ALP > 1.67*ULN and 45% using Paris II criteria. M-URS accuracy was "very good" (AUROC = 0.87, sensitivity = 0.62, and specificity = 0.82) for ALP > 1.67*ULN and "moderate" (AUROC = 0.74, sensitivity = 0.57, and specificity = 0.70) for Paris II. Our dynamic model significantly improved accuracy for both definitions of ITR (ALP > 1.67*ULN: AUROC = 0.91; Paris II: AUROC = 0.81); specificity approached 100%. Roughly 9% of patients in our cohort were at the highest risk of ITR. CONCLUSIONS: Early identification of patients who will not respond to UDCA treatment using a dynamic prediction model based on longitudinal, repeated risk factor measurements may facilitate earlier introduction of adjuvant treatment.

Public Health Sciences

Macki M, **Hamilton T**, **Lim S**, **Mansour TR**, **Telemi E**, **Bazydlo M**, **Schultz L**, **Nerenz DR**, Park P, **Chang V**, **Schwalb J**, and **Abdulhak MM**. The role of postoperative antibiotic duration on surgical site infection after lumbar surgery. *J Neurosurg Spine* 2021;1-7. Epub ahead of print. PMID: 34534952. Full Text

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OBJECTIVE: Despite a general consensus regarding the administration of preoperative antibiotics, poorly defined comparison groups and underpowered studies prevent clear guidelines for postoperative antibiotics. Utilizing a data set tailored specifically to spine surgery outcomes, in this clinical study the authors aimed to determine whether there is a role for postoperative antibiotics in the prevention of

surgical site infection (SSI). METHODS: The Michigan Spine Surgery Improvement Collaborative registry was queried for all lumbar operations performed for degenerative spinal pathologies over a 5-year period from 2014 to 2019. Preoperative prophylactic antibiotics were administered for all surgical procedures. The study population was divided into three cohorts: no postoperative antibiotics, postoperative antibiotics ≤ 24 hours, and postoperative antibiotics > 24 hours. This categorization was intended to determine 1) whether postoperative antibiotics are helpful and 2) the appropriate duration of postoperative antibiotics. First, multivariable analysis with generalized estimating equations (GEEs) was used to determine the association between antibiotic duration and all-type SSI with adjusted odds ratios; second, a three-tiered outcome-no SSI, superficial SSI, and deep SSI-was calculated with multivariable multinomial logistical GEE analysis. RESULTS: Among 37,161 patients, the postoperative antibiotics > 24 hours cohort had more men with older average age, greater body mass index, and greater comorbidity burden. The postoperative antibiotics > 24 hours cohort had a 3% rate of SSI, which was significantly higher than the 2% rate of SSI of the other two cohorts (p = 0.004). On multivariable GEE analysis, neither postoperative antibiotics > 24 hours nor postoperative antibiotics ≤ 24 hours, as compared with no postoperative antibiotics, was associated with a lower rate of all-type postoperative SSIs. On multivariable multinomial logistical GEE analysis, neither postoperative antibiotics ≤ 24 hours nor postoperative antibiotics > 24 hours was associated with rate of superficial SSI, as compared with no antibiotic use at all. The odds of deep SSI decreased by 45% with postoperative antibiotics ≤ 24 hours (p = 0.002) and by 40% with postoperative antibiotics > 24 hours (p = 0.008). CONCLUSIONS: Although the incidence of all-type SSI was highest in the antibiotics > 24 hours cohort, which also had the highest proportions of risk factors, duration of antibiotics failed to predict all-type SSI. On multinomial subanalysis, administration of postoperative antibiotics for both ≤ 24 hours and > 24 hours was associated with decreased risk of only deep SSI but not superficial SSI. Spine surgeons can safely consider antibiotics for 24 hours, which is equally as effective as long-term administration for prophylaxis against deep SSI.

Public Health Sciences

Mansi ET, Johnson ES, Thorp ML, Go AS, Lee MS, Shen AY, Park KJ, **Budzynska K**, **Markin A**, Sung SH, Thompson JH, Slaughter MT, Luong TQ, An J, Reynolds K, Roblin DW, **Cassidy-Bushrow AE**, Kuntz JL, Schlienger RG, Behr S, and Smith DH. Physician adjudication of angioedema diagnosis codes in a population of patients with heart failure prescribed angiotensin-converting enzyme inhibitor therapy. *Pharmacoepidemiol Drug Saf* 2021; Epub ahead of print. PMID: 34558760. Full Text

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PURPOSE: Our objective was to calculate the positive predictive value (PPV) of the ICD-9 diagnosis code for angioedema when physicians adjudicate the events by electronic health record review. Our secondary objective was to evaluate the inter-rater reliability of physician adjudication. METHODS: Patients from the Cardiovascular Research Network previously diagnosed with heart failure who were started on angiotensin-converting enzyme inhibitors (ACEI) during the study period (July 1, 2006 through September 30, 2015) were included. A team of two physicians per participating site adjudicated possible events using electronic health records for all patients coded for angioedema for a total of five sites. The PPV was calculated as the number of physician-adjudicated cases divided by all cases with the diagnosis code of angioedema (ICD-9-CM code 995.1) meeting the inclusion criteria. The inter-rater reliability of physician teams, or kappa statistic, was also calculated. RESULTS: There were 38 061 adults with heart

failure initiating ACEI in the study (21 489 patient-years). Of 114 coded events that were adjudicated by physicians, 98 angioedema events were confirmed for a PPV of 86% (95% CI: 80%, 92%). The kappa statistic based on physician inter-rater reliability was 0.65 (95% CI: 0.47, 0.82). CONCLUSIONS: ICD-9 diagnosis code of 995.1 (angioneurotic edema, not elsewhere classified) is highly predictive of angioedema in adults with heart failure exposed to ACEI.

Public Health Sciences

Sen A, **Li P**, Ye W, and Franzblau A. Bayesian inference of dependent kappa for binary ratings. *Stat Med* 2021; Epub ahead of print. PMID: 34542193. Full Text

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In medical and social science research, reliability of testing methods measured through inter- and intraobserver agreement is critical in disease diagnosis. Often comparison of agreement across multiple testing methods is sought in situations where testing is carried out on the same experimental units rendering the outcomes to be correlated. In this article, we first developed a Bayesian method for comparing dependent agreement measures under a grouped data setting. Simulation studies showed that the proposed methodology outperforms the competing methods in terms of power, while maintaining a decent type I error rate. We further developed a Bayesian joint model for comparing dependent agreement measures adjusting for subject and rater-level heterogeneity. Simulation studies indicate that our model outperforms a competing method that is used in this context. The developed methodology was implemented on a key measure on a dichotomous rating scale from a study with six raters evaluating three classification methods for chest radiographs for pneumoconiosis developed by the International Labor Office.

Pulmonary and Critical Care Medicine

Adawi Awdish RL. You Don't Ever Let Go of the Thread. *Ann Intern Med* 2021; Epub ahead of print. PMID: 34570600. Full Text

Henry Ford Health System, Detroit, Michigan (R.L.A.).

Pulmonary and Critical Care Medicine

Martinez-Zayas G, Almeida FA, Yarmus L, Steinfort D, Lazarus DR, **Simoff MJ**, Saettele T, Murgu S, Dammad T, Duong DK, Mudambi L, Filner JJ, Molina S, Aravena C, Thiboutot J, Bonney A, Rueda AM, **Debiane LG**, Hogarth DK, Bedi H, Deffebach M, Sagar AS, Cicenia J, Yu DH, **Cohen A**, Frye L, Grosu HB, Gildea T, Feller-Kopman D, Casal RF, Machuzak M, Arain MH, Sethi S, Eapen GA, Lam L, Jimenez CA, Ribeiro M, Noor LZ, Mehta A, Song J, Choi H, Ma J, Li L, and Ost DE. Predicting Lymph Node Metastasis in Non-small Cell Lung Cancer: Prospective External and Temporal Validation of the HAL and HOMER Models. *Chest* 2021; 160(3):1108-1120. PMID: 33932466. Full Text

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BACKGROUND: Two models, the Help with the Assessment of Adenopathy in Lung cancer (HAL) and Help with Oncologic Mediastinal Evaluation for Radiation (HOMER), were recently developed to estimate the probability of nodal disease in patients with non-small cell lung cancer (NSCLC) as determined by endobronchial ultrasound-transbronchial needle aspiration (EBUS-TBNA). The objective of this study was to prospectively externally validate both models at multiple centers. RESEARCH QUESTION: Are the HAL and HOMER models valid across multiple centers? STUDY DESIGN AND METHODS: This multicenter prospective observational cohort study enrolled consecutive patients with PET-CT clinical-radiographic stages T1-3, N0-3, M0 NSCLC undergoing EBUS-TBNA staging. HOMER was used to predict the probability of N0 vs N1 vs N2 or N3 (N2|3) disease, and HAL was used to predict the probability of N2|3 (vs N0 or N1) disease. Model discrimination was assessed using the area under the receiver operating characteristics curve (ROC-AUC), and calibration was assessed using the Brier score, calibration plots, and the Hosmer-Lemeshow test. RESULTS: Thirteen centers enrolled 1,799 patients. HAL and HOMER demonstrated good discrimination: HAL ROC-AUC = 0.873 (95%CI, 0.856-0.891) and HOMER ROC-AUC = 0.837 (95%CI, 0.814-0.859) for predicting N1 disease or higher (N1|2|3) and 0.876 (95%CI, 0.855-0.897) for predicting N2|3 disease. Brier scores were 0.117 and 0.349, respectively. Calibration plots demonstrated good calibration for both models. For HAL, the difference between forecast and observed probability of N2|3 disease was +0.012; for HOMER, the difference for N1|2|3 was -0.018 and for N2|3 was +0.002. The Hosmer-Lemeshow test was significant for both models (P = .034 and .002), indicating a small but statistically significant calibration error. INTERPRETATION: HAL and HOMER demonstrated good discrimination and calibration in multiple centers. Although calibration error was present, the magnitude of the error is small, such that the models are informative.

Radiation Oncology

Amini A, Verma V, Simone CB, 2nd, **Chetty IJ**, Chun SG, Donington J, Edelman MJ, Higgins KA, Kestin LL, Movsas B, Rodrigues GB, Rosenzweig KE, Rybkin, II, Slotman BJ, Wolf A, and Chang JY. American Radium Society™ Appropriate Use Criteria on Radiation Therapy in Oligometastatic or Oligoprogressive Non-Small Cell Lung Cancer. *Int J Radiat Oncol Biol Phys* 2021; Epub ahead of print. PMID: 34571054.
Full Text

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Emory University Winship Cancer Institute, Atlanta, GA.
MHP Cancer Institute, Pontiac, MI.
London Health Sciences Centre, London, ON.
Mount Sinai School of Medicine, New York, NY.
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PURPOSE: Recent randomized studies have suggested improvements in progression-free and overall survival with the addition of stereotactic body radiation therapy (SBRT, also known as stereotactic ablative radiotherapy, SABR) in oligometastatic NSCLC patients. Given the novelty and complexity of incorporating SBRT in the oligometastatic setting, the multidisciplinary American Radium Society (ARS) Lung Cancer Panel was assigned to create Appropriate Use Criteria (AUC) on SBRT as part of consolidative local therapy for oligometastatic and oligoprogressive NSCLC patients. METHODS AND MATERIALS: A review of the current literature was conducted from January 1, 2008 to December 25, 2020 using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines to systematically search the PubMed database to retrieve a comprehensive set of relevant articles. RESULTS: Based on representation in existing randomized trials, the panel defined the term "oligometastasis" as ≤3 metastatic deposits (not including the primary tumor) in the previously-untreated setting or after first-line systemic therapy following the initial diagnosis. "Oligoprogression" also referred to ≤3 discrete areas of progression in the setting of prior or ongoing receipt of systemic therapy. In all appropriate patients, the panel strongly recommends enrollment on a clinical trial whenever available. For oligometastatic disease, administering first-line systemic therapy followed by consolidative radiotherapy (to all sites plus the primary/nodal disease) is preferred over up-front radiotherapy. Owing to a dearth of data, the panel recommended that consolidative radiotherapy be considered on a case-by-case basis for 4-5 sites of oligometastatic disease, driver mutation-positive oligometastatic disease without progression on up-front targeted therapy, and oligoprogressive cases. CONCLUSIONS: Although SBRT/SABR appears to be both safe and effective in treating patients with limited metastatic sites of disease, many clinical circumstances require individualized management and strong multidisciplinary discussion on account of the limited existing data.

Radiation Oncology

Chang SS, and **Movsas B**. How Vital are Patient Reported Outcomes? *J Natl Cancer Inst* 2021; Epub ahead of print. PMID: 34508599. Full Text

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Radiation Oncology

Foster CC, Couey MA, Kochanny SE, Khattri A, Acharya RK, Tan YC, **Brisson RJ**, Leidner RS, and Seiwert TY. Immune-related adverse events are associated with improved response, progression-free survival, and overall survival for patients with head and neck cancer receiving immune checkpoint inhibitors. *Cancer* 2021; Epub ahead of print. PMID: 34547103. Full Text

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BACKGROUND: The authors hypothesized that patients developing immune-related adverse events (irAEs) while receiving immune checkpoint inhibition (ICI) for recurrent/metastatic head and neck cancer (HNC) would have improved oncologic outcomes. METHODS: Patients with recurrent/metastatic HNC received ICI at 2 centers. Univariate and multivariate logistic regression, Kaplan-Meier methods, and Cox proportional hazards regression were used to associate the irAE status with the overall response rate (ORR), progression-free survival (PFS), and overall survival (OS) in cohort 1 (n = 108). These outcomes were also analyzed in an independent cohort of patients receiving ICI (cohort 2; 47 evaluable for irAEs). RESULTS: The median follow-up was 8.4 months for patients treated in cohort 1. Sixty irAEs occurred in 49 of 108 patients with 5 grade 3 or higher irAEs (10.2%). ORR was higher for irAE+ patients (30.6%) in comparison with irAE- patients (12.3%; P = .02). The median PFS was 6.9 months for irAE+ patients and 2.1 months for irAE- patients (P = .0004), and the median OS was 12.5 and 6.8 months, respectively

(P = .007). Experiencing 1 or more irAEs remained associated with ORR (P = .03), PFS (P = .003), and OS (P = .004) in multivariate analyses. The association between development of irAEs and prolonged OS persisted in a 22-week landmark analysis (P = .049). The association between development of irAEs and favorable outcomes was verified in cohort 2. CONCLUSIONS: The development of irAEs was strongly associated with an ICI benefit, including overall response, PFS, and OS, in 2 separate cohorts of patients with recurrent/metastatic HNC.

Radiation Oncology

Kim H, Pedersen K, Olsen JR, Mutch MG, Chin RI, Glasgow SC, Wise PE, Silviera ML, Tan BR, Wang-Gillam A, Lim KH, Suresh R, Amin M, Huang Y, Henke LE, Park H, Ciorba MA, Badiyan S, **Parikh PJ**, Roach MC, and Hunt SR. Nonoperative Rectal Cancer Management With Short-Course Radiation Followed by Chemotherapy: A Nonrandomized Control Trial. *Clin Colorectal Cancer* 2021; 20(3):e185-e193. PMID: 34001462. Full Text

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PURPOSE: Short-course radiation therapy (SCRT) and nonoperative management are emerging paradigms for rectal cancer treatment. This clinical trial is the first to evaluate SCRT followed by chemotherapy as a nonoperative treatment modality. METHODS: Patients with nonmetastatic rectal adenocarcinoma were treated on the single-arm, Nonoperative Radiation Management of Adenocarcinoma of the Lower Rectum study of SCRT followed by chemotherapy. Patients received 25 Gy in 5 fractions to the pelvis followed by FOLFOX ×8 or CAPOX ×5 cycles. Patients with clinical complete response (cCR) underwent nonoperative surveillance. The primary end point was cCR at 1 year. Secondary end points included safety profile and anorectal function. RESULTS: From June 2016 to March 2019, 19 patients were treated (21% stage I, 32% stage II, and 47% stage III disease). At a median follow-up of 27.7 months for living patients, the 1-year cCR rate was 68%. Eighteen of 19 patients are alive without evidence of disease. Patients with cCR versus without had improved 2-year disease-free survival (93% vs 67%; P = .006), distant metastasis-free survival (100% vs 67%; P = .03), and overall survival (100% vs 67%; P = .03). Involved versus uninvolved circumferential resection margin on magnetic resonance imaging was associated with less initial cCR (40% vs 93%; P = .04). Anorectal function by Functional Assessment of Cancer Therapy-Colorectal cancer score at 1 year was not different than baseline. There were no severe late effects. CONCLUSIONS: Treatment with SCRT and chemotherapy resulted in high cCR rate, intact anorectal function, and no severe late effects. NCT02641691.

Radiation Oncology

Mickevicius NJ, **Kim JP**, Zhao J, Morris ZS, Hurst NJ, Jr., and Glide-Hurst CK. Toward magnetic resonance fingerprinting for low-field MR-guided radiation therapy. *Med Phys* 2021; Epub ahead of print. PMID: 34487357. Full Text

Department of Human Oncology, University of Wisconsin-Madison, Madison, Wisconsin, USA.
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PURPOSE: The acquisition of multiparametric quantitative magnetic resonance imaging (qMRI) is becoming increasingly important for functional characterization of cancer prior to- and throughout the course of radiation therapy. The feasibility of a qMRI method known as magnetic resonance fingerprinting (MRF) for rapid T(1) and T(2) mapping was assessed on a low-field MR-linac system. METHODS: A three-dimensional MRF sequence was implemented on a 0.35T MR-guided radiotherapy system. MRF-derived measurements of T(1) and T(2) were compared to those obtained with gold standard single spin echo methods, and the impacts of the radiofrequency field homogeneity and scan times ranging between 6 and 48 min were analyzed by acquiring between 1 and 8 spokes per time point in a standard quantitative system phantom. The short-term repeatability of MRF was assessed over three measurements taken over a 10-h period. To evaluate transferability, MRF measurements were acquired on two additional MR-guided radiotherapy systems. Preliminary human volunteer studies were performed. RESULTS: The phantom benchmarking studies showed that MRF is capable of mapping T(1) and T(2) values within 8% and 10% of gold standard measures, respectively, at 0.35T. The coefficient of variation of T(1) and T(2) estimates over three repeated scans was < 5% over a broad range of relaxation times. The T(1) and T(2) times derived using a single-spoke MRF acquisition across three scanners were near unity and mean percent errors in T(1) and T(2) estimates using the same phantom were < 3%. The mean percent differences in T(1) and T(2) as a result of truncating the scan time to 6 min over the large range of relaxation times in the system phantom were 0.65% and 4.05%, respectively. CONCLUSIONS: The technical feasibility and accuracy of MRF on a low-field MR-guided radiation therapy device has been demonstrated. MRF can be used to measure accurate T(1) and T(2) maps in three dimensions from a brief 6-min scan, offering strong potential for efficient and reproducible qMRI for future clinical trials in functional plan adaptation and tumor/normal tissue response assessment.

Radiation Oncology

Nagaraja TN, **Bartlett S**, **Farmer KG**, **Cabral G**, **Knight RA**, **Valadie OG**, **Brown SL**, **Ewing JR**, and **Lee IY**. Adaptation of laser interstitial thermal therapy for tumor ablation under MRI monitoring in a rat orthotopic model of glioblastoma. *Acta Neurochir (Wien)* 2021; Epub ahead of print. PMID: 34554269.
Full Text

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BACKGROUND: Laser interstitial thermal therapy (LITT) under magnetic resonance imaging (MRI) monitoring is being increasingly used in cytoreductive surgery of recurrent brain tumors and tumors located in eloquent brain areas. The objective of this study was to adapt this technique to an animal glioma model. METHODS: A rat model of U251 glioblastoma (GBM) was employed. Tumor location and extent were determined by MRI and dynamic contrast-enhanced (DCE) MRI. A day after assessing tumor appearance, tumors were ablated during diffusion-weighted imaging (DWI)-MRI using a Visualase LITT system (n = 5). Brain images were obtained immediately after ablation and again at 24 h post-ablation to confirm the efficacy of tumor cytoablation. Untreated tumors served as controls (n = 3). Rats were injected with fluorescent isothiocyanate (FITC) dextran and Evans blue that circulated for 10 min after post-LITT MRI. The brains were then removed for fluorescence microscopy and histopathology evaluations using hematoxylin and eosin (H&E) and major histocompatibility complex (MHC) staining. RESULTS: All rats showed a space-occupying tumor with T2 and T1 contrast-enhancement at pre-LITT imaging. The rats that underwent the LITT procedure showed a well-demarcated ablation zone with near-complete ablation of tumor tissue and with peri-ablation contrast enhancement at 24 h post-ablation. Tumor cytoreduction

by ablation as seen on MRI was confirmed by H&E and MHC staining. CONCLUSIONS: Data showed that tumor cytoablation using MRI-monitored LITT was possible in preclinical glioma models. Real-time MRI monitoring facilitated visualizing and controlling the area of ablation as it is otherwise performed in clinical applications.

Radiation Oncology

Speers C, Murthy VL, **Walker EM**, Glide-Hurst CK, Marsh R, Tang M, Morris EL, Schipper MJ, Weinberg RL, Gits HC, Hayman J, Feng M, Balter J, Moran J, Jagsi R, and Pierce LJ. Cardiac MRI and blood biomarkers for evaluation of radiation-induced cardiotoxicity in breast cancer patients: results of a phase II clinical trial. *Int J Radiat Oncol Biol Phys* 2021; Epub ahead of print. PMID: 34509552. Full Text

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PURPOSE: Radiotherapy (RT) can increase the risk of cardiac events in patients with breast cancer (BC), but biomarkers predicting risk for developing RT-induced cardiac disease are currently lacking. We report results from a prospective clinical trial evaluating early magnetic resonance imaging (MRI) and serum biomarker changes as predictors of cardiac injury and risk of subsequent cardiac events following RT for left-sided disease. METHODS: Women with node-negative and node-positive (N-/+) left-sided BC were enrolled on 2 IRB-approved protocols at 2 institutions. MRI was conducted pretreatment (within one week of starting radiation), at the end of treatment (last day of treatment +/- 1 week), and 3 months post-last day of treatment (+/- 2 weeks) to quantify left and right ventricular volumes and function, myocardial fibrosis, and edema. Perfusion changes during regadenoson stress perfusion were also assessed on a subset of patients (N=28). Serum was collected at the same time points. Whole heart and cardiac substructures were contoured using CT and MRI. Models were constructed using baseline cardiac and clinical risk factors. Associations between MRI-measured changes and dose were evaluated. RESULTS: Among 51 women enrolled, mean heart dose ranged from 0.80-4.7 Gy and mean left ventricular (LV) dose from 1.1-8.2 Gy, with mean heart dose 2.0 Gy. T1 time, a marker of fibrosis, and right ventricular (RV) ejection fraction (EF) significantly changed with treatment; these were not dose dependent. T2 (marker of edema) and LV EF did not significantly change. No risk factors were associated with baseline global perfusion. Prior receipt of doxorubicin was marginally associated with decreased myocardial perfusion after RT (p=0.059) and mean MHD was not associated with perfusion changes. Significant correlation between baseline IL6 and MHD at the end of RT (ρ 0.44, p=0.007) and and a strong trend between Troponin I and MHD at 3-months post-treatment (ρ 0.33, p=0.07) were observed. No other significant correlations were identified. CONCLUSIONS: In this prospective study of women with left-sided breast cancer treated with contemporary treatment planning, cardiac radiation doses were very low relative to historical doses reported by Darby et al. Although we observed significant changes in T1 and RV EF shortly after RT, these changes were not correlated with whole heart or substructure doses. Serum biomarker analysis of cardiac injury demonstrates an interesting trend between markers and MHD that warrants further investigation.

Research Administration

Cattarinussi G, Aarabi MH, Moghaddam HS, Homayoun M, Ashrafi M, **Soltanian-Zadeh H**, and Sambataro F. Effect of parental depressive symptoms on offspring's brain structure and function: A systematic review of neuroimaging studies. *Neurosci Biobehav Rev* 2021; Epub ahead of print. PMID: 34592256. Request Article

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Control and Intelligent Processing Center of Excellence (CIPCE), School of Electrical and Computer Engineering, College of Engineering, University of Tehran, Tehran, Iran; Neuroimage Signal and Image Analysis Group, School of Cognitive Sciences, Institute for Research in Fundamental Sciences (IPM), Tehran, Iran; Medical Image Analysis Laboratory, Departments of Radiology and Research Administration, Henry Ford Health System, Detroit, MI, United States.

Perinatal Depression (PND) is a severe mental disorder that appears during pregnancy or in the post-partum. Although PND has been associated with behavioral problems in the offspring, its effects on brain development are unclear. With this review we aimed at summarizing the existing literature on the effects of perinatal depressive symptoms on children's brains. A search on PubMed and Embase of structural, functional Magnetic Resonance Imaging (MRI) and Diffusion Tensor Imaging (DTI) studies exploring the effect of PND on offspring's brain was conducted. We selected twenty-six studies, ten structural MRI, five DTI, six fMRI and five with combined techniques. Overall, the studies showed: a) gray matter alterations in amygdala and fronto-temporal lobes; b) microstructural alterations in amygdala, frontal lobe, cingulum, longitudinal fasciculus and fornix; and c) functional alterations between limbic and mesocortical networks. The small sample size and the heterogeneity in populations and methodologies limit this review. In conclusion, PND seems to influence structure and function of offspring, that may contribute to the risk of behavioral disturbances later in life.

Research Administration

Shojaeilangari S, Radman N, Taghizadeh ME, and **Soltanian-Zadeh H**. rsfMRI based evidence for functional connectivity alterations in adults with developmental stuttering. *Heliyon* 2021; 7(9):e07855. PMID: 34504967. Full Text

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Persistent developmental stuttering (PDS) is defined as a speech disorder mainly characterized by intermittent involuntary disruption in normal fluency, time patterning, and rhythm of speech. Although extensive functional neuroimaging studies have explored brain activation alterations in stuttering, the main affected brain regions/networks in PDS still remain unclear. Here, using functional magnetic resonance imaging (fMRI), we investigated resting-state whole-brain functional connectivity of 15 adults who stutter (PDS group) and 15 age-matched control individuals to reveal the connectivity abnormalities associated with stuttering. We were also interested in exploring how the severity of stuttering varies across individuals to understand the compensatory mechanism of connectivity pattern in patients showing less symptoms. Our results revealed decreased connectivity of left frontal pole and left middle frontal

gyrus (MidFG) with right precentral/postcentral gyrus in stuttering individuals compared with control participants, while less symptomatic PDS individuals showed greater functional connectivity between left MidFG and left caudate. Additionally, our finding indicated reduced connectivity in the PDS group between the left superior temporal gyrus (STG) and several brain regions including the right limbic lobe, right fusiform, and right cerebellum, as well as the left middle temporal gyrus (MTG). We also observed that PDS individuals with less severe symptoms had stronger connectivity between right MTG and several left hemispheric regions including inferior frontal gyrus (IFG) and STG. The connectivity between right fronto-orbital and right MTG was also negatively correlated with stuttering severity. These findings may suggest the involvement of right MTG and left MidFG in successful compensatory mechanisms in more fluent stutterers.

Sleep Medicine

Cheng P, Casement MD, **Kalmbach DA**, **Cuamatzi Castelan A**, and **Drake CL**. Self-efficacy in Insomnia Symptom Management after Digital CBT-I Mediates Insomnia Severity during the COVID-19 Pandemic. *Behav Sleep Med* 2021;1-11. Epub ahead of print. PMID: 34511016. Request Article

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STUDY OBJECTIVES: Digital cognitive behavioral therapy for insomnia (dCBT-I) can reduce acute insomnia and depressive symptoms and prevent symptom recurrence. The current study evaluated self-efficacy in managing insomnia symptoms as a potential mediator of the relationship between prior dCBT-I and subsequent insomnia and depressive symptoms assessed during the coronavirus 2019 (COVID-19) pandemic. METHOD: Participants were 208 adults who completed a randomized controlled trial of dCBT-I versus sleep education in 2016-2017 and also completed self-report assessments of insomnia, depression, and self-efficacy in managing insomnia symptoms. Data were collected in May 2020, five weeks into state-wide COVID-19 stay-at-home orders. Regression and mediation analyses were used to evaluate the extent to which self-efficacy accounted for the relationship between treatment condition and improvement in insomnia and depressive symptoms from pre-treatment to COVID-19 follow-up. RESULTS: Prior dCBT-I predicted greater self-efficacy in managing insomnia symptoms. Self-efficacy accounted for 49% and 67% of the protective effect of dCBT-I against COVID-era insomnia and depressive symptoms, respectively. CONCLUSIONS: This study affirms the importance of self-efficacy as a key intervention outcome and potential mechanism by which dCBT-I predicts future sleep and mental health. Future studies that evaluate the role of self-efficacy in treatment effectiveness and resilience can provide additional clues about how to optimize dCBT-I for maximum benefit to public health.

Sleep Medicine

Johnson DA, **Cheng P**, FarrHenderson M, and Knutson K. Understanding the determinants of circadian health disparities and cardiovascular disease. *Chronobiol Int* 2021;1-8. Epub ahead of print. PMID: 34547974. Request Article

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Emerging research suggests that sleep contributes to racial disparities in cardiovascular disease (CVD). Racial/ethnic minorities are disproportionately affected by poor cardiovascular outcomes including obesity, hypertension and diabetes. Although circadian rhythms affect sleep patterns, few studies have examined disparities in circadian health or the contribution of circadian disparities to CVD. In this paper, we provide an overview of the relation between circadian health and CVD in the context of health disparities. We discuss (1) the current knowledge on racial disparities in circadian health; (2) social and environmental determinants of circadian health disparities; (3) the cardiovascular consequences of circadian disparities; and (4) future opportunities to advance the field of circadian disparities. In brief, our findings demonstrated that among a small literature, racial minorities (mainly African American) were more likely to have a shorter circadian period, delayed phase shifts, and were more likely to be shift

workers, which are associated with CVD risk factors. Given racial minorities are disproportionately affected by CVD and CVD risk factors, it is important to further understand circadian health as an intervention target and support more research among racial minorities to understand circadian health in these populations.

Surgery

Acho C, **Morita Y**, **Fernandez V**, **Safwan M**, **Galusca D**, **Abouljoud M**, **Yoshida A**, **El-Bashir J**, and **Nagai S**. Immediate Postoperative Extubation Decreases Pulmonary Complications in Liver Transplant Patients. *Transplantation* 2021; 105(9):2018-2028. PMID: 32890127. Full Text

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BACKGROUND: Fast-track anesthesia in liver transplantation (LT) has been discussed over the past few decades; however, factors associated with immediate extubation after LT surgery are not well defined. This study aimed to identify predictive factors and examine impacts of immediate extubation on post-LT outcomes. METHODS: A total of 279 LT patients between January 2014 and May 2017 were included. Primary outcome was immediate extubation after LT. Other postoperative outcomes included reintubation, intensive care unit stay and cost, pulmonary complications within 90 days, and 90-day graft survival. Logistic regression was performed to identify factors that were predictive for immediate extubation. A matched control was used to study immediate extubation effect on the other postoperative outcomes. RESULTS: Of these 279 patients, 80 (28.7%) underwent immediate extubation. Patients with anhepatic time >75 minutes and with total intraoperative blood transfusion ≥12 units were less likely to be immediately extubated (odds ratio [OR], 0.48; 95% confidence interval [CI], 0.26-0.89; P = 0.02; OR, 0.11; 95% CI, 0.05-0.21; P < 0.001). The multivariable analysis showed immediate extubation significantly decreased the risk of pulmonary complications (OR, 0.34; 95% CI, 0.15-0.77; P = 0.01). According to a matched case-control model (immediate group [n = 72], delayed group [n = 72]), the immediate group had a significantly lower rate of pulmonary complications (11.1% versus 27.8%; P = 0.012). Intensive care unit stay and cost were relatively lower in the immediate group (2 versus 3 d; P = 0.082; $5700 versus $7710; P = 0.11). Reintubation rates (2.8% versus 2.8%; P > 0.9) and 90-day graft survival rates (95.8% versus 98.6%; P = 0.31) were similar. CONCLUSIONS: Immediate extubation post-LT in appropriate patients is safe and may improve patient outcomes and resource allocation.

Surgery

Ivanics T, **Leonard-Murali S**, **Mouzaihem H**, **Moonka D**, **Kitajima T**, **Yeddula S**, **Shamaa T**, **Rizzari M**, **Collins K**, **Yoshida A**, **Abouljoud M**, and **Nagai S**. Extreme Hyponatremia as a Risk Factor for Early Mortality after Liver Transplantation in the MELD-Sodium Era. *Transpl Int* 2021; Epub ahead of print. PMID: 34580929. Full Text

Division of Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, MI, United States.
Division of Gastroenterology and Hepatology, Henry Ford Hospital, Detroit, MI, United States.

BACKGROUND: The impact of hyponatremia on waitlist and post-transplant outcomes following the implementation of MELD-Na-based liver allocation remains unclear. We investigated waitlist and post-liver transplant(LT) outcomes in patients with hyponatremia before and after implementing MELD-Na-based allocation. METHODS: Adult patients registered for a primary LT between 2009 and 2021 were identified in the OPTN/UNOS database. Two eras were defined; pre-MELD-Na and post-MELD-Na. Extreme hyponatremia was defined as a serum sodium concentration≤120mEq/L. 90-day waitlist outcomes and post-LT survival were compared using Fine-Gray proportional hazard and mixed-effects Cox proportional hazard models. RESULTS: 118,487 patients were eligible (n=64,940:pre-MELD-Na;n=53,547:post-MELD-Na). In the pre-MELD-Na era, extreme hyponatremia at listing was associated with an increased risk of 90-day waitlist mortality ([ref:135-145]HR:3.80;95%CI:2.97-4.87;p<0.001) and higher transplant probability (HR: 1.67;95%CI:1.38-2.01;p<0.001). In the post-MELD-Na era, patients with extreme hyponatremia had a proportionally lower relative risk of waitlist mortality (HR:2.27;95%CI1.60-3.23;p<0.001) and proportionally higher transplant probability (HR:2.12;95%CI1.76-2.55;p<0.001) as patients with normal serum sodium levels(135-145). Extreme hyponatremia was associated with a higher

risk of 90, 180, and 365-day post-LT survival compared to patients with normal serum sodium levels. CONCLUSION: With the introduction of MELD-Na-based allocation, waitlist outcomes have improved in patients with extreme hyponatremia but continue to have worse short-term post-LT survival.

Surgery

Lehman H, **Acho R**, and **Hans SS**. Achenbach syndrome as a rare cause of painful, blue finger. *J Vasc Surg Cases Innov Tech* 2021; 7(3):589-592. PMID: 34541431. Full Text

Division of Vascular Surgery, Department of Surgery, Henry Ford Macomb Hospital, Clinton Township, Mich.

Paroxysmal finger hematoma, also known as Achenbach syndrome, is an underdiagnosed condition that causes apprehension in patients owing to the alarming appearance. It usually presents as a blue-purple discoloration of the volar aspect of one or more digits and can be associated with pain and paresthesia. This condition is benign and is usually self-limiting.

Surgery

Oyedeji O, **Sheqwara J**, **Onwubiko I**, **Lopez-Plaza I**, **Nagai S**, and **Otrock ZK**. Thrombocytapheresis for acquired von Willebrand syndrome in a patient with essential thrombocythemia and recent multivisceral transplantation. *Transfusion* 2021; Epub ahead of print. PMID: 34569071. Full Text

Transfusion Medicine Division, Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Michigan, USA.
Division of Hematology and Oncology, Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA.
Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, Michigan, USA.

BACKGROUND: Essential thrombocythemia (ET) is associated with increased risk of bleeding secondary to acquired von Willebrand syndrome (AVWS). Bleeding in ET requires urgent platelet reduction by cytoreductive therapy such as hydroxyurea or thrombocytapheresis. We report on the efficacy and safety of thrombocytapheresis in managing AVWS in a patient with ET and multivisceral transplantation. CASE REPORT: The patient was a 51-year-old female who underwent multivisceral transplantation. Her postoperative course was complicated by bleeding from oral cavity, IV lines, gastrointestinal and upper respiratory tracts as well as vaginal bleeding, which coincided with ET flare with a platelet count of 1512 × 10(9) /L. Coagulation studies including von Willebrand factor (vWF) antigen and activity, vWF propeptide antigen, and vWF multimer analysis were consistent with AVWS. Hydroxyurea was initiated. However, due to major bleeding, rapidly increasing platelet count, and uncertainty of response to hydroxyurea being given through the enteral tube, thrombocytapheresis was initiated for rapid platelet reduction. The patient tolerated the procedure well. Platelet count was reduced from 1636 × 10(9) /L to 275 × 10(9) /L with rapid cessation of bleeding. The patient's condition stabilized over the next few days; however, bleeding recurred with increasing platelet count, which required a second thrombocytapheresis 8 days after the first one. The patient was maintained on hydroxyurea 500 mg twice/day. At 11-month follow-up, she had a normal platelet count and no recurrence of bleeding. DISCUSSION: Thrombocytapheresis is safe and efficient in managing postoperative bleeding due to ET/AVWS in solid organ transplant patients. The procedure can be an adjunct to bridging therapy before response to hydroxyurea is achieved.

Surgery

Shamaa T, **Yoshida A**, **Borchert A**, **McEvoy T**, **Jeong W**, and **Malinzak L**. Robot-assisted Transplant Ureteral Repair after Robot-assisted Kidney Transplant. *Urology Video Journal* 2021; 11. PMID: Not assigned. Request Article

T. Shamaa, Henry Ford Hospital, Detroit, MI, United States

Objective: To use a video to describe steps of robotic-assisted transplant ureteral repair (RATUR) for treating transplant ureteral stricture (TUS) in a patient who had undergone robot assisted kidney

transplant (RAKT). Method: We recorded and edited the operation of a patient who experienced TUS by distal obstruction due to a calcification after RAKT and underwent RATUR in 2020. Results: We present a case of a 65-year-old male who developed graft dysfunction. He was found to have a short intrinsic obstruction of the distal transplant ureter due to a calcification that formed around the suture line at the ureteroneocystostomy. The video covers the steps of the operation which include positioning, placement of the ports, orientation, dissection of the paravesicle space, identification and dissection of the ureter, stent placement, reconstruction and post-operative course. We try to include tips and tricks that could be useful in other similar robotic cases. Conclusion: Open surgical repair of the transplant ureter is the standard of care for transplant ureteral stenosis. However, it requires the morbidity of a large surgical incision. Robotic assisted transplant ureteral repair can be done successfully while limiting convalescence from an open reoperation.

Surgery

Stefanou AJ, Sentovich SM, and Peters WR. What Every Colorectal Surgeon Should Know About the No Surprises Act. *Dis Colon Rectum* 2021; 64(9):1038-1040. PMID: 34397556. Full Text

Division of Colon and Rectal Surgery, Department of Surgery, Henry Ford Hospital, Detroit, Michigan.
Division of Colorectal Surgery, Department of Surgery, City of Hope National Medical Center, Duarte, California.
Baylor Scott & White Health, Dallas, Texas.

Urology

Budzyn J, and **Leavitt D**. Life threatening hepatic hemorrhage after shockwave lithotripsy - A case report and review of literature. *Urol Case Rep* 2021; 38:101724. PMID: 34136358. Full Text

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We report a 31 year old female with urologic history significant for right ureteropelvic junction obstruction managed with open right pyeloplasty in 1996 with recurrent stricture managed with right ureterocalycostomy in 1997 along with right distal ureteroneocystostomy for iatrogenic distal ureteral stricture. She developed symptomatic stone episodes and recurrent urinary tract infections and elected to proceed with shockwave lithotripsy. Postoperatively she developed a large liver hemorrhage requiring supportive care and endovascular embolization.

Urology

Delto JC, Fleishman A, Chang P, Jiang DD, Hyde S, McAnally K, Crociani C, **Jamil M**, Patel HD, Pavlinec J, **Budzyn J**, Durant A, Eilender B, Gordon AO, Huang MM, Pierorazio PM, Raman JD, **Rogers C**, Su LM, and Wagner AA. Perioperative Aspirin Use is Associated with Bleeding Complications During Robotic Partial Nephrectomy. *J Urol* 2021; Epub ahead of print. PMID: 34555934. Full Text

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Icahn School of Medicine, New York, New York.
The James Buchanan Brady Urological Institute, Johns Hopkins School of Medicine, Baltimore, Maryland.

INTRODUCTION AND OBJECTIVE: Daily aspirin use following cardiovascular intervention is commonplace and creates concern regarding bleeding risk in patients undergoing surgery. Despite its cardio-protective role, aspirin is often discontinued 5-7 days prior to major surgery due to bleeding concerns. Single institution studies have investigated perioperative outcomes of aspirin use in robotic partial nephrectomy (RPN). We sought to evaluate the outcomes of perioperative aspirin (pASA) use during RPN in a multicenter setting. METHODS: We performed a retrospective evaluation of patients undergoing RPN at 5 high volume RPN institutions. We compared perioperative outcomes of patients

taking pASA (81 mg) to those not on aspirin. We analyzed the association between pASA use and perioperative transfusion. RESULTS: Of 1565 patients undergoing RPN, 228 (14.5%) patients continued pASA and were older (62.8 vs. 56.8 years, p <0.001) with higher Charlson scores (mean 3 vs. 2, p <0.001). pASA was associated with increased perioperative blood transfusions (11% vs. 4%, p <0.001) and major complications (10% vs. 3%, p <0.001). On multivariable analysis, pASA was associated with increased transfusion risk (OR 1.94, 1.10-3.45, 95% CI). CONCLUSIONS: In experienced hands, perioperative aspirin 81 mg use during RPN is reasonable and safe, however, there is a higher risk of blood transfusions and major complications. Future studies are needed to clarify the role of antiplatelet therapy in RPN patients requiring pASA for primary or secondary prevention of cardiovascular events.

Urology

Ginsburg KB, Johnson K, Moldovan T, **Peabody J**, Qi J, Dunn RL, **Rogers C**, Weizer A, Kaul S, Johnson A, Traver M, and Lane BR. A statewide quality improvement collaborative's adherence to the 2017 AUA guidelines regarding initial evaluation of patients with cT1 renal masses. *Urology* 2021; Epub ahead of print. PMID: 34499969. Full Text

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OBJECTIVES: To evaluate MUSIC-KIDNEY's adherence to the AUA guidelines regarding initial evaluation of patient's with clinical T1 (cT1) renal masses. METHODS: We reviewed MUSIC-KIDNEY registry data for patients with newly diagnosed cT1 renal masses to assess for adherence with the 2017 AUA guideline statements regarding recommendations to obtain 1) CMP, 2) CBC 3) UA, 4) abdominal cross-sectional imaging and 5) chest imaging. An evaluation consisting of all 5 guideline measures was considered "complete compliance". Variation with guideline adherence was assessed by contributing practice, management strategy and renal mass size. RESULTS: We identified 1,808 patients with cT1 renal masses in the MUSIC-KIDNEY registry, of which 30% met the definition of complete compliance. Most patients received care that was compliant with recommendations to obtain laboratory testing with 1,448 (80%), 1,545 (85%), and 1,472 (81%) patients obtaining a CMP, CBC, and UA respectively. Only 862 (48%) of patients underwent chest imaging. Significant variation exists in complete guideline compliance for contributing practices, ranging from 0-45% as well as for patients which underwent immediate intervention compared with initial observation (37% vs. 23%) and patients with cT1b masses compared with cT1a masses (36% vs. 28%). CONCLUSION: Complete guideline compliance in the initial evaluation of cT1 renal masses is poor, which is mainly driven by omission of chest imaging. Significant variation in guideline adherence is seen across practices, as well as patients undergoing an intervention vs. observation, and cT1a vs. cT1b masses. There are ample quality improvement opportunities to increase adherence and decrease variability with guideline recommendations.

Urology

Goel S, Bhatia V, Kundu S, Biswas T, **Carskadon S**, **Gupta N**, Asim M, Morrissey C, **Palanisamy N**, and Ateeq B. Transcriptional network involving ERG and AR orchestrates Distal-less homeobox-1 mediated prostate cancer progression. *Nat Commun* 2021; 12(1):5325. PMID: 34493733. Full Text

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Distal-less homeobox-1 (DLX1) is a well-established non-invasive biomarker for prostate cancer (PCa) diagnosis, however, its mechanistic underpinnings in disease pathobiology are not known. Here, we reveal the oncogenic role of DLX1 and show that abrogating its function leads to reduced tumorigenesis and metastases. We observed that ~60% of advanced-stage and metastatic patients display higher DLX1 levels. Moreover, ~96% of TMPRSS2-ERG fusion-positive and ~70% of androgen receptor (AR)-positive patients show elevated DLX1, associated with aggressive disease and poor survival. Mechanistically, ERG coordinates with enhancer-bound AR and FOXA1 to drive transcriptional upregulation of DLX1 in ERG-positive background. However, in ERG-negative context, AR/AR-V7 and FOXA1 suffice to upregulate DLX1. Notably, inhibiting ERG/AR-mediated DLX1 transcription using BET inhibitor (BETi) or/and anti-androgen drugs reduce its expression and downstream oncogenic effects. Conclusively, this study establishes DLX1 as a direct-target of ERG/AR with an oncogenic role and demonstrates the clinical significance of BETi and anti-androgens for DLX1-positive patients.

Conference Abstracts

Cardiology/Cardiovascular Research

Kazem A, **Al-Darzi W**, **Mohammed M**, **Lemor A**, **Lee J**, **Wang D**, **Basir M**, **Alaswad K**, **O'Neill B**, **Frisoli T**, **Eng M**, **O'Neill W**, and **Villablanca P**. Safety, feasibility, and outcomes of transcaval access for the delivery of Impella microaxial-flow pump 5.0 in patients with acute heart failure. *Eur J Heart Fail* 2021; 23(SUPPL 2):206.

A. Kazem, Henry Ford Hospital, Detroit, United States

Background: Transcaval access (TCA) may enable fully percutaneous mechanical circulatory support (MCS) without the hazards of vascular complication in patients with heart failure that require left ventricular unloading. Purpose: To review the safety, feasibility, and outcomes of using TCA to deliver Impella 5.0 MCS in patients with ischemic and non-ischemic systolic acute heart failure. Methods: This single center retrospective study included all patients that underwent TCA placement of a 5.0 Impella from June 2015 to January 2021. Demographic, clinical and procedural variables, and in-hospital outcomes were collected. The procedure was performed by electrifying a caval guidewire and advancing it into a pre-positioned aortic snare. After exchanging for a rigid guidewire, a 22 or 24Fr sheath was delivered into the aorta and then the Impella 5.0 was placed in the left ventricle through TCA sheaths. Results: A total of 43 patients were included in the analysis. The average age was 56.9 years (interquartile range [IQR], 52-65.5), of which, 70%(n=30) were males. Fifteen patients had non-ischemic cardiomyopathy and 28 had ischemic cardiomyopathy. Baseline average left ventricular ejection fraction prior to implantation was 23.6% (IQR, 13.75-29.75). 86% of the patients were in category C-D of the SCAI classification schema for cardiogenic shock (CS), 39.5% required inotropes and 48.8% required pressors prior to the procedure; 54% had a prior MCS in place. Only 18.6% of the cases had prior CT imaging reviewed for planning. TCA was successful in all attempted patients and the MCS delivery was achieved in 100% of the cohort. The available hemodynamic parameters prior and after Impella 5.0 implantation via Table 1 TCA are summarized in table 1. From the total cohort, only 29 patients survived to explant device and TCA sheath. The explant was successful in all patients using nitinol occluders; two patients required a covered stent at the arteriotomy site due to right sided heart failure from residual fistula; no surgical repair was necessary. All residual fistulous tracks were graded as<or =2. In-hospital survival was 46.5% for the entire cohort; 53.3%(n=8) for the non-ischemic group and 42.8%(n=12) in the ischemic group. BARC bleeding >1 from Impella insertion/removal site was observed in 9.3%,which didn't require further intervention. No vascular complication of the access site was observed with TCA. During hospitalization, 20.9% had VT/VF and 4.7% a PEA after implantation (all CS patients). 13.9% of the patients had AKI requiring hemodialysis and no stroke was observed in the entire group. The average length of stay for entire cohort was 16.3 days (IQR, 3.25-18.75). Conclusions: Transcaval access of 5.0 Impella is safe and feasible under expert hands for patients where more conventional MCS devices do not provide enough support or have inadequate peripheral arterial access.

Cardiology/Cardiovascular Research

Kourkoveli P, Mazimba S, Hage A, Goldschmidt M, Simmons L, Moe G, **Cowger J**, Mishkin J, Marcoff L, Toma M, and Grayburn P. 2-year outcomes for transcatheter repair in patients with functional mitral regurgitation from the CLASP study. *Eur J Heart Fail* 2021; 23(SUPPL 2):242.

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Background: Transcatheter mitral valve repair has emerged as a favourable option in patient care for treating functional mitral regurgitation (FMR) with a need for longer term data. We herein report two-year outcomes from the FMR group of the multicentre, prospective, single arm CLASP study with the PASCAL transcatheter valve repair system. Methods: Patients with symptomatic, clinically significant FMR ≥3+ as evaluated by the core laboratory and deemed candidates for transcatheter repair by the local heart team were eligible for the study. Follow-up was conducted at 30 days, one year, and two years with echocardiographic outcomes evaluated by the core laboratory at all timepoints and major adverse events (MAEs) evaluated by an independent clinical events committee to one year (site-reported thereafter).

Results: Eighty-five FMR patients were treated with mean age 72 years, 55% male, 65% in NYHA Class III-IVa, 37% LVEF, and 100% MR grade ≥3+. Successful implantation was achieved in 96% of patients. MAEs included one cardiovascular mortality (1.2%) and one conversion tomitral valve replacement surgery (1.2%) at 30 days, and two reinterventions between 30 days and two years. Kaplan-Meier (KM) estimates for survival were 88% at one year and 72% at two years. Freedom from heart failure (HF) rehospitalization KM estimates were 81% at one year and 78% for two years. The reduction in annualized HF hospitalization rate was 81% at two years (p<0.001). MR ≤1+ was achieved in 73% of patients at 30 days, 75% at one year, and 84% at two years; MR ≤2+ was achieved in 96% of patients at 30 days, 100% at one year, and 95% two years (all p<0.001). Mean LVEDV of 199 mL at baseline decreased by 9 mL at 30 days (p=0.039), 29 mL at one year (p<0.001), and 31 mL at two years (p<0.001). NYHA class I/II was achieved in 87% of patients at 30 days, 86% at one year, and 88% at two years (all p<0.001). Six-minute walk distance (6MWD) improved by 22 m at 30 days (p=0.004) and 40 m at one year (p=0.003). Kansas City Cardiomyopathy Questionnaire (KCCQ) score improved by 16 points at 30 days and one year (all p<0.001). Conclusions: In the CLASP study, the PASCAL transcatheter valve repair system demonstrated sustained favourable outcomes at two years in patients with FMR. Results showed a high survival rate of 72% and freedom from HF rehospitalization of 78% at two years. An 81% reduction in annualized HF hospitalization rate was observed. At two years, sustained MR reduction of MR ≤2+ was achieved in 95% andMR ≤1+ in 84% of patients, with evidence of left ventricular reverse remodelling. Improvements in functional status were significant and sustained at two years. The CLASP IIF randomized pivotal trial is ongoing.

Dermatology

Alavi A, **Hamzavi IH**, Baradaran S, Mathias SD, Colwell HH, Song M, and Han C. 27630 Assessing signs and symptoms of hidradenitis suppurativa from the patient perspective. *J Am Acad Dermatol* 2021; 85(3):AB157.

Background: Qualitative research was conducted to develop a patient reported outcome (PRO) measure assessing symptoms/signs of hidradenitis suppurativa (HS), the HS Symptom Diary (HSSD). Methods: Concept elicitation (CE) and combined CE/cognitive debriefing (CD) interviews were conducted with adult patients with moderate-to-severe HS from 5 dermatology practices in North America. The CE portion of the interview sought to fully understand important concepts of HS. Subjects then completed the draft HSSD, and answered questions to evaluate its content, clarity, and relevance. Revisions were made iteratively to the HSSD. The study received institutional review board approval; subjects provided written informed consent. Results: 36 subjects were interviewed [6 = CE and 30 = CE/CD, 65% female; mean age = 39]. The most commonly reported lesion locations were armpits (81%), groin (75%), or under the breasts (31%). Subjects reported pain (100%), drainage (100%), itching (100%), swelling/ inflammation (94%), odor (86%), tenderness (81%), heat (64%), and pressure (64%) related to their lesions. The most bothersome symptoms were pain (94%), drainage (50%), swelling/inflammation (42%), and itching (33%). Pain was the most difficult symptom to manage (53%). In general, respondents were able to paraphrase each item and found the content to be clear and relevant. The final HSSD, developed as a daily diary with a 24-hour recall period, contains 8 items evaluating severity of each symptom/sign using an 11-point numeric rating scale. A 7-day version was also developed. Conclusion: Content validity of the HSSD in patients with moderate-to-severe HS has been demonstrated. Its measurement properties will be assessed using data from upcoming clinical studies.

Dermatology

Arora H, and McHargue C. 28353 Hemorrhagic cellulitis secondary to vibrio fluvialis infection. *J Am Acad Dermatol* 2021; 85(3):AB184.

A 75-year-old male with a medical history of heart failure, interstitial lung disease, end stage renal disease on hemodialysis, and carcinoid tumor presented to the ER due to diarrhea and abdominal rash. His abdominal rash started as asymptomatic bruising along the left abdomen which spread to the right. He developed myalgias, lethargy, and altered mental status; he later developed fever, tachycardia, and hypovolemia and was found to be in septic shock. Labwork revealed a leukocytosis with neutrophilic predominance, elevated lactate, and negative Clostridium difficile. Blood cultures grew Gram-negative bacilli which later speciated as Vibrio fluvialis. Biopsy revealed neutrophilic dermatitis and panniculitis with

hemorrhage consistent with hemorrhagic cellulitis. The patient was treated with IV piperacillin/tazobactam and oral doxycycline with which he had improvement of his abdominal rash, mental status, and systemic symptoms. V fluvialis is a Gram-negative bacterium which occurs widely in aquatic environments. V fluvialis has been detected in mollusks, oysters, mussels, among other marine creatures commonly consumed as seafood. Upon questioning, this patient did admit to eating uncooked clams three days prior to presentation. This organism is known to cause gastroenteritis with diarrheal illness as in this patient. Cases of peritonitis, suppurative cholangitis, and bacteremia have been noted with V fluvialis. There is one reported case of hemorrhagic cellulitis and cerebritis in a patient who swam in brackish water following multiple fire ant stings. We report a novel case of hemorrhagic cellulitis and bacteremia leading to septic shock secondary to V fluvialis infection following raw clam ingestion.

Dermatology

Braunberger TL, Adelman M, **Shwayder TA**, Clarke LE, and **Friedman BJ**. 26856 Proliferative nodule resembling angiomatoid Spitz with pronounced degenerative atypia arising within a giant congenital nevus. *J Am Acad Dermatol* 2021; 85(3):AB118.

Proliferative nodules arising within congenital melanocytic nevi present a diagnostic challenge for dematopathologists given their close resemblance to melanoma. In difficult cases, ancillary molecular tests can be used to better exclude the possibility of malignancy. We report case of a biopsy and subsequent excision of an unusual proliferative nodule with overlapping features of angiomatoid Spitz tumor and ancient melanocytic nevus which demonstrated normal findings on both chromosomal microarray and a gene expression profiling assay. Our case is noteworthy given its striking resemblance to what has been reported for an angiomatoid Spitz tumor. To our knowledge, this particular morphologic subset of Spitz has been described primarily in the context of spontaneous melanocytic tumors arising de novo outside the context of a congenital lesion. The pathology showed bizarre cytological features along with a myxoid and highly vascularized stroma which is thought to represent degenerative atypia characteristic of an “ancient nevus.” The lesions described as ancient nevi have some overlapping stromal features with angiomatoid Spitz tumors. A low proliferation index and paucity of mitotic figures is characteristic of these neoplasms. We hypothesize that continued host response to the lesion may be responsible for inducing the observed cytological and stromal derangement. Interestingly, these changes increased from the time of biopsy to the excision. Future studies should aim to define the genetic and immunologic signature of these lesions to help predict prognosis. The relationship between angiomatoid Spitz tumor, ancient change, and regressing nevi should also be investigated.

Dermatology

Braunberger TL, Vakharia P, **Ezekwe N**, Nicholson CL, **Parks-Miller A**, and **Hamzavi IH**. 26843 Carbon dioxide laser excision for hidradenitis suppurativa patients—Healing, complications, and recurrence in patients with diabetes mellitus and history of smoking. *J Am Acad Dermatol* 2021; 85(3):AB25.

Introduction: Hidradenitis suppurativa (HS) is often refractory to medical and surgical interventions. Carbon dioxide (CO2) laser excision has demonstrated promising results for HS treatment. Objective: We characterized the efficacy and safety of CO2 laser excision for HS in smokers and diabetics. Methods: On initial data pull, 72 patients were identified. This number was reduced to 38 patients by including HS patients with all data points at Henry Ford Hospital who underwent CO2 laser excision between August 2014 to May 2017. Data were obtained from medical charts including healing and recurrence rates, complications, smoking status, and history of diabetes mellitus. Results: The average age of our cohort was 37.5 years and mean BMI was 34.9. In total, 3 patients had recurrence at a mean of 6 months following the procedure. Postoperative complications included: infection (n = 2), contracture (n = 2), dehiscence (n = 2), and paresthesia (n = 1). Patients with dehiscence were not smokers or diabetics. Twelve patients were smokers, and 26 patients were nonsmokers. The mean healing time in both smokers and nonsmokers was 6 months. Nine patients had a history of diabetes mellitus (DM), and 29 patients were not diabetic. The mean healing time was not significantly prolonged in diabetics compared to nondiabetics and was 7.3 months and 5.4 months, respectively. Conclusion: Both smokers and nonsmokers demonstrated similar healing time, recurrence rates, and postoperative complications. Patients with DM had prolonged healing times when compared to those without DM. Our study identifies

important characteristics that clinicians should consider when assessing HS patients for CO2 laser excision.

Dermatology
Draelos ZD, Lebwohl MG, Lynde CW, Nahm WK, Papp KA, Pariser DM, **Gold LS**, Stewart D, Higham RC, Navale L, and Berk DR. 28043 Roflumilast cream significantly improves chronic plaque psoriasis in patients with steroid-sensitive area involvement. *J Am Acad Dermatol* 2021; 85(3):AB171.

Roflumilast cream is a nonsteroidal, selective phosphodiesterase-4 inhibitor in development for plaque psoriasis (PsO). A double-blind, phase 2b trial randomized adults with PsO to once daily roflumilast 0.3%, 0.15%, or vehicle for 12 weeks (NCT03638258).(1) Efficacy was assessed using Investigator Global Assessment (IGA), Worst Itch Numeric Rating Scale (WI–NRS), and Psoriasis Symptom Diary (PSD). This posthoc analysis reports efficacy and safety in patients with steroid-sensitive area involvement (plaques on the face, neck, or in intertriginous areas). Of 331 patients, 160 had steroid-sensitive area involvement. The primary endpoint in the study, IGA status clear/almost clear at Week 6 was met by 27.2% patients with steroid sensitive areas (P =.007 vs vehicle), 22.3% (P =.026), and 6.3% on roflumilast 0.3%, roflumilast 0.15%, and vehicle, respectively; relative to 30.1% (P =.026), 24.1% (P =.098), and 12.0% patients without steroid-sensitive areas. Among patients with baseline WI–NRS score ≥4, 73.5%, 55.6%, and 32.6% of those with steroid-sensitive areas and 45.9%, 72.7%, and 23.7% of those without steroid-sensitive areas achieved a 4-point reduction with roflumilast 0.3%, 0.15%, or vehicle at Week 12. PSD improvement from baseline at Week 12 for patients with steroid-sensitive areas was -48.3 (P <.001), -43.1 (P =.012), and -24.9, and for patients without steroid-sensitive areas -35.7 (P =.003), -44.6 (P <.001), and -17.1. Most treatment emergent adverse events were mild to moderate and there was no evidence of local irritation. Once-daily roflumilast cream was well tolerated with significant improvements in investigator and patient assessed PsO outcomes in patients with steroid-sensitive area involvement on the face, neck, or intertriginous areas.

Dermatology
Duffin KC, **Gold LS**, Leonardi C, Pariser D, Green L, Sofen H, Strober B, Chen M, Inc, Yao Wang A, and Papp K. 26085 Key efficacy and safety of apremilast in patients with mild to moderate plaque psoriasis in the phase 3 ADVANCE trial. *J Am Acad Dermatol* 2021; 85(3):AB83.

Background: In ADVANCE, apremilast 30 mg BID (APR) demonstrated efficacy in mild-to-moderate psoriasis vs placebo (PBO). We report subgroup analyses by baseline psoriasis-involved BSA (≤5%, >5%). Methods: Biologic-naive adults with mild-to-moderate psoriasis (sPGA 2-3, BSA 2%-15%, PASI 2-15) inadequately controlled with or intolerant to ≥1 topical were randomized to APR or PBO for 16 weeks. At Week 16, endpoints were compared between treatment groups and by baseline BSA. Results: At baseline, 284 patients had BSA ≤5% (APR: 143; PBO: 141); 311 had BSA >5% (APR: 154; PBO: 157). Overall, a greater proportion of APR patients achieved the primary endpoint, sPGA response (score 0/1 [clear/almost clear] with ≥2-point reduction at Week 16) vs PBO (21.6% vs 4.1%, P 5%: 54.6% vs 14.9%, P 5%: 45.4% vs 17.6%, P 5%: 50.6% vs 19.2%, P 5%: 11.0 vs 10.0 DLQI 5-point improvement (baseline DLQI >5): - BSA≤5%: 56.6% vs 31.2%, P =.0002 - BSA>5%: 64.4% vs 36.4%, P <.0001. Conclusions: Greater proportions of patients achieved efficacy outcomes and greater improvements in QOL with APR vs PBO. Comparable improvements were observed between mild and moderate subgroups.

Dermatology
Ezekwe N, Smith J, **Pourang A**, and **Hamzavi I**. 26914 Ustekinumab-induced myositis: A case series. *J Am Acad Dermatol* 2021; 85(3):AB122.

Ustekinumab (UST) is a monoclonal antibody that blocks proinflammatory cytokines IL-12 and IL-23. Off-label use of UST has shown promising results for moderate to severe hidradenitis suppurativa (HS) in patients who have failed to respond to or unable to tolerate adalimumab, the only Food and Drug Administration (FDA) approved treatment for HS. Previously, myositis has not been reported as an adverse effect of UST. We present two patients with poorly controlled HS who experienced new onset myositis shortly after beginning treatment with UST. Abnormal electromyography (EMG) demonstrated myopathic appearing motor units in the bilateral biceps in patient 1. Creatinine kinase was elevated

greater than three times normal in patient 1, and normal in patient 2. Patient 2 had marked reduction in ambulation requiring use of a cane. Both patients experienced a sequela of symptoms such as generalized muscle weakness, muscle swelling with warmth to the areas, and myalgias with improvement of symptoms shortly after discontinuation of UST. A proposed mechanism may be related to the overexpression of IL-12 and IL-23 secondary to UST's receptor blockade. IL-12 can initiate IL-32 production, a cytokine that has been shown to be overexpressed in HS.3 Il-32 induces the production of IFNy and IL-17, byproducts of TH1 and TH17 helper cells which have been implicated in autoimmune myositis. As the use of UST increases in HS patients, it is important for clinicians to consider the potential risk of drug-induced myositis. Long-term clinical surveillance is needed to evaluate the significance and frequency of this occurrence.

Dermatology

Gold LS, Alonso-Llamazares J, Draelos ZD, Gooderham MJ, Kempers SE, Lebwohl MG, Toth DP, Yosipovitch G, Higham RC, Navale L, and Berk DR. 27874 Correlation of itch response to roflumilast cream with disease severity and patient-reported outcomes in patients with chronic plaque psoriasis. *J Am Acad Dermatol* 2021; 85(3):AB164.

Roflumilast cream is a nonsteroidal, selective phosphodiesterase-4 inhibitor in development for plaque psoriasis (PsO). A Phase 2b, double-blinded trial randomized adults with PsO (2-20% body surface area) to once daily roflumilast 0.3%, roflumilast 0.15%, or vehicle for 12 weeks (NCT03638258). Throughout the trial, itch and its impact were evaluated via patient reported outcomes (PROs): Worst Itch Numeric Rating Scale (WI–NRS), Itch related Sleep Loss (IRSL), and Dermatology Life Quality Index (DLQI). This posthoc analysis reports correlation of WI–NRS with other PROs and with disease severity. Overall, 331 patients were randomized (109 to roflumilast 0.3%, 113 to 0.15%, and 109 to vehicle). At baseline, the mean WI–NRS score was 5.87. Throughout the trial, both roflumilast doses showed similar improvements in WI–NRS starting at Week 2 and were significantly superior to vehicle (P ≤.002). At baseline, Pearson correlation coefficients (PCCs) for WI–NRS and Psoriasis Area and Severity Index (PASI) were 0.189, 0.282, 0.205 for roflumilast 0.3%, roflumilast 0.15%, and vehicle, respectively (P ≤.033 for all correlations); for WI–NRS and IRSL: 0.548, 0.646, 0.652 (P <.001); for WI–NRS and DLQI: 0.445, 0.617, 0.422 (P <.001). At Week 8, PCCs for WI–NRS and PASI were 0.420, 0.409, 0.365 (P <.001); for WI–NRS and IRSL: 0.673, 0.725, 0.696 (P <.001); for WI–NRS and DLQI: 0.607, 0.823, 0.529. Treatment with roflumilast resulted in rapid and robust improvement in the severity of itch associated with PsO. Itch response to roflumilast was independent of disease severity and positively correlated with patient-reported sleep loss and quality of life improvement.

Dermatology

Gold LS, Blauvelt A, Armstrong A, Desai SR, Sofen H, Green LJ, Tyring SK, Ferris LK, Brown PM, Rubenstein DS, and Piscitelli SC. 25750 Tapinarof cream 1% once daily for plaque psoriasis: Secondary efficacy outcomes from two pivotal phase 3 trials. *J Am Acad Dermatol* 2021; 85(3):AB69.

Tapinarof is a novel therapeutic aryl hydrocarbon receptor modulating agent (TAMA) in development for treatment of psoriasis and atopic dermatitis. Tapinarof cream 1% once daily (QD) demonstrated highly statistically significant efficacy vs vehicle QD at 12 weeks and was well-tolerated in adults with mild to severe plaque psoriasis in two identical Phase 3 trials: PSOARING 1 (N = 510) and PSOARING 2 (N = 515). Here, we present secondary efficacy endpoints, including Physician Global Assessment (PGA) scores, body surface area (BSA) affected, and ≥90% reduction in Psoriasis Area and Severity Index (PASI90) – an endpoint more commonly assessed for systemic agents. Mean overall baseline PASI was 8.9 and 9.1 and BSA affected was 7.9% and 7.6% in PSOARING 1 and 2, respectively. At Week 12, significantly more patients achieved PGA score of 0 or 1 with tapinarof vs vehicle: 37.8% vs 9.9% (P =.0001) and 43.6% vs 8.1% (P <.0001); and mean BSA affected was significantly reduced with tapinarof vs vehicle: −3.5 vs −0.2 and −4.2 vs 0.1 (both P <.0001). A significantly higher proportion of tapinarof-treated patients achieved PASI90 at Week 12 vs vehicle: 18.8% vs 1.6% (P =.0005) and 20.9% vs 2.5% (P <.0001). All secondary endpoints were highly statistically significant, confirming the efficacy on the primary endpoint. Tapinarof significantly improved all measures of disease activity and showed clear and consistent separation vs vehicle. Tapinarof cream has the potential to provide physicians and patients with a novel nonsteroidal topical treatment option that is effective and well-tolerated.

Dermatology

Gold LS, Jalili A, Danic DL, Nyholm N, Thoning H, and Calzavara-Pinton P. 26607 Proactive management using Cal/BD foam in patients with plaque psoriasis prolongs time with a health-related quality of life improvement, compared with reactive management. *J Am Acad Dermatol* 2021; 85(3):AB109.

Introduction: The Phase III PSO-LONG study (NCT02899962) showed that proactive (PM) vs reactive management (RM) using calcipotriene 0.005%/betamethasone dipropionate 0.064% (Cal/BD) foam for up to 52 weeks in adults with psoriasis, resulted in superior efficacy. The patient-reported outcome measure Dermatology Life Quality Index (DLQI) evaluates patient-perception of psoriasis on health-related quality of life (HRQoL). In this post hoc analysis of PSO-LONG we evaluate whether initial DLQI responses, obtained following open-label Cal/BD foam treatment, were better sustained using subsequent PM or RM. Methods: PSO-LONG included an initial 4-week open-label phase (OLP) (once-daily Cal/BD foam) and a 52-week, double-blind, maintenance phase (MP) where patients were randomized to twice-weekly Cal/BD or vehicle foam (PM or RM, respectively), with 4-weeks once-daily Cal/BD foam rescue treatment for relapse (Physician's Global Assessment [PGA] ≥2). The proportion of patients achieving DLQI = 0/1 following OLP was assessed during MP to evaluate how long patients sustained initially gained responses. Survival analysis curves and hazard ratios (HR) for time with response in each group, were evaluated. Results: The analysis included 521 patients with predominantly PGA-moderate psoriasis (85.2%). During OLP, 49% of patients achieved DLQI = 0/1. During MP, RM vs PM was associated with almost double the risk (hazard) of losing DLQI = 0/1 (HR: 1.92; P <.001) and median time to lost response was almost 3.5 times shorter (57 vs 197 days, respectively). Conclusion: In a subset of patients achieving a DLQI = 0/1 HRQoL response following initial open-label Cal/BD foam, subsequent PM with Cal/BD foam significantly prolonged time with DLQI response vs RM.

Dermatology

Gold LS, Lain E, Bagel J, and Jacobson A. 27611 Fixed-combination halobetasol propionate 0.01%/tazarotene 0.045% (HP/TAZ) lotion for the treatment of plaque psoriasis in patients with 3-5% body surface area (BSA) and poor quality of life (QoL). *J Am Acad Dermatol* 2021; 85(3):AB156.

Use of TAZ with topical steroids, such as superpotent HP, is recommended for mild-to-moderate psoriasis as the combination may provide synergistic efficacy while increasing duration of treatment effect and remission. The objective of this analysis was to investigate HP 0.01%/TAZ 0.045% lotion in patients with relatively low affected BSA and poor QoL, as objective measures such as BSA may underestimate disease severity. Two phase 3, multicenter, double-blind studies enrolled 418 adults with 3-12% BSA and Investigator's Global Assessment (IGA) score of 3 or 4 ('moderate' or 'severe') at baseline. Participants were randomized (2:1) to receive HP/TAZ or vehicle lotion once-daily for 8 weeks, with a 4-week posttreatment follow-up. Pooled, post hoc analyses were conducted in a subset of 65 participants with baseline BSA of 3-5% and Dermatology Life Quality Index (DLQI) score ≥11. At week 8, 50.3% of HP/TAZ-treated participants achieved treatment success (≥2-grade reduction from baseline in IGA and score of 0 or 1 ['clear' or 'almost clear']), vs 14.6% of vehicle-treated participants (P <.05). BSA was significantly reduced with HP/TAZ (39.2%) vs vehicle lotion (+15.9%; P <.05). The percentage of participants experiencing a clinically meaningful ≥4-point reduction in DLQI score was greater for HP/TAZ (85.3%) vs vehicle (55.6%). Numerical improvements with HP/TAZ lotion were maintained 4-weeks posttreatment for efficacy measures and DLQI, consistent with the overall population. Though analyses were limited by the small population, HP/TAZ lotion provided significantly greater efficacy vs vehicle in participants with low BSA and poor QoL, with clinically relevant improvements in QoL.

Dermatology

Graber E, Baldwin H, Harper J, Alexis A, **Gold LS**, Hebert A, Fried R, Rieder E, Kircik L, Del Rosso J, Kasujee I, and Grada A. LB756 Patient-reported outcomes for sarecycline effectiveness in Acne Vulgaris in real-world settings: PROSES study protocol. *J Invest Dermatol* 2021; 141(9):B12.

Introduction: The detrimental psychosocial impact of acne vulgaris is well established. Patient-reported outcomes are needed to fully understand the psychosocial benefits of acne treatment. Sarecycline, a novel narrow-spectrum antibiotic, demonstrated efficacy, safety, and improvement in health-related quality of life (HRQOL) in clinical trials and is approved for treatment of moderate-to-severe acne. In 2020, a consensus panel generated a 10-question expert panel questionnaire (EPQ), which, along with the validated acne symptom and impact scale (ASIS), was considered a high-quality tool for real-world assessment of patient-reported HRQOL. The HRQOL benefits of sarecycline will be assessed using these instruments. Methods: This single-group, prospective, 12-week cohort study is expected to enroll 300 patients (age, ≥9 years) with moderate-to-severe acne treated with sarecycline as part of routine care in up to 50 US community practices. The primary endpoint is patient-reported outcomes at week 12. At the baseline and week-12 visits, patients and caregivers of pediatric patients will complete the EPQ and ASIS. Additional endpoints include sarecycline effectiveness (success on investigator global assessment), satisfaction, safety, and tolerability. Conclusions: This real-world study of sarecycline will be the first to use the most recent expert panel recommendations to evaluate HRQOL for patients with acne.

Dermatology

Grayson C, **Awosika O**, and Pritchett E. 28666 Global initiatives in dermatology and education. *J Am Acad Dermatol* 2021; 85(3):AB204.

Background: Coronavirus disease 2019 (COVID-19) resulted in a global pandemic that has adversely affected the economy, healthcare, and education around the world. The resulting travel restrictions, physical distancing policies, and limited social interactions have led to an inevitable change in the medical education system. The use of technology platforms to teach, connect, and collaborate is crucial to maintain education standards and research projects. We present an international exchange program with a videoconferencing series that allows residency programs to sustain international educational partnerships during COVID-19 and thereafter. Description: A series of 60-minute videoconferencing lectures were held for residents at both Henry Ford Hospital (HFH) in Detroit, Michigan and Universidad El Bosque in Bogotá, Colombia to participate in simultaneously. Sessions were hosted by faculty members from HFH on subjects including but not limited to: oncodermatology, comparative dermoscopy, and cutaneous T-cell lymphoma. Learning objectives were developed for each videoconference and participants answered a series of questions to assess (a) their knowledge and (b) lecture content. Results of the surveys serve as the core of our evaluation. Goals: Teach residents about new approaches to diagnosis and treatment, improve social and intercultural competencies, and increase interest in global health and caring for the underserved. Conclusion: The videoconferencing series component of this mutually beneficial international exchange partnership is of utmost importance given the circumstances of COVID-19. In addition to continuing education and collaboration, videoconferencing allows the interactive format of in-person lectures to be maintained while adhering to distancing guidelines.

Dermatology

Hamzavi I, Rosmarin D, Butler K, Kuo F, Zhu Z, and Sun K. 25486 Correlation of the Vitiligo Area Scoring Index with patient- and physician-reported measures of clinical improvement in a randomized, double-blind phase 2 study. *J Am Acad Dermatol* 2021; 85(3):AB60.

The Vitiligo Area Scoring Index (VASI) is a quantitative clinical tool that estimates the overall area of vitiligo patches (ie, skin depigmentation) and the degree of macular repigmentation within these patches over time. This analysis aimed to evaluate the correlation between facial and total VASI (F-VASI and T-VASI, respectively) with patient- and physician-reported measures of clinical improvement (Patient Global Impression of Change-Vitiligo [PaGIC-V; 7-point scale] and Physician's Global Vitiligo Assessment [PhGVA]) in a randomized, double-blind phase 2 study of 157 patients with vitiligo. Among stable patients (ie, no change from baseline in PaGIC-V [score of 4]), VASI scores showed excellent test-retest reliability (≥0.95) at Weeks 12 and 24. Significant differences in VASI were detected among PhGVA categories (mild, moderate, severe) at baseline. The VASI detected change in disease status during the treatment period; the changes were significantly different between patients who showed improvement (PaGIC-V, 1-3) or worsening (PaGIC-V, 5-6) and were related to the PaGIC-V (Pearson's r ~0.45, P <.0001). To assess interpretability, an anchor-based approach used PaGIC-V (score of 1 or 2) to define clinically meaningful change (CMC) on the VASI at Week 24; mean percentage CMC was 57% for F-VASI and

42% for T-VASI. Results indicated that a higher percentage of patients treated with 1.5% ruxolitinib cream met or exceeded CMC thresholds vs vehicle on F-VASI (39.4% vs 3.1%; P =.0005) and T-VASI (27.3% vs 0%; P =.002). Analyses of efficacy using the F-VASI and T-VASI reflect meaningful and relevant changes in patients with vitiligo.

Dermatology
Jiang A, and **Kerr H**. 27099 Actinomyces infection within red pigment of a tattoo. *J Am Acad Dermatol* 2021; 85(3):AB129.

Patient history: A Caucasian woman in her 40s presented with a one-year history of a raised, dry, pruritic papules on the tattoo on the left medial lower leg she received six months prior. Examination revealed multiple open comedones and pustules coalescing into an edematous plaque, limited to the red portions of the tattoo. Biopsies: Histologic examination revealed pseudoepitheliomatous hyperplasia, tattoo and brisk lymphohistiocytic inflammation, suggestive of an infectious process. Laboratory data: A wound culture grew Actinomyces neuii. Diagnosis and treatment: Patient was diagnosed with Actinomyces infection of red pigment of her tattoo and was started on amoxicillin 500 mg TID for six months and mupirocin ointment topically. Red pigment within tattoos is the most common cause of cutaneous reactions to tattoos. We describe a case of PEH secondary to Actinomyces neuii infection limited to the red portions of a tattoo. To our knowledge, this is the first case in which Actinomyces species has been implicated in a tattoo infection. Primary cutaneous actinomycosis is rare; it is typically chronic, recurs after short courses of antibiotic treatment and leads to the formation of granules. While reactions within red tattoos and bacterial infections of tattoos may be relatively common, infection of the red component of a tattoo with Actinomyces has not yet been described. Biopsy and evaluation for bacterial infections such as Actinomyces should be considered within the differential of a red tattoo reaction.

Dermatology
Kim KM, and **Friedman B**. 28139 A case of IgA vasculitis associated with underlying cytomegalovirus colitis. *J Am Acad Dermatol* 2021; 85(3):AB175.

A 62-year-old Caucasian female with history of treated hepatitis C virus (HCV) infection in remission, secondary liver cirrhosis, and idiopathic CD4 deficiency presented for admission with hematochezia and gastrointestinal discomfort. She also endorsed a 2-week history of petechial rash on her feet. A colonoscopy revealed ulcerated, friable mucosa at the hepatic flexure with a biopsy confirming CMV colitis. The patient was promptly started on IV valgalanyclovir. Dermatology was consulted for the rash with examination revealing numerous scattered purpuric macules and papules on the legs and feet. A punch biopsy revealed leukocytoclastic vasculitis, while a direct immunofluorescence (DIF) assay demonstrated 2+ granular staining in superficial dermal vessels for IgA, IgM, IgG, C3, and fibrinogen. The patient's hospital course was complicated by worsening renal function, hematuria, and Staphylococcus epidermidis bacteremia treated with IV daptomycin. The patient was felt to have IgA vasculitis, but given her concurrent infections systemic immunosuppression was not recommended. Her cutaneous lesions, hematochezia, hematuria and renal function all ultimately improved with treatment of the patient's underlying colitis. To our knowledge, this is the third case of IgA vasculitis as a complication of underlying CMV infection of the gastrointestinal tract.

Dermatology
Kurland E, Myers B, **Friedman B**, and **Rambhatla P**. 28367 A case of chronic prurigo nodularis, angiolymphoid hyperplasia with eosinophilia, and reactive lymphadenopathy: Intersection of multiple processes, or a novel clinical entity? *J Am Acad Dermatol* 2021; 85(3):AB185.

Background: Prurigo nodularis (PN) is a chronic skin disease characterized by intensely pruritic, hyperkeratotic nodules that can have significant deleterious effects on patient quality of life and are often difficult to treat. Various etiologies have been shown to trigger the development of PN lesions by initiating the itch-scratch cycle. Angiolymphoid hyperplasia with eosinophilia (AHLE) is a rare benign vascular tumor which may cause pain, bleeding or pruritus. We present a case of PN-like lesions with features of AHLE on pathology, which has been recalcitrant to several topical and systemic therapies. Case: A 64-year-old female with a past medical history of breast cancer presented for management of long-standing

PN resistant to several topical therapies, antihistamines, systemic medications (including methotrexate, mycophenolate mofetil, flutamide, minocycline, allopurinol, infliximab, cyclosporine, etanercept, oral prednisone) and phototherapy. On physical examination, she had diffusely scattered hyperpigmented, excoriated papules and nodules over her arms, legs, chest, and upper back. Multiple lesional biopsies revealed superficial and deep lymphoid infiltrate with multiple eosinophils, consistent with AHLE. Additionally, left axillary lymph node biopsy demonstrated reactive lymphoid hyperplasia with focal dermatopathic changes. Future systemic treatment options for this patient include dupilumab, thalidomide, apremilast and omalizumab. Conclusion: To our knowledge, PN associated with AHLE has not been reported.This case emphasizes the utility of clinicopathological correlations and the importance of a systemic approach to investigate the underlying etiology of PN especially in treatment-resistant cases.

Dermatology

Kwa M, Kang R, Cherupally M, Aikman C, and Ackermann R. LB762 Initiation patterns among novel systemic agents for U.S. adults with Psoriasis and Psoriatic Arthritis. *J Invest Dermatol* 2021; 141(9):B13.

Background: Biologic agents and PDE-4 inhibitors are a growing, but high cost drug class for severe psoriasis patients, especially those refractory to conventional therapies. Factors that drive treatment selection are unknown. Type of Study: Retrospective cohort study. Methods: Commercial and Medicare Advantage adult enrollees with a pharmacy claim for a TNF-a, IL-12/23, IL-17, or PDE-4 between 2015 and 2018 were grouped into psoriasis only (1-Ps, n=8013) or those with psoriasis plus psoriatic arthritis (2-Ps+PsA, n=5233). Multinomial logistic regression was used to generate odds ratios and 95% confidence intervals for receiving IL-12/23, IL-17, or PDE-4 compared with TNF-a and adjusted for demographics, prescriber specialty, insurance, and Charlson Comorbidity Index. Results: TNF-a (referent) was the most common biologic for both groups (1-Ps 36%, 2-Ps+PsA 55%), followed by PDE-4 (1-Ps: 38%, 2-Ps+PsA: 27%), IL-12/23 (1-Ps: 21%, 2-Ps+PsA: 12%) and IL-17 (1-Ps: 5%, 2-Ps+PsA: 6%). Only 1.1% of 1-Ps patients were prescribed by a rheumatologist and 43% of 2-Ps+PsA. From 2015 to 2018, the proportion of IL-17 and PDE-4 increased, but TNF-a remained the most common. Prescribing of IL-12/23 is also increasing over time driven by the newer IL-23 medications. For 2-Ps+PsA patients, patients seen by rheumatologists were less likely to have a claim for non-TNF-a treatment i.e. IL-12/23 (OR=0.22[0.18-0.27)], IL-17 (0.36[0.28-0.46]) and PDE-4 (0.53[0.27-0.46]) versus those seen by dermatology. For 1-Ps, fills for IL-12/23 and PDE-4 (0.45[0.33-0.61], 0.48[0.38-0.60]) were less likely to be observed in Medicare compared to commercial. Conclusion: IL-17 and PDE-4 inhibitors have been increasingly utilized compared to older biologics, however TNF-a remained the most commonly used. IL-23s should be monitored as their prescribing increases. Psoriasis type, insurance, and provider specialty were associated with selection of these agents.

Dermatology

Lyons AB, **Awosika O**, and **Lim HW**. 28545 A man with halo nevi and premature hair graying. *J Am Acad Dermatol* 2021; 85(3):AB197.

Case presentation: A 20-year-old male presented with a 5-month history of asymptomatic depigmented lesions on the trunk and patchy graying of hair. He noted an acute onset of depigmented patches slowly enlarging around nevi on his chest and abdomen. Three months later, he developed similar appearing areas of involvement disassociated from nevi on his chest and back and graying of his scalp hair. He denied any new or changing moles and reported no associated symptoms. Personal and family histories were negative for vitiligo, autoimmune conditions, and skin cancer. On physical examination, there were numerous depigmented macules and patches on the trunk and depigmented patches surrounding symmetric, evenly pigmented, well-demarcated 3-6 mm brown-black macules on the trunk. There was also patchy graying of the scalp hair. Wood's lamp examination revealed fluorescence of depigmented macules and patches on the trunk. Labs were notable for mild anemia and TSH within normal limits. The patient also had a normal ocular exam by ophthalmology. Betamethasone dipropionate 0.05% ointment BID, gingko biloba (60 mg BID), and alpha lipoic acid (100 mg daily) were started with no improvement at 4 months. Discussion: Halo nevi may be associated with nonsegmental vitiligo or melanoma-associated leukoderma. In patients with multiple halo nevi, premature hair graying may represent a robust immune response that warrants a search for melanoma as a possible trigger. Melanoma was ruled out in this case

with full skin and ocular examinations. This clinical presentation of halo nevi, nonsegmental vitiligo, and premature hair graying represents a rare triad.

Dermatology
Pandya AG, Harris JE, Lebwohl M, **Hamzavi I**, Butler K, Kuo F, Wei S, and Rosmarin D. 27636 Addition of narrow-band ultraviolet light B phototherapy to ruxolitinib cream in patients with vitiligo. *J Am Acad Dermatol* 2021; 85(3):AB158.

Previous reports with Janus kinase (JAK) inhibitors have suggested additional therapeutic benefit with concomitant phototherapy in patients with vitiligo. In a phase 2, randomized, dose-ranging study in adult patients with vitiligo (NCT03099304), ruxolitinib cream, a JAK1/JAK2 inhibitor, was associated with substantial repigmentation for up to 52 weeks of treatment as assessed by ≥50% improvement in facial and total Vitiligo Area Scoring Index (F-VASI50 and T-VASI50). After Week 52, patients were allowed to add narrow-band ultraviolet-B (NB-UVB) therapy while continuing open-label treatment with twice-daily 1.5% ruxolitinib cream. Nineteen patients (mean age, 47 years) received add-on NB-UVB for ≥12 weeks (mean [range] duration, 40 [15–51] weeks) at various frequencies based on investigator site's standard phototherapy protocol, most commonly 3 times/week (n = 9). Only 4 patients (21%) had adverse events (AEs; all grade 1/2 in severity) after receiving add-on NB-UVB, and no AEs were related to treatment. No AEs related to skin application site reaction, skin malignancies, or laboratory abnormalities were reported. All 19 patients who received ruxolitinib cream with add-on phototherapy experienced improvement in repigmentation (before vs after add-on NB-UVB: F-VASI75, 42% vs 68%; F-VASI90, 21% vs 58%; T-VASI50, 42% vs 68%). The benefit was more apparent in the 12 patients who had not achieved F-VASI50 at Week 24. In summary, the addition of phototherapy to ruxolitinib cream in patients with vitiligo was well tolerated and demonstrated further improvement in repigmentation. Larger studies are needed to confirm these findings.

Dermatology
Papp K, Van Voorhees A, **Gold LS**, Lebwohl M, Strober B, Zhang Z, and Wang Y. 25602 Improvements and response achievement in PASI subscale domains for head scaling and erythema in apremilast-treated patients with moderate to severe plaque psoriasis of the scalp: Results from the STYLE study. *J Am Acad Dermatol* 2021; 85(3):AB63.

Background: Up to 80% of patients with psoriasis have scalp involvement. Apremilast 30 mg BID (APR) demonstrated efficacy in the phase 3 STYLE study of moderate-to-severe scalp psoriasis. We report a post hoc analysis of the head scaling and head erythema PASI subscale domains. Methods: Patients with moderate-to-severe plaque psoriasis (PASI ≥12, BSA ≥10%, sPGA ≥3) and moderate-to-severe scalp psoriasis (baseline Scalp PGA score ≥3, psoriasis-involved scalp surface area ≥20%) with inadequate response/intolerance to ≥1 topical therapy were randomized to double-blind treatment with APR or placebo (PBO) for 16 weeks. Results: Baseline mean (SD) PASI head scaling scores were 2.8 (0.7) for APR (n = 201) and PBO (n = 102); head erythema scores were 2.9 (0.6) and 2.8 (0.6). Significantly greater mean percentage changes from baseline were observed at Week 16 with APR vs PBO in head scaling (APR: −52.2 [95% CI: −57.9, −46.4] vs PBO: −26.9 [95% CI: −34.4, −19.4]) and head erythema scores (APR: −53.1 [95% CI: −59.1, −47.2] vs PBO: −25.0 [95% CI: −32.0, −17.9]). Improvements were observed as early as Week 2. Significantly more APR vs PBO patients achieved Week 16 responses (score of 0 [none] or 1 [slight]) on head scaling (55.4% [95% CI: 47.5, 63.0] vs 31.0% [95% CI: 21.3, 42.0]; P =.0002) and erythema (55.4% [95% CI: 47.5, 63.0] vs 23.8% [95% CI: 15.2, 34.3]; P <.0001). Conclusions: Patients with moderate-to-severe scalp psoriasis had greater improvements in PASI subscale scores (head scaling, head erythema); greater proportions of patients achieved head scaling and erythema responses with APR vs PBO.

Dermatology
Pourang A, Dourra M, **Ezekwe N**, **Kohli I**, **Hamzavi I**, and **Lim HW**. 26905 The effect of Polypodium leucotomos extract (Fernblock) on visible light and UV-induced photoaging. *J Am Acad Dermatol* 2021; 85(3):AB26.

Traditional sunscreens containing organic ultraviolet (UV) filters have increasingly been scrutinized for their effects on the environment. As a result there has been an interest in environmentally safe polyphenol compounds as adjuvants which also provide systemic protection against different wavelengths of solar radiation. Fernblock the patented, standardized extract of Polypodium leucotomos, herein referred to as PLE, is an antioxidant widely available as oral supplement for photoprotection. We performed a comprehensive review of the available literature on the effect of PLE on UV and visible light (VL) induced photoaging. PLE increases TGF-β, type I and V collagen and elastin in UV-irradiated fibroblasts, as well as increased elastin and fibrillin 1 expression and decreased MMP-1 expression in VL-irradiated fibroblasts. PLE also decreases UVR-induced TNF-α, NO, iNOS, NF-kB and AP1 in keratinocytes. In murine models PLE increases catalase and glutathione peroxidase activity in the epidermis, inhibits dermal elastosis, decreases skin inflammatory cells and COX-2 levels, and reinforces dermal elastic fibers. In human skin, PLE prevents both VL and UV-induced COX-2 expression and VL-induced MMP-1 expression. Enhanced antioxidative protection of the skin was noted in human skin in vivo after consumption of an antioxidant supplement containing non-Fernblock extract of P leucotomos. PLE may protect against UV- and VL-induced photoaging through regulation of extracellular matrix (ECM) modeling, specifically via TGF-β signaling and MMP transcription factors, and downregulation of inflammation due to its anti-inflammatory and antioxidant properties. Future large-scale studies assessing the photoprotective effects of PLE in humans are warranted.

Dermatology

Pourang A, Olds H, **Ezekwe N**, **Lim HW**, and **Hamzavi I**. 28522 The impact of the SARS-CoV-2 pandemic on phototherapy utilization. *J Am Acad Dermatol* 2021; 85(3):AB194.

Phototherapy is a mainstay of treatment for several dermatologic conditions. Patients often require multiple treatments per week for several weeks to months to achieve treatment efficacy. The SARS-CoV-2 global pandemic caused many dermatology clinics to close completely or significantly reduce patient volumes, which may have limited patient access to this beneficial treatment. This retrospective study examines the pandemic's impact on phototherapy treatment rates and reimbursement at one major tertiary care center and five locations of a private dermatology clinic in Southeast Michigan. Phototherapy CPT reimbursement data from March 1-June 30, 2020 was compared with the same timeframe in 2019. Units of phototherapy performed decreased by an average of 84%, and there was an average decrease of 43% in the number of unique patients receiving treatments. Reimbursement for phototherapy decreased by an average of 83%. The drastic decline in phototherapy reimbursement is a reflection of the pandemic's financial impact and likely correlates to a larger scale of revenue loss in dermatology practices. Adequate phototherapy treatment was also likely delayed for many patients. As the pandemic continues, implementation of home phototherapy treatments may be necessary for patients to receive proper treatment and to minimize the impact of loss of revenue due to limited in-office phototherapy. Precautions will need to be taken to guarantee the safety of patients and the care team for patients to receive optimal in-office phototherapy treatment. The pandemic's impact on medical dermatology finances could potentially destabilize access to patients who need this safe and effective treatment.

Dermatology

Ramachandran V, and **Konda S**. 28206 Disseminated gonococcal infection manifesting as embolic septic vasculitis. *J Am Acad Dermatol* 2021; 85(3):AB179.

Patient history and physical: A pregnant 21-year-old African American female (G5P2, 34w2d) presented with one day of painful, red bumps of her upper and lower extremities. Associated symptoms included chills, malaise, headache, photophobia, phonophobia, and edematous arthralgias (left shoulder, left ankle). Personal and family history were negative for thromboembolic phenomena, autoimmune disorders, or coagulopathies. She denied intravenous drug use, new sexual partners, blood transfusions, sick contacts, or recent travel. Physical examination demonstrated sparse, irregularly distributed, exquisitely tender erythematous to necrotic pinpoint papules and pustules of the abdomen and distal extremities. Vital signs were notable only for mild tachycardia. Biopsies: Punch biopsies of lesions of the left ankle and left thigh revealed large neutrophilic aggregates surrounding dermal vessels featuring sludging and engorgement within the vessels themselves. This perivascular suppurative dermatitis was suspicious for infection. Tissue culture ultimately indicated presence of Neisseria gonorrhea. Laboratory

data: Inpatient work-up revealed: elevated ESR (122 mm/hr), elevated CRP (8.8 mg/dL), negative CSF studies (VZV/CMV/EBV/HSV/cryptococcal antigen/bacterial culture), three negative peripheral blood cultures, negative syphilis serologies, normal WBC count, and normal transthoracic echocardiogram. Neisseria gonorrhea and Chlamydia trachomatis rRNA (cervical swabs) were negative 10 days prior to presentation to the hospital. However, following the biopsy and tissue culture results, urine gonococcal and chlamydial rRNA were rechecked and found to be positive. Diagnosis: Disseminated gonococcal infection (acute arthritis-dermatitis syndrome). Clinical course and treatment: Patient was treated with one week of intravenous ceftriaxone and single-dose oral azithromycin for chlamydial coinfection. At 3-week outpatient follow-up, all symptoms and cutaneous findings had resolved.

Dermatology

Robinson G, **Friedman B**, and **McHargue C**. 28714 Primary cutaneous Fusarium infection in an immunocompetent host. *J Am Acad Dermatol* 2021; 85(3):AB206.

Introduction: Fusarium is a ubiquitous hyalohyphomycete found in the soil and air in many parts of the world. While well recognized as cause of severe disseminated disease in immunocompromised hosts, reports of cutaneous Fusarium infection in immunocompetent hosts are rare. Clinical case: A 67-year-old immunocompetent African American female with a history of diabetes mellitus complicated by neuropathy (A1c 7.7%) presented with a 2-year history of an asymptomatic nonhealing sore on the dorsal aspect of her left foot. It had begun as a small red papule that subsequently developed peripheral pustules and ulcerated. Examination revealed a firm brawny plaque over the left dorsal midfoot with a central 3-cm indurated pink plaque containing two shallow ulcers with yellow fibrinous bases. The patient was started on doxycycline after wound culture grew Staphylococcus aureus but was then lost to follow-up for five months. On representation, the ulcerative plaque had grown and become more cribriform in nature. Biopsy at that time revealed hyalohyphomycosis and tissue culture grew Fusarium spp. The patient was admitted to the hospital where she underwent operative debridement and was started on an extended course of voriconazole. Workup for systemic involvement was negative. She is currently being followed as an outpatient and improving. Conclusion: We report a rare case of primary cutaneous Fusarium infection in an immunocompetent patient. Physicians should consider hyalohyphomycosis during evaluation of patients with indolent ulcers, even in the absence of immunocompromise or systemic symptoms.

Dermatology

Rosmarin D, Pandya AG, Grimes P, Lebwohl M, Gottlieb AB, **Hamzavi I**, Butler K, Kuo F, Wei S, Rumberger B, and Harris JE. 27568 Maintenance of repigmentation after discontinuation of ruxolitinib cream in patients with vitiligo. *J Am Acad Dermatol* 2021; 85(3):AB36.

Treatment with ruxolitinib cream (Janus kinase [JAK] 1/JAK2 inhibitor) in adult patients with vitiligo resulted in substantial repigmentation over 52 weeks in a phase 2 dose-ranging study (NCT03099304). We assessed maintenance of repigmentation among responders from the phase 2 study following ruxolitinib discontinuation after 104 weeks of treatment. Patients initially randomized to ruxolitinib cream (1.5% twice daily [BID], 1.5% once daily [QD], 0.5% QD, or 0.15% QD) with evidence of facial repigmentation at Week 24 who completed ≥1 follow-up visit 1, 3, or 6 months after an additional 52 weeks of 1.5% ruxolitinib cream BID monotherapy (Weeks 52-104) were analyzed. Loss of repigmentation was defined as an increase in Vitiligo Area Severity Index score during the last follow-up visit vs Week 104 on ruxolitinib cream. Sixteen patients were included in the analysis (1.5% BID, n = 3; 1.5% QD, n = 5; 0.5% QD, n = 3; 0.15% QD, n = 5 [including 2 patients rerandomized to 1.5% BID/0.5% QD after Week 24]). Four patients (25.0%; 1.5% QD, n = 1; 0.5% QD, n = 1; 0.15% QD, n = 2) had repigmentation loss over 1-6 months of follow-up; no patients from the 1.5% ruxolitinib BID treatment group (with 2 years' exposure) experienced repigmentation loss. There were no significant differences in baseline serum levels of chemokine (C-X-C motif) ligand (CXCL) 9, CXCL10, or interleukin-15 in patients who experienced loss vs maintenance of repigmentation after ruxolitinib cream discontinuation. This exploratory analysis suggests that repigmentation with ruxolitinib cream monotherapy may be maintained postdiscontinuation; larger follow-up studies are required to confirm these findings.

Dermatology

Sagher E, and **Axelson A**. 27426 A young man with an impressive ulcer on the chest. *J Am Acad Dermatol* 2021; 85(3):AB143.

Diffuse large B cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma (NHL), and when cutaneous, may be limited to the skin or internal with metastasis to the skin. Morphologies of cutaneous metastases may be variable, and lymphomas most commonly present with pink-violet to red-brown papulonodules. Although less common, it is important to consider malignancy in the differential when evaluating an ulcer. Here we present the case of a 23-year-old morbidly obese Hispanic male who was hospitalized for inability to ambulate and was found to have nodal diffuse large B cell lymphoma, with full body imaging concerning for metastatic spread. Dermatology was consulted for a 3-month history of an ulcer on his chest, which was originally treated by the surgery team with debridement and antibiotics without improvement. On examination, he had a 8 × 7 × 5 cm ulcer over his left breast with a surrounding violaceous indurated plaque. Punch biopsy showed sheets of large atypical cells in the dermis with immunohistochemistry mirroring that of the lymph node biopsy (positive CD20 and BCL6, negative CD10, and MUM-1). As such, the ulcer was diagnosed as a cutaneous metastasis of nodal DLBCL, and he was started on chemotherapy with rituximab, doxorubicin, vincristine, and prednisone (R-CHOP) followed by radiation to the chest wound.

Dermatology

Wang Y, **Gold LS**, Lebwohl M, Strober B, Zhang Z, and Van Voorhees A. 25603 Improvement in scalp psoriasis and quality of life with apremilast in patients with moderate to severe scalp psoriasis regardless of prior systemic treatment: Results from the phase 3, randomized STYLE study. *J Am Acad Dermatol* 2021; 85(3):AB63.

Background: Apremilast 30 mg BID (APR) provided greater improvements in scalp psoriasis and quality of life vs placebo (PBO) in a phase 3 study in patients with moderate-to-severe plaque psoriasis of the scalp. We present subgroup analyses based on systemic treatment history. Methods: Patients with moderate-to-severe scalp psoriasis (Scalp Physician's Global Assessment ≥3, psoriasis-involved scalp surface area [SSA] ≥20%) and moderate-to-severe plaque psoriasis with inadequate response/intolerance to ≥1 topical therapy were randomized to double-blind APR or PBO for 16 weeks. SSA (last observation carried forward) and Dermatology Life Quality Index (DLQI; multiple imputation) changes were analyzed by ANCOVA in intent-to-treat (ITT) population subgroups based on prior systemic treatment. Results: 303 patients were randomized to APR (ITT: 201; prior systemic: 99; no prior systemic: 102) or PBO (ITT: 102; prior systemic: 49; no prior systemic: 53). Mean baseline assessments were similar with APR vs PBO for SSA involvement and DLQI: SSA - Prior systemic: 61.9% vs 56.2% - No prior systemic: 61.8% vs 60.0% DLQI - Prior systemic: 13.3 vs 12.8 - No prior systemic: 12.0 vs 12.5 At Week 16, APR patients achieved greater improvements vs PBO (least-squares mean differences): SSA - Prior systemic: −27.3%, P =.0003 - No prior systemic: −33.6%, P <.0001 DLQI - Prior systemic: −3.4, P =.0003 - No prior systemic: −2.6, P =.0016. Conclusions: APR demonstrated a consistent treatment effect vs PBO in moderate-to-severe scalp psoriasis patients with and without a history of prior systemic treatment.

Dermatology

Zirwas M, Draelos ZD, DuBois J, Kircik L, Moore A, **Gold LS**, Higham RC, Navale L, Burnett P, and Berk DR. 28588 Efficacy and safety of roflumilast foam 0.3% in patients with seborrheic dermatitis in a randomized, double-blind, vehicle-controlled phase 2 study. *J Am Acad Dermatol* 2021; 85(3):AB47.

Seborrheic dermatitis is a chronic inflammatory skin condition that may cause physical discomfort and emotional burden for patients including itching, stress, and embarrassment. Topical treatments, such as antifungals, steroids, immunomodulators, and dandruff shampoos are used, but there is a need for efficacious and safe options, especially for long-term use. A phase 2, 8-week study investigated roflumilast foam 0.3%, a potent, phosphodiesterase-4 inhibitor designed for once-daily treatment of lesions on the scalp, face, and body. Patients with at least moderate severity (mean IGA 3.1) and mean BSA 3.2% were randomized to roflumilast foam 0.3% (n = 154) or vehicle foam (n = 72). For the primary endpoint, IGA success at Week 8, 73.8% and 40.9% patients achieved IGA of clear/almost clear in the roflumilast foam and vehicle groups, respectively (P <.0001). Improvement in IGA success was

statistically significant starting at first postbaseline visit (Week 2, P =.0033) and continuing through Week 8 (P <.0001). Scaling and erythema were both significantly reduced at Week 8 in patients on roflumilast foam compared with vehicle (P ≤.002). Among patients with baseline Worst Itch Numeric Rating Scale (WI–NRS) score ≥4 (n = 184/226), statistically significant 4-point reduction in WI-NRS was achieved as early as Week 2 with roflumilast foam compared with vehicle (P ≤.0007). Rates of application-site pain, treatment-related adverse events, and discontinuations due to adverse events were low and comparable to vehicle. Once-daily roflumilast foam 0.3% was safe, well tolerated, and effective in treating erythema, scaling, and itch of seborrheic dermatitis, and represents a promising and mechanistically novel treatment with early onset of action.

Hematology-Oncology

Balanchivadze N, **Nasser Z**, **Shahid M**, **McKay C**, **Li P**, **Sohaney R**, and **Gadgeel SM**. 1317P Renal toxicity in black patients with non-squamous non-small cell lung cancer treated with combination platinum-pemetrexed-pembrolizumab therapy. *Ann Oncol* 2021; 32:S1013.

Background: In Keynote 189, an increased incidence of renal toxicity was observed with combination platinum-pemetrexed-pembrolizumab (PPP) therapy compared to chemotherapy alone. Studies have shown that compared to White Americans, Black Americans are at higher risk of morbidity and mortality associated with chronic kidney disease (CKD). We conducted a retrospective analysis of patients treated with PPP to assess the rate of renal toxicity in Black and White patients. Methods: Data of self-identified non-hispanic (NH) Black and NH White patients with advanced NS-NSCLC who were treated with PPP between January 1, 2017, and November 1, 2020, at the Henry Ford Health System was analyzed. Serum creatinine (Cr) and calculated glomerular filtration rate (GFR) before the first cycle of PPP and over the duration of PPP therapy were assessed. Acute kidney injury (AKI) was defined as an increase in Cr 1.5 times the baseline value. Reduction in GFR of ≥ 30% was considered significant. Multiple variables and outcomes were analyzed by two-group comparisons, univariate analysis, and Cox regression. Results: A total of 134 patients were included in the analysis. The mean age was 66.5 (SD 8.6) years, and 65 (48.5%) patients were men. A total of 33 (24%) patients were NH Black and 101 (75.4%) were NH White. There were 10 (8.1%) patients who developed AKI, and the median time to development of AKI was 4.5 months. No significant association of Black (3) or White (7) ethnicity with AKI was observed (p =.57). The odds of developing AKI was not increased in patients with a history of hypertension (p =.67), diabetes mellitus (p =.33), cardiovascular disease (p =.68), or CKD (p =.33). A total of 17 out of 127 (13.4%) patients had significantly reduced GFR, and patients with CKD were more likely to have reduced GFR (OR 4.8, p =.02). At the median follow-up of 24.5 months, the median survival was 15.2 months (95% CI, 12.7-22.2). Black ethnicity (HR 1.21, p =.46) and development of AKI (HR 1.13; 95% CI, 0.45–2.86) were not associated with increased mortality. Conclusions: Black patients with NS-NSCLC treated with PPP are not at higher risk of AKI or death than White patients. Development of AKI after PPP therapy was not associated with increased mortality. Legal entity responsible for the study: The authors. Funding: Has not received any funding.

Hematology-Oncology

Dziadziuszko R, Peters S, **Gadgeel SM**, Mathisen MS, Shagan SM, Felip E, Morabito A, Cheema P, Dols MC, Andric Z, Barrios CH, Yamaguchi M, Dansin E, Danchaivijitr P, Johnson M, Novello S, Gandara DR, Schleifman E, Wang J, and Mok TSK. 1281O Atezolizumab (atezo) vs platinum-based chemo in blood-based tumour mutational burden-positive (bTMB+) patients (pts) with first-line (1L) advanced/metastatic (m)NSCLC: Results of the Blood First Assay Screening Trial (BFAST) phase III cohort C. *Ann Oncol* 2021; 32:S950-S951.

Background: TMB is a promising biomarker for immunotherapy in NSCLC, but current data are mostly retrospective. As not all pts may have sufficient tissue for comprehensive biomarker testing, bTMB was prospectively tested as a novel biomarker using targeted next-generation sequencing. BFAST (NCT03178552), a global, open-label, multi-cohort trial, evaluated safety and efficacy of targeted therapies or immunotherapy in biomarker-selected pts with unresectable mNSCLC. Here we present results from Cohort C of 1L atezo vs platinum-based chemo in pts with bTMB+ mNSCLC. Methods: We planned to randomise ≈440 pts with 1L mNSCLC with measurable disease per RECIST 1.1 and bTMB ≥10 (9.1 mut/Mb; FMI bTMB assay) 1:1 to atezo 1200 mg IV every 3 weeks or chemo and stratified by

tissue availability, ECOG PS, bTMB and histology. The primary endpoint was INV-PFS per RECIST 1.1 in bTMB ≥16 (14.5 mut/Mb) pts. Key secondary endpoints included OS in bTMB ≥10 (intent to treat, ITT) and bTMB ≥16 pts, and INV-PFS in ITT pts. Results: 471 pts were assigned to atezo (n=234) or chemo (n=237). At baseline, 72% had non-squamous histology, 2% never smoked and median SLD was 103 mm. 145 pts with bTMB ≥16 were assigned to atezo and 146 to chemo. At data cutoff (21 May 2020) minimum follow up was 6 mo. INV-PFS difference in bTMB ≥16 pts for atezo vs chemo was not significant (P=0.053; Table). Grade 3-4 TRAEs occurred in 18% (atezo) vs 46% (chemo) of pts. Serious TRAEs occurred in 12% (atezo) vs 14% (chemo). Results at other bTMB thresholds and by F1L CDx will also be presented as an exploratory analysis. Conclusions: The primary PFS endpoint in bTMB ≥16 pts was not met. OS was numerically better with atezo vs chemo but the difference was not statistically significant. The safety profile of atezo vs chemo was favourable and consistent with atezo monotherapy across indications. [Formula presented] Clinical trial identification: NCT03178552.

Hematology-Oncology

Esakia T, Melkadze T, Tsiklauri K, Mariamidze E, Tsitsilashvili S, Otkhozoria N, Abuladze M, Jokhadze N, and **Balanchivadze N**. 1632P At home androgen deprivation therapy for patients with prostate cancer during the COVID-19 pandemic. One center experience. *Ann Oncol* 2021; 32:S1156-S1157.

Background: COVID-19 pandemic created major challenges in cancer care. Studies have shown increased risk for COVID-19 infectivity, severe disease and death in patients with cancer. Cancer centers worldwide adapted by modifying and often delaying treatment to minimize contact with patients. Methods: To provide safe and uninterrupted care for patients, a home care program was created for patients with prostate cancer at Acad. F. Todua Medical center. Men with locally advanced or metastatic prostate cancer (MPC) receiving androgen deprivation therapy (ADT) were enrolled. Patients and their caretakers were instructed on gonadotropin-releasing hormone (GnRH) subcutaneous injections (SQ) for home administration. Monthly at home laboratory testing and virtual consultations with medical oncologists every 1-3 months were arranged. Results: A total of 52 patients were enrolled during the period of March 2020 – March 2021. All men were White and had ECOG 0/1. The mean age was 71 [±6.3 y] years. Sixteen (31%) patients had stage IIIB PC and 36 (69%) patients had stage IV disease. Stage IIIB patients were receiving adjuvant ADT with SQ Goserelin Acetate 10,8mg every 8 weeks and bicalutamide 50mg daily for two weeks after definitive local treatment. Thirty-one (86%) patients had hormone sensitive metastatic PC and were receiving SQ Goserelin Acetate 10.8mg (28) every 8 weeks or SQ Leuprolide Acetate 22,5mg every 8 weeks (3) with 2 weeks of Bicalutamide 50mg daily. Five (14%) patients had castration resistant (CR) PC and were receiving SQ Goserelin Acetate 10,8mg every 8 weeks with Enzalutamide 160mg daily. Thirty-three (63%) patients had Gleason's score of 8/9. All patients were compliant with home injections, laboratory tests and virtual physician visits. Thirty-nine (75%) patients administered injections by themselves. Forty-two (80%) patients had PSA reduction >50%. Ten (20%) patients had disease progression and required clinic visits for investigations. Median time to progression was 12 months. Only 1 (2%) patient acquired COVID-19 infection, was hospitalized and died of respiratory failure. Conclusions: At home ADT with appropriate patient/caregiver education and close follow up may be safe for patients with PC during the COVID-19 pandemic.

Hematology-Oncology

Graff JN, Tagawa S, Hoimes C, Gerritsen W, Vaishampayan UN, Elliott T, **Hwang C**, Tije AJT, Omlin AG, McDermott RS, De Wit R, Qiu P, Poehlein C, Kim J, Suttner L, Cristescu R, Marton MJ, Schloss C, de Bono JS, and Antonarakis ES. 61MO Biomarker analysis of men with enzalutamide (enza)-resistant metastatic castration-resistant prostate cancer (mCRPC) treated with pembrolizumab (pembro) + enza in KEYNOTE-199. *Ann Oncol* 2021; 32:S383.

Background: In KEYNOTE-199 (NCT02787005), pembro + enza had durable antitumor activity in enza-refractory mCRPC. We evaluated the association between prespecified biomarkers and clinical outcomes. Methods: Cohorts 4 (C4; RECIST-measurable disease) and 5 (C5; nonmeasurable, bone-predominant disease) enrolled men with chemotherapy-naive mCRPC, irrespective of PD-L1 status, that progressed after initial response to enza. We evaluated TMB by whole exome sequencing (n = 64), PD-L1 combined positive score (CPS) by IHC (n = 124), and 18-gene T-cell–inflamed gene expression profile (TcellinfGEP) by NanoString (n = 51). Outcomes were DCR, PFS, PSA response, PSA progression, OS,

and ORR per blinded independent review (C4 only). Significance of continuous biomarkers (CPS, TMB, GEP) was prespecified at 0.05 for 1-sided P values from logistic (ORR, DCR, PSA response) and Cox proportional hazard (PFS, OS, PSA progression) regression adjusted for ECOG PS. Results: In C4, ORR was 10% (5/48) in pts with evaluable TMB data and 12% (10/81) in pts with CPS data. In C4 and C5, 16% (10/64) and 14% (17/124) of pts with TMB and CPS data, respectively, achieved a PSA response. TMB was significantly associated with DCR (P = 0.03) and trended toward an association with PSA response (P = 0.08). TMB (AUROC [95% CI]: 0.68 [0.51-0.86]), but not CPS (0.54 [0.41-0.67]) or TcellinfGEP (0.55 [0.37-0.74]), enriched for PSA response. TMB (P = 0.04), but not CPS (P = 0.57) or TcellinfGEP (P = 0.32), was significantly associated with PSA progression. There was 1 MSI-H pt (per Promega PCR assay); this pt achieved an objective and PSA response and had PFS >6 months. TMB, CPS, and TcellinfGEP were not associated with PFS or OS. There was a low prevalence of TMB ≥175 mut/exome (11%) and TcellinfGEP-high (≥−0.318; 16%). Conclusions: In this biomarker analysis of KEYNOTE-199 C4-C5, PD-L1 CPS and TcellinfGEP were not significantly associated with clinical outcome. Despite the low prevalence of TMB ≥175 mut/exome, TMB was positively associated with outcomes of pembro + enza in pts with mCRPC. The sample sizes for the exploratory analyses were small, and results should be interpreted with caution. Clinical trial identification: NCT02787005

Hematology-Oncology

Lawal O, Lupak O, Udo I, and **Emole J**. CT-423: Neuropsychiatric Disorders in Hospitalized Patients Undergoing Chimeric Antigen Receptor T-Cell Therapy for Multiple Myeloma. *Clin Lymphoma Myeloma Leuk* 2021; 21:S454.

Context: Chimeric antigen receptor T-cell (CAR-T) therapies have shown efficacy in treatment of relapsed/refractory multiple myeloma (MM). Neuropsychiatric disorders (NPD) in patients undergoing CAR-T have not been well described. Objective: To evaluate prevalence of NPD in patients who underwent in-hospital CAR-T therapy for MM and explore association of NPD with in-hospital outcomes of CAR-T therapy. Design: Retrospective. Setting: We evaluated NPD among patients undergoing in-hospital CAR-T therapy for MM in 2018 using data from the National Inpatient Sample (NIS). We applied discharge level weights to extrapolate findings to hospitalizations across the nation. Patients: Hospitalizations for patients ≥ 18 years who received investigational CAR-T therapy for MM were selected from the NIS database using International Classification of Disease, Tenth Revision (ICD-10) procedure and diagnostic codes. Demographic and CAR-T treatment variables were collected. Regression models were fit to assess association of NPD with clinical variables, and odds ratios (OR) were reported. Main Outcomes Measures: The primary outcome was prevalence and distribution of NPD. The secondary outcome was association of NPD with CAR-T outcomes. Results: A total of 200 CAR-T procedures met inclusion criteria; 65% males, 71% Caucasians, and 15.8% African Americans, with a median age of 59 years. Most CAR-T procedures (95%) were performed in urban teaching hospitals. Prevalence of NPD was 27.5%. Anxiety was the most common NPD, then depression and insomnia. Patients with NPD, compared to those without, were more likely to have Charlson comorbidity index (CCI) > 3 (54.5% versus 20.7%, p= 0.01). There were no observed differences in the distribution of NPD with regard to race, age, gender, insurance, or prior receipt of bone marrow transplantation. Association was noted between NPD and CCI ≥ 3 (OR= 4.60, 95% CI= 1.29–16.40), between NPD and fever (OR= 0.16, 95% CI= 0.04–0.70). No significant association were found between NPD and neurotoxicity, in-hospital mortality, respiratory or renal failure, length of stay, or hospital charges. Conclusions: One in every four patients who underwent CART therapy for MM in 2018 had NPD. Patients with multiple comorbidities were at higher risk, while patients with fever during CART therapy were likely underdiagnosed with NPD.

Hematology-Oncology

Leal TA, Berz D, **Rybkin I**, Iams WT, Bruno D, Blakely C, Spira A, Patel MR, Waterhouse DM, Richards D, Pham A, Jotte R, Garon EB, Hong D, Shazer R, Yan X, Latven L, and He K. 1191O MRTX-500: Phase II trial of sitravatinib (sitra) + nivolumab (nivo) in patients (pts) with non-squamous (NSQ) non-small cell lung cancer (NSCLC) progressing on or after prior checkpoint inhibitor (CPI) therapy. *Ann Oncol* 2021; 32:S949.

Background: Therapy with CPI has improved OS across many tumor types, including in a subset of pts with NSCLC. Mechanisms of CPI resistance, however, have been described, including an

immunosuppressive TME, which may include recruitment of immunosuppressive myeloid-derived suppressor cells (MDSCs), regulatory T cells (Tregs), and M2-polarized macrophages within the TME. Sitra, a spectrum-selective TKI targeting TAM (Tyro3/Axl/MerTK) receptors and VEGFR2, reduces the number of MDSCs and Tregs while increasing the ratio of M1/M2-polarized macrophages, and thus is hypothesized to overcome an immunosuppressive TME and augment antitumor immune responses. Methods: MRTX-500 (NCT02954991) is a phase II study evaluating sitra (120 mg QD) + nivo (Q2W or Q4W) in pts with NSQ NSCLC who have progressed on or after treatment, with a CPI-based regimen (anti-PD1/PD-L1) and/or platinum doublet chemotherapy. The primary endpoint is ORR per RECIST 1.1. Secondary endpoints include OS, PFS, and safety. We report updated efficacy data for pts with NSCLC with PCB (prior clinical benefit; CR, PR, or SD ≥12 weeks) from a CPI who were treated with sitra + nivo as either 2L or 3L therapy. Results: As of 17 October 2020, 68 pts with PCB (57% female; median age, 66 years; ECOG PS 0/1/2, 27%/66%/7%) were treated. Median follow-up was 28 months, median OS was 15 months (95% CI 9.3, 21.1),1- and 2-year OS rates were 56% and 32%, respectively. Median PFS was 6 months, and ORR was 16% (11/68), including 2 CRs. Median duration of response was 13 months. In all CPI-experienced pts evaluable for safety (n=124), treatment related adverse events (TRAEs) occurred in 91% of pts, with Gr 3/4 TRAEs occurring in 60% of pts. The most common (≥10%) Gr 3/4 TRAEs were hypertension and diarrhea. There were no Gr 5 TRAEs. Discontinuation rates for sitra and nivo due to any AE were 30% and 27%, respectively. Conclusions: Sitra + nivo demonstrated antitumor activity and encouraging OS compared to historical controls and no new safety signals were observed in pts with NSQ NSCLC who progressed on prior CPI. This combination is being evaluated in the phase III SAPPHIRE study. Clinical trial identification: NCT02954991.

Hematology-Oncology

Posner MR, Ho AL, Niu J, Nabell L, Leidner RS, Nieva J, Richardson DL, Pearson AT, **Wang D**, Chung K, Adkins DR, Pimentel A, Wong S, Lacobucci C, Qing X, Katchar K, Schlienger K, Matushansky I, Fu S, and Pfister DG. 961MO Safety, efficacy, immunogenicity of arenavirus-based vectors HB-201 and HB-202 in patients with HPV16+ cancers. *Ann Oncol* 2021; 32:S831-S832.

Background: Human papillomavirus 16 positive (HPV16+) cancers are caused by stable expression of HPV16-specific E7 and E6 oncoproteins, also a source of immunogenic neoantigens. Replicating arenavirus vectors HB-201 (LCMV) and HB-202 (Pichinde virus), expressing the same non-oncogenic HPV16 E7E6 fusion protein, induce tumour-specific T-cell responses. Methods: A phase I first-in-human study assessed HB-201 monotherapy and HB-201 & HB-202 alternating 2-vector therapy (HB-201/HB-202) intravenously (IV) with or without 1 intratumoral dose (IT/IV) in HPV16+ cancers. Safety, tolerability, and preliminary anti-tumour activity by Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 or immune RECIST were evaluated, as well as immunogenicity and pharmacodynamic biomarkers in blood and tumour tissue samples. Results: The study treated 38 patients (29 with ≥1 efficacy scan) with confirmed HPV16+ cancers with a median (range) of 3 (1–10) prior anticancer therapies. The most common primary cancer site was oropharynx (76%), followed by cervical (7.9%). Eighteen patients received HB-201 monotherapy IV and 9 IT/IV; 11 patients received HB-201/HB-202 alternating therapy. Treatment was generally well tolerated. Twenty patients (53%) reported treatment-related adverse events (all Grade ≤2). Two of 11 evaluable patients treated with HB-201 IV every 3 weeks had partial response (including 1 unconfirmed immune complete response of target lesion) and 6 had stable disease...

Internal Medicine

Balanchivadze N, **Nasser Z**, **Shahid M**, **McKay C**, **Li P**, **Sohaney R**, and **Gadgeel SM**. 1317P Renal toxicity in black patients with non-squamous non-small cell lung cancer treated with combination platinum-pemetrexed-pembrolizumab therapy. *Ann Oncol* 2021; 32:S1013.

Background: In Keynote 189, an increased incidence of renal toxicity was observed with combination platinum-pemetrexed-pembrolizumab (PPP) therapy compared to chemotherapy alone. Studies have shown that compared to White Americans, Black Americans are at higher risk of morbidity and mortality associated with chronic kidney disease (CKD). We conducted a retrospective analysis of patients treated with PPP to assess the rate of renal toxicity in Black and White patients. Methods: Data of self-identified non-hispanic (NH) Black and NH White patients with advanced NS-NSCLC who were treated with PPP between January 1, 2017, and November 1, 2020, at the Henry Ford Health System was analyzed.

Serum creatinine (Cr) and calculated glomerular filtration rate (GFR) before the first cycle of PPP and over the duration of PPP therapy were assessed. Acute kidney injury (AKI) was defined as an increase in Cr 1.5 times the baseline value. Reduction in GFR of ≥ 30% was considered significant. Multiple variables and outcomes were analyzed by two-group comparisons, univariate analysis, and Cox regression. Results: A total of 134 patients were included in the analysis. The mean age was 66.5 (SD 8.6) years, and 65 (48.5%) patients were men. A total of 33 (24%) patients were NH Black and 101 (75.4%) were NH White. There were 10 (8.1%) patients who developed AKI, and the median time to development of AKI was 4.5 months. No significant association of Black (3) or White (7) ethnicity with AKI was observed (p =.57). The odds of developing AKI was not increased in patients with a history of hypertension (p =.67), diabetes mellitus (p =.33), cardiovascular disease (p =.68), or CKD (p =.33). A total of 17 out of 127 (13.4%) patients had significantly reduced GFR, and patients with CKD were more likely to have reduced GFR (OR 4.8, p =.02). At the median follow-up of 24.5 months, the median survival was 15.2 months (95% CI, 12.7-22.2). Black ethnicity (HR 1.21, p =.46) and development of AKI (HR 1.13; 95% CI, 0.45–2.86) were not associated with increased mortality. Conclusions: Black patients with NS-NSCLC treated with PPP are not at higher risk of AKI or death than White patients. Development of AKI after PPP therapy was not associated with increased mortality. Legal entity responsible for the study: The authors. Funding: Has not received any funding. Disclosure: S.M. Gadgeel: Financial Interests, Personal, Advisory Role, Honoraria: AstraZeneca; Financial Interests, Personal, Advisory Role, Honoraria: Roche/Genentech; Financial Interests, Personal, Advisory Role, Honoraria: Takeda; Financial Interests, Personal, Advisory Role, serve on IDMC on a phase III trial sponsored by AstraZeneca: Pfizer; Financial Interests, Personal, Advisory Role, Honoraria: Bristol Myers Squibb; Financial Interests, Personal, Advisory Role, Honoraria: Novartis; Financial Interests, Personal, Advisory Role, Honoraria: Janssen; Financial Interests, Personal, Advisory Role, Honoraria: Merck; Financial Interests, Personal, Advisory Role, Honoraria: Eli Lilly; Financial Interests, Personal, Advisory Role, Honoraria: Blueprint. All other authors have declared no conflicts of interest.

Internal Medicine

Chidharla A, Rabbani R, Agarwal K, Abdelwahed S, Bhandari R, Manaktala PS, Singh A, Patel K, Singh P, Mehta D, Malik P, Patel U, **Pillai S**, and Koritala T. 1825P Prevalence of cancer among e-cigarette smokers compared to non-smokers: A retrospective cross-sectional survey study of NHANES-CDC. *Ann Oncol* 2021; 32:S1236.

Background: Current e-cigarette use has been rising, assuming as a safe alternative to traditional smoking. Therefore, we aim to evaluate the prevalence of cancer and types of cancers amongst e-cigarette and traditional smokers. Methods: A retrospective cross-sectional survey study was performed using NHANES (National Health And Nutrition Examination Survey) database from 2015 to 2018. History of cancer (MCQ220), type of cancers (MCQ230a), and smoking status (E-cigarette: SMQ900 or SMQ905 and Traditional smoking: SMQ020) were identified. Univariate and multivariable logistic regression analysis was performed to find out prevalence and association between e-cigarette smoking and cancer. We have excluded respondents with dual smoking. Results: Out of 154,856 participants, 7756 (5.01%) were e-cigarette users, 48625 (31.4%) were traditional smokers, 98475 (63.59%) were non-smokers. Females (49 vs 38%), Mexican Americans (20 vs 13%), high annual household income (>$100,000: 23 vs 15%) were having a higher prevalence of e-cigarette smoking in comparison with traditional smoking. (p<0.0001) Prevalence of cancer (any type) was 11.61%. Cancer prevalence was higher amongst traditional smokers in comparison with e-cigarette smokers. (16.77 vs 2.32%; p<0.0001) E-cigarette smokers were younger at the diagnosis of 1st cancer in comparison with traditional smokers. (median: 45 vs 63-years; p<0.0001) Cervical (21.99 vs 2.01%), thyroid (10.64 vs 2.45%), leukemias (8.51 vs 1.08%), and breast (12.06 vs 12.01%) cancers were more prevalent amongst e-cigarette smokers in comparison to traditional smokers. (p<0.0001) In adjusted multivariable regression analysis, e-cigarette smokers [aOR: 1.3 (95%CI: 1.32-1.33); p<0.0001] and traditional smokers [1.6 (1.64-1.65); p<0.0001] were having higher odds of prevalence of cancer in comparison with non-smoker. Conclusions: E-cigarette smokers had an early age of cancer onset and higher odds of cancer prevalence. Females had higher use of e-cigarette and cervical, thyroid, and breast cancers were prevalent amongst e-cigarette users. More prospective studies should be planned to mitigate the risk and before considering e-cigarette as a safe alternative to traditional smoking. Legal entity responsible for the study: The authors. Funding: Has not received any funding. Disclosure: All authors have declared no conflicts of interest.

Internal Medicine

Kazem A, **Al-Darzi W**, **Mohammed M**, **Lemor A**, **Lee J**, **Wang D**, **Basir M**, **Alaswad K**, **O'Neill B**, **Frisoli T**, **Eng M**, **O'Neill W**, and **Villablanca P**. Safety, feasibility, and outcomes of transcaval access for the delivery of Impella microaxial-flow pump 5.0 in patients with acute heart failure. *Eur J Heart Fail* 2021; 23(SUPPL 2):206.

A. Kazem, Henry Ford Hospital, Detroit, United States

Background: Transcaval access (TCA) may enable fully percutaneous mechanical circulatory support (MCS) without the hazards of vascular complication in patients with heart failure that require left ventricular unloading. Purpose: To review the safety, feasibility, and outcomes of using TCA to deliver Impella 5.0 MCS in patients with ischemic and non-ischemic systolic acute heart failure. Methods: This single center retrospective study included all patients that underwent TCA placement of a 5.0 Impella from June 2015 to January 2021. Demographic, clinical and procedural variables, and in-hospital outcomes were collected. The procedure was performed by electrifying a caval guidewire and advancing it into a pre-positioned aortic snare. After exchanging for a rigid guidewire, a 22 or 24Fr sheath was delivered into the aorta and then the Impella 5.0 was placed in the left ventricle through TCA sheaths. Results: A total of 43 patients were included in the analysis. The average age was 56.9 years (interquartile range [IQR], 52-65.5), of which, 70%(n=30) were males. Fifteen patients had non-ischemic cardiomyopathy and 28 had ischemic cardiomyopathy. Baseline average left ventricular ejection fraction prior to implantation was 23.6% (IQR, 13.75-29.75). 86% of the patients were in category C-D of the SCAI classification schema for cardiogenic shock (CS), 39.5% required inotropes and 48.8% required pressors prior to the procedure; 54% had a prior MCS in place. Only 18.6% of the cases had prior CT imaging reviewed for planning. TCA was successful in all attempted patients and the MCS delivery was achieved in 100% of the cohort. The available hemodynamic parameters prior and after Impella 5.0 implantation via Table 1 TCA are summarized in table 1. From the total cohort, only 29 patients survived to explant device and TCA sheath. The explant was successful in all patients using nitinol occluders; two patients required a covered stent at the arteriotomy site due to right sided heart failure from residual fistula; no surgical repair was necessary. All residual fistulous tracks were graded as<or =2. In-hospital survival was 46.5% for the entire cohort; 53.3%(n=8) for the non-ischemic group and 42.8%(n=12) in the ischemic group. BARC bleeding >1 from Impella insertion/removal site was observed in 9.3%,which didn't require further intervention. No vascular complication of the access site was observed with TCA. During hospitalization, 20.9% had VT/VF and 4.7% a PEA after implantation (all CS patients). 13.9% of the patients had AKI requiring hemodialysis and no stroke was observed in the entire group. The average length of stay for entire cohort was 16.3 days (IQR, 3.25-18.75). Conclusions: Transcaval access of 5.0 Impella is safe and feasible under expert hands for patients where more conventional MCS devices do not provide enough support or have inadequate peripheral arterial access.

Nephrology

Balanchivadze N, **Nasser Z**, **Shahid M**, **McKay C**, **Li P**, **Sohaney R**, and **Gadgeel SM**. 1317P Renal toxicity in black patients with non-squamous non-small cell lung cancer treated with combination platinum-pemetrexed-pembrolizumab therapy. *Ann Oncol* 2021; 32:S1013.

Background: In Keynote 189, an increased incidence of renal toxicity was observed with combination platinum-pemetrexed-pembrolizumab (PPP) therapy compared to chemotherapy alone. Studies have shown that compared to White Americans, Black Americans are at higher risk of morbidity and mortality associated with chronic kidney disease (CKD). We conducted a retrospective analysis of patients treated with PPP to assess the rate of renal toxicity in Black and White patients. Methods: Data of self-identified non-hispanic (NH) Black and NH White patients with advanced NS-NSCLC who were treated with PPP between January 1, 2017, and November 1, 2020, at the Henry Ford Health System was analyzed. Serum creatinine (Cr) and calculated glomerular filtration rate (GFR) before the first cycle of PPP and over the duration of PPP therapy were assessed. Acute kidney injury (AKI) was defined as an increase in Cr 1.5 times the baseline value. Reduction in GFR of ≥ 30% was considered significant. Multiple variables and outcomes were analyzed by two-group comparisons, univariate analysis, and Cox regression. Results: A total of 134 patients were included in the analysis. The mean age was 66.5 (SD 8.6) years,

and 65 (48.5%) patients were men. A total of 33 (24%) patients were NH Black and 101 (75.4%) were NH White. There were 10 (8.1%) patients who developed AKI, and the median time to development of AKI was 4.5 months. No significant association of Black (3) or White (7) ethnicity with AKI was observed (p =.57). The odds of developing AKI was not increased in patients with a history of hypertension (p =.67), diabetes mellitus (p =.33), cardiovascular disease (p =.68), or CKD (p =.33). A total of 17 out of 127 (13.4%) patients had significantly reduced GFR, and patients with CKD were more likely to have reduced GFR (OR 4.8, p =.02). At the median follow-up of 24.5 months, the median survival was 15.2 months (95% CI, 12.7-22.2). Black ethnicity (HR 1.21, p =.46) and development of AKI (HR 1.13; 95% CI, 0.45–2.86) were not associated with increased mortality. Conclusions: Black patients with NS-NSCLC treated with PPP are not at higher risk of AKI or death than White patients. Development of AKI after PPP therapy was not associated with increased mortality.

Public Health Sciences

Balanchivadze N, **Nasser Z**, **Shahid M**, **McKay C**, **Li P**, **Sohaney R**, and **Gadgeel SM**. 1317P Renal toxicity in black patients with non-squamous non-small cell lung cancer treated with combination platinum-pemetrexed-pembrolizumab therapy. *Ann Oncol* 2021; 32:S1013.

Background: In Keynote 189, an increased incidence of renal toxicity was observed with combination platinum-pemetrexed-pembrolizumab (PPP) therapy compared to chemotherapy alone. Studies have shown that compared to White Americans, Black Americans are at higher risk of morbidity and mortality associated with chronic kidney disease (CKD). We conducted a retrospective analysis of patients treated with PPP to assess the rate of renal toxicity in Black and White patients. Methods: Data of self-identified non-hispanic (NH) Black and NH White patients with advanced NS-NSCLC who were treated with PPP between January 1, 2017, and November 1, 2020, at the Henry Ford Health System was analyzed. Serum creatinine (Cr) and calculated glomerular filtration rate (GFR) before the first cycle of PPP and over the duration of PPP therapy were assessed. Acute kidney injury (AKI) was defined as an increase in Cr 1.5 times the baseline value. Reduction in GFR of ≥ 30% was considered significant. Multiple variables and outcomes were analyzed by two-group comparisons, univariate analysis, and Cox regression. Results: A total of 134 patients were included in the analysis. The mean age was 66.5 (SD 8.6) years, and 65 (48.5%) patients were men. A total of 33 (24%) patients were NH Black and 101 (75.4%) were NH White. There were 10 (8.1%) patients who developed AKI, and the median time to development of AKI was 4.5 months. No significant association of Black (3) or White (7) ethnicity with AKI was observed (p =.57). The odds of developing AKI was not increased in patients with a history of hypertension (p =.67), diabetes mellitus (p =.33), cardiovascular disease (p =.68), or CKD (p =.33). A total of 17 out of 127 (13.4%) patients had significantly reduced GFR, and patients with CKD were more likely to have reduced GFR (OR 4.8, p =.02). At the median follow-up of 24.5 months, the median survival was 15.2 months (95% CI, 12.7-22.2). Black ethnicity (HR 1.21, p =.46) and development of AKI (HR 1.13; 95% CI, 0.45–2.86) were not associated with increased mortality. Conclusions: Black patients with NS-NSCLC treated with PPP are not at higher risk of AKI or death than White patients. Development of AKI after PPP therapy was not associated with increased mortality.

Surgery

Mitchell MA, **Natour AK**, **Hares K**, King AH, **Kabbani L**, Kashyap VS, and Cho JS. The Effect of Neutrophil-lymphocyte Ratio on 10-year Survival Outcomes Following Elective Open and EVAR Procedures. *J Vasc Surg* 2021; 74(3):E229-E230.

[Mitchell, Megan A.; Kashyap, Vikram S.] Case Western Reserve Univ, Sch Med, Cleveland, OH USA. [Natour, Abdul Kader; Hares, Keinnan; Kabbani, Loay] Henry Ford Hlth Syst, Detroit, MI USA. [King, Alexander H.] Univ Hosp Cleveland, Med Ctr, Cleveland, OH 44106 USA. [Cho, Jae S.] Univ Hosp Case Med Ctr, Cleveland, OH USA.

Objectives: The neutrophil-lymphocyte ratio (NLR) is a useful and inexpensive inflammatory marker associated with surgical outcomes. This study evaluates the effects of NLR on survival after elective endovascular (EVAR) and open aortic repair (OAR) of abdominal aortic aneurysm. Methods: We retrospectively reviewed patients from 1989 to 2019 who underwent elective OAR or EVAR at two separate academic centers. Baseline comorbidities were assessed. A receiver operating characteristic

(ROC) curve was used to determine a cutoff point where NLR was associated with outcome. Kaplan-Meier survival analysis was used to compare survival through 10-year follow-up. Results: Overall, 437 patients (mean age, 72.0 6 10.1 years; 74.1% male) underwent 213 EVARs and 224 OARs. Median duration of follow-up was 4.55 years. The analysis of the ROC curve yielded an NLR of 3.94 with the highest specificity and sensitivity for 10-year survival. Baseline characteristics were similar between groups, except for an increased age in the group with NLR >3.94 (73.5 vs 70.9 years; P ¼ .008) (Table). KaplanMeier analysis revealed that patients with NLR >3.94 had decreased 10-year survival (37.2% vs 54.2%; P ¼ .0001) (Fig). By univariate analysis, NLR >3.94 (P ¼ .0001), chronic obstructive pulmonary disease (P ¼ .006), and increased age (P ¼ .0001) were associated with increased mortality. On multivariable cox regression analysis, an NLR >3.94 (odds ratio [OR], 1.69; 95% confidence interval [CI], 1.19-2.40), increased age (OR, 1.05; 95% CI, 1.03-1.07), and chronic obstructive pulmonary disease (OR, 1.44; 95% CI, 1.01-2.07) were associated with increased risk of mortality. Between OAR and EVAR, no difference in late survival was noted (49.9% vs 43.5%; P ¼ .24). Conclusions: An NLR >3.94 is associated with increased mortality over a 10-year follow-up period after open and endovascular aortic repair. Future studies to further understand the driving force between an elevated NLR and increased mortality are warranted.

Surgery

Potti C, **Eby J**, **Rteil A**, **Woodward A**, **Shepard A**, and **Kabbani L**. "Stronger but Not Faster": Flipped Classroom Teaching Significantly Improves Resident's Skills but Not Speed. *J Vasc Surg* 2021; 74(3):E159-E160.

[Potti, Chinmayee; Eby, Joshua; Rteil, Ali; Woodward, Ann; Shepard, Alexander; Kabbani, Loay] Henry Ford Hlth Syst, Detroit, MI USA.

Objective: Flipped classroom teaching is a nontraditional education model where instructional content is delivered outside the classroom. This constructivist approach emphasizes self-direction, active inquiry; the instructor’s role is to foster critical reflection and facilitate the application and understanding of concepts. Our objective was to study the difference in time taken and quality of patch graft angioplasty performed by residents with and without flipped teaching. Methods: The study was set in a skills simulation teaching session overseen by attending surgeons. The intervention consisted of introducing a video outlining the technical aspects of patch graft angioplasty, watched before the session. The first group (2018 postgraduate year [PGY] 1 and 2 residents) was given instructions at the time of the class without a prior educational video or resources (Figs 1 and 2). The second group (2019, 2020 PGY 1 and 2 residents) was asked to watch a 20-minute video on the technical aspects of the procedure before the class. Participants then performed a standardized patch graft closure of a 1 cm arteriotomy using a polytetrafluoroethylene patch. The groups were timed. The quality of the closure was tested by assessing the number of leaks and the quantity of leak of the patch (Fig 3). Bivariate analysis sample t-tests were used for statistical analysis. P value <.05 was considered significant. Pre- and post-session surveys were conducted to assess residents’ experience. Results: 1Forty-two residents (PGY 1 and 2) were enrolled in the study, 15 in nonintervention group 1 and 27 in intervention group 2, compared with 7 staff vascular surgeons. The mean completion time was 26 minutes (group 1) vs 27 minutes (group 2), P ¼ .6. The staff completion time was 12 minutes, P ¼ .001. The number of major leaks (not needle holes) was 2.0 (group 1) vs 1.6 (group 2), P ¼ .007, none for staff. The total quantity of leak was 42 mL (group 1) vs 15 mL (group 2), P ¼ .0001 (Table I). There was perceived improvement in skill on analyzing pre- and post-session surveys (Table II). Conclusions: A structured educational intervention, watching a video of a procedure before the skills session, did not change the time needed to complete the skill. There was improvement in the technical outcome of the procedure defined by a decrease in the total quantity of leak. Reversed classroom teaching significantly improves resident’s skill, not speed. There was also a perceived improvement in skill by participants. This is a pilot study and further instructional outcomes are being studied.

Surgery

Sharma V, and **Hans S**. Carotid Endarterectomy During Index Hospital Admission for Patients With Acute Mild to Moderate Stroke. *J Vasc Surg* 2021; 74(3):E144-E145.

[Sharma, Vicki] St John Ascens Hosp Macomb Oakland, Warren, MI USA. [Hans, Sachinder] Henry Ford Hosp, Detroit, MI 48202 USA.

Objective: The timing of carotid endarterectomy (CEA) after acute stroke due to an infarct in themiddle cerebral artery territory with ipsilateral internal carotid artery stenosis remains controversial. We evaluated the results of CEA in this group of patients during the index hospital admission. Methods: We performed a retrospective review of all patients admitted with acute, mild (National Institutes of Health [NIH] stroke scale score, 1-5) and moderate stroke (NIH stroke scale score, 6-14) in the distribution of the middle cerebral artery with $70% ipsilateral internal carotid artery stenosis admitted to two midsize teaching hospitals with stroke certification from 2005 to 2020. Patients with focal transient ischemic attacks were excluded. An indwelling shunt was placed if the patient developed a new neurologic deficit with carotid cross-clamping or ischemic electroencephalographic changes under general anesthesia. Results: A total of 74 patients (45 men) aged 35 to 87 years (mean age, 70.1 6 10.8 years). Of the 74 patients, 61 had a NIH stroke scale score of 1 to 5) and 13 an NIH stroke scale score of 6 to 14. Twelve patients were given intravenous tissue plasminogen activator. Of the 74 patients, 21 had undergone CEA 3 to 5 days after stroke and 53 had done so 6 to 8 days after stroke. Cervical block anesthesia was used for 54 patients (20 with general anesthesia), and a shunt was required for 15 patients (20%). Four patients (5.4%) had experienced severe postoperative stroke (three new ischemic infarcts and one intracerebral hemorrhage), resulting in death in all four. Two patients (2.7%) had developed postoperative seizures. Two patients (2.7%) had experienced temporary cranial nerve palsy (hypoglossal in one, ramus mandibularis in one). Conclusions: CEA for acute mild to moderate stroke can be performed with satisfactory results during the index admission. This strategy is useful to prevent recurrent stroke.

HFHS Publications on COVID-19

Cardiology/Cardiovascular Research
Beatty AL, Brown TM, Corbett M, Diersing D, **Keteyian SJ**, Mola A, Stolp H, Wall HK, and Sperling LS. Million Hearts Cardiac Rehabilitation Think Tank: Accelerating New Care Models. *Circ Cardiovasc Qual Outcomes* 2021; Epub ahead of print. PMID: 34587751. Full Text

Cardiology/Cardiovascular Research
Raad M, **Gorgis S**, Abshire C, Yost M, **Dabbagh MF**, Chehab O, **Aurora L**, **Patel S**, **Nona P**, **Yan J**, **Singh G**, Syrjamaki J, **Kaatz S**, and **Parikh S**. COVID-19 risk index (CRI): a simple and validated emergency department risk score that predicts mortality and the need for mechanical ventilation. *J Thromb Thrombolysis* 2021;1-9. Epub ahead of print. PMID: 34554359. Full Text

Cardiology/Cardiovascular Research
Shero ST, Benzo R, Cooper LS, Finkelstein J, Forman DE, Gaalema DE, Joseph L, **Keteyian SJ**, Peterson PN, Punturieri A, Zieman S, and Fleg JL. Update on RFA Increasing Use of Cardiac and Pulmonary Rehabilitation in Traditional and Community Settings NIH-Funded Trials: ADDRESSING CLINICAL TRIAL CHALLENGES PRESENTED BY THE COVID-19 PANDEMIC. *J Cardiopulm Rehabil Prev* 2021; Epub ahead of print. PMID: 34508036. Full Text

Dermatology
Fathy RA, McMahon DE, Lee C, Chamberlin GC, Rosenbach M, Lipoff JB, Tyagi A, Desai SR, French LE, **Lim HW**, Thiers BH, Hruza GJ, Fassett M, Fox LP, Greenberg HL, Blumenthal K, and Freeman EE. Varicella Zoster and Herpes Simplex Virus Reactivation Post-COVID-19 Vaccination: A Review of 40 Cases in an International Dermatology Registry. *J Eur Acad Dermatol Venereol* 2021; Epub ahead of print. PMID: 34487581. Full Text

Dermatology
Grayson C, **Awosika O**, and Pritchett E. 28666 Global initiatives in dermatology and education. *J Am Acad Dermatol* 2021; 85(3):AB204. Conference Abstract.

Dermatology
Ko D, **Lyons AB**, **Kohli I**, Narla S, Torres AE, **Miller A**, **Ozog D**, **Hamzavi I**, and **Lim HW**. The value of photomedicine in a global health crisis: Utilizing ultraviolet C to decontaminate N95 respirators during the COVID-19 pandemic. *Photodermatol Photoimmunol Photomed* 2021; Epub ahead of print. PMID: 34467568. Full Text

Dermatology
McMahon DE, Kovarik CL, Damsky W, Rosenbach M, Lipoff JB, Tyagi A, Chamberlin G, Fathy R, Nazarian RM, Desai SR, **Lim HW**, Thiers BH, Hruza GJ, French LE, Blumenthal K, Fox LP, and Freeman EE. Clinical and Pathologic Correlation of Cutaneous COVID-19 Vaccine Reactions including V-REPP: A Registry Based Study. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34517079. Full Text

Dermatology
Pourang A, Olds H, **Ezekwe N**, **Lim HW**, and **Hamzavi I**. 28522 The impact of the SARS-CoV-2 pandemic on phototherapy utilization. *J Am Acad Dermatol* 2021; 85(3):AB194. Conference Abstract.

Hematology-Oncology
Esakia T, Melkadze T, Tsiklauri K, Mariamidze E, Tsitsilashvili S, Otkhozoria N, Abuladze M, Jokhadze N, and **Balanchivadze N**. 1632P At home androgen deprivation therapy for patients with prostate cancer during the COVID-19 pandemic. One center experience. *Ann Oncol* 2021; 32:S1156-S1157. Conference Abstract.

Hospital Medicine

Raad M, **Gorgis S**, Abshire C, Yost M, **Dabbagh MF**, Chehab O, **Aurora L**, **Patel S**, **Nona P**, **Yan J**, **Singh G**, Syrjamaki J, **Kaatz S**, and **Parikh S**. COVID-19 risk index (CRI): a simple and validated emergency department risk score that predicts mortality and the need for mechanical ventilation. *J Thromb Thrombolysis* 2021; Epub ahead of print.:1-9. PMID: 34554359. Full Text

Infectious Diseases

Bhargava P. Response to "Tocilizumab therapy and COVID-19". *J Osteopath Med* 2021; Epub ahead of print. PMID: 34492174. Full Text

Infectious Diseases

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