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Henry Ford Health System

Henry Ford Health System Publication List – December 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 **114 unique citations** listed this month, with **11 articles** and **2 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

Administration
Allergy and Immunology
Behavioral Health Services/Psychiatry/Neuropsychology
Cardiology/Cardiovascular Research
Center for Health Policy and Health Services Research
Center for Individualized and Genomic Medicine Research
Dermatology
Diagnostic Radiology
Emergency Medicine
Family Medicine
Gastroenterology
Graduate Medical Education
Hematology-Oncology
Hospital Medicine
Hypertension and Vascular Research
Infectious Diseases
Internal Medicine
Nephrology
Neurology
Neurosurgery
Nursing
Obstetrics, Gynecology and Women's Health Services
Ophthalmology and Eye Care Services
Orthopedics/Bone and Joint Center
Otolaryngology – Head and Neck Surgery
Pathology and Laboratory Medicine
Pharmacy
Public Health Sciences
Pulmonary and Critical Care Medicine
Radiation Oncology
Research Administration
Rheumatology
Sleep Medicine
Surgery
Urology

Conference Abstracts

Cardiology/Cardiovascular Research
Gastroenterology
Hematology-Oncology
Hospital Medicine
Internal Medicine
Neurology
Pathology and Laboratory Medicine
Public Health Sciences

Articles

Administration
Gifford L, **Johnson CC**, **Haque N**, **Passalacqua KD**, **Swiderek J**, and **Kalkanis S**. COVID-19 in the hotspot of Metropolitan Detroit: A multi-faceted health system experience. *Int J Health Plann Manage* 2021; Epub ahead of print. PMID: 34859491. Full Text

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Health systems were abruptly plunged into a crisis as SARS-CoV-2 exploded into a pandemic in spring 2020. In March-April 2020, Metropolitan Detroit was a US "hotspot." As a large health system with five hospitals and two behavioural health inpatient facilities, a health insurance company, a medical group and physician network, and 41 ambulatory clinics normally hosting over 10,000 daily patient encounters, the Henry Ford Health System deployed numerous strategies in the management of this upheaval. As hospitals and Emergency Departments were inundated with COVID-19 patients, other services and activities needed to shut down as state-mandated policies were promulgated, new internal and external communication networks established, and management of employees and resources such as ventilators, ICU beds, personal protective equipment, and laboratory supplies became critical challenges. We describe herein the system-wide strategies implemented and lessons learned in the operation of a health system in the initial throes of a global pandemic.

Administration
Suleyman G, and **Alangaden GJ**. Nosocomial Fungal Infections: Epidemiology, Infection Control, and Prevention. *Infect Dis Clin North Am* 2021; 35(4):1027-1053. PMID: 34752219. Full Text

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Invasive fungal infections are an important cause of morbidity and mortality in hospitalized patients and in the immunocompromised population. This article reviews the current epidemiology of nosocomial fungal infections in adult patients, with an emphasis on invasive candidiasis (IC) and invasive aspergillosis (IA). Included are descriptions of nosocomial infections caused by Candida auris, an emerging pathogen, and IC- and IA-associated with coronavirus disease 2019. The characteristics and availability of newer nonculture-based tests for identification of nosocomial fungal pathogens are discussed. Recently published recommendations and guidelines for the control and prevention of these nosocomial fungal infections are summarized.

Administration
Xiao S, **Sahasrabudhe N**, **Hochstadt S**, **Cabral W**, **Simons S**, **Yang M**, **Lanfear DE**, and **Williams LK**. Predicting death from COVID-19 using pre-existing conditions: implications for vaccination triage. *BMJ Open Respir Res* 2021; 8(1). PMID: 34949575. Full Text

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INTRODUCTION: Global shortages in the supply of SARS-CoV-2 vaccines have resulted in campaigns to first inoculate individuals at highest risk for death from COVID-19. Here, we develop a predictive model of COVID-19-related death using longitudinal clinical data from patients in metropolitan Detroit. METHODS: All individuals included in the analysis had a laboratory-confirmed SARS-CoV-2 infection. Thirty-six pre-existing conditions with a false discovery rate $p<0.05$ were combined with other demographic variables to develop a parsimonious prediction model using least absolute shrinkage and selection operator regression. The model was then prospectively validated in a separate set of individuals with confirmed COVID-19. RESULTS: The study population consisted of 15 502 individuals with laboratory-confirmed SARS-CoV-2. The main prediction model was developed using data from 11 635 individuals with 709 reported deaths (case fatality ratio 6.1%). The final prediction model consisted of 14 variables with 11 comorbidities. This model was then prospectively assessed among the remaining 3867 individuals (185 deaths; case fatality ratio 4.8%). When compared with using an age threshold of 65 years, the 14-variable model detected 6% more of the individuals who would die from COVID-19. However, below age 45 years and its risk equivalent, there was no benefit to using the prediction model over age alone. DISCUSSION: Using a prediction model, such as the one described here, may help identify individuals who would most benefit from COVID-19 inoculation, and thereby may produce more dramatic initial drops in deaths through targeted vaccination.

Allergy and Immunology

Fonseca W, Asai N, Yagi K, Malinczak CA, **Savickas G**, **Johnson CC**, **Murray S**, **Zoratti EM**, Lukacs NW, **Li J**, and Schuler Iv CF. COVID-19 Modulates Inflammatory and Renal Markers That May Predict Hospital Outcomes among African American Males. *Viruses* 2021; 13(12). PMID: 34960684. Full Text

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BACKGROUND AND OBJECTIVES: African Americans and males have elevated risks of infection, hospitalization, and death from SARS-CoV-2 in comparison with other populations. We report immune responses and renal injury markers in African American male patients hospitalized for COVID-19. METHODS: This was a single-center, retrospective study of 56 COVID-19 infected hospitalized African American males 50+ years of age selected from among non-intensive care unit (ICU) and ICU status patients. Demographics, hospitalization-related variables, and medical history were collected from electronic medical records. Plasma samples collected close to admission (≤2 days) were evaluated for cytokines and renal markers; results were compared to a control group (n = 31) and related to COVID-19 in-hospital mortality. RESULTS: Among COVID-19 patients, eight (14.2%) suffered in-hospital mortality; seven (23.3%) in the ICU and one (3.8%) among non-ICU patients. Interleukin (IL)-18 and IL-33 were elevated at admission in COVID-19 patients in comparison with controls. IL-6, IL-18, MCP-1/CCL2, MIP-1α/CCL3, IL-33, GST, and osteopontin were upregulated at admission in ICU patients in comparison with controls. In addition to clinical factors, MCP-1 and GST may provide incremental value for risk prediction of COVID-19 in-hospital mortality. CONCLUSIONS: Qualitatively similar inflammatory responses were observed in comparison to other populations reported in the literature, suggesting non-immunologic factors may account for outcome differences. Further, we provide initial evidence for cytokine and renal toxicity markers as prognostic factors for COVID-19 in-hospital mortality among African American males.

Behavioral Health Services/Psychiatry/Neuropsychology

Jesse MT, Clifton E, **Kim DY**, **Nicholson D**, **Patil R**, **Bhavsar S**, **Desai S**, **Gartrelle K**, **Eshelman A**, **Fleagle E**, **Ahmedani B**, Carlozzi NE, **Tang A**, and **Patel A**. Prerenal Transplant Education and Evaluation Positively Impacts Outcomes. *Prog Transplant* 2021; Epub ahead of print. PMID: 34860614. Full Text

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Introduction: An outstanding question in kidney transplantation is how to prepare candidates and their social supports for optimal posttransplant outcomes. Project Aims: This program evaluation assessed whether a pretransplant quality improvement clinic improved clinical outcomes in the year posttransplant compared to recipients receiving standard of care. Design: The Countdown to Transplant Clinic was implemented with kidney transplant candidates expected to receive a transplant within the next few months. The clinic included an enhanced education session on posttransplant lifestyle management, confirmation of support (≥2 adults), and evaluations by transplant social work, psychology, and nephrology. Results: Seventy-five patients participated in the clinic and underwent a transplant. A retrospective chart review of posttransplant laboratory values, rehospitalizations (within 3-months posttransplant), biopsy-confirmed graft failure, and mortality (within 1-year posttransplant) were collected from both groups. Univariate and multivariate propensity score-weighted linear or logistic regression models were used to evaluate the association between clinic participation and outcomes. In models adjusting for relevant covariates, participation in The Countdown to Transplant Clinic (vs standard care) was associated with a lower coefficient of variation of serum tacrolimus (all values collected 3-12 months posttransplant), 30-day posttransplant white blood cell counts (but not 90-day), 90-day posttransplant potassium, and 30 and 31 to 90 days rehospitalizations. Clinic participation did not predict serum glucose levels at 30- or 90-days posttransplant. Due to low rates of rejection and mortality, meaningful comparisons were not possible. Conclusion: Participation in a pretransplant, multicomponent clinic may improve certain outcomes of interest posttransplantation. Pilot testing for feasibility for randomized controlled trials is a necessary next step.

Cardiology/Cardiovascular Research

Ananthasubramaniam K, and Arumugam P. Can we "REFINE" the art of predicting ischemia on SPECT myocardial perfusion imaging? *J Nucl Cardiol* 2021; Epub ahead of print. PMID: 34873645. Full Text

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Cardiology/Cardiovascular Research

Arslan F, Núñez-Gil IJ, Rodríguez-Olivares R, Cerrato E, Bollati M, Nombela-Franco L, Terol B, Alfonso-Rodríguez E, Camacho Freire SJ, **Villablanca PA**, Amat Santos IJ, De la Torre Hernández JM, Pascual I, Liebetrau C, Alkhouli M, and Fernández-Ortiz A. Sex differences in treatment strategy for coronary artery aneurysms: Insights from the international Coronary Artery Aneurysm Registry. *Neth Heart J* 2021; Epub ahead of print. PMID: 34910278. Full Text

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INTRODUCTION: Sex disparities exist in coronary artery disease (CAD) in terms of risk profile, clinical management and outcome. It is unclear if differences are also present in coronary aneurysms, a rare variant of CAD. METHODS: Patients were selected from the international Coronary Artery Aneurysm Registry (CAAR; ClinicalTrials.gov: NCT02563626), and differences between groups were analysed according to sex. The CAAR database is a prospective multicentre registry of 1565 patients with coronary aneurysms (336 females). Kaplan-Meier method was used for event-free survival analysis for death, major adverse cardiac events (MACE: composite endpoint of death, heart failure and acute coronary syndrome) and bleeding. RESULTS: Female patients were older, were more often hypertensive and less frequently smoker. They were treated conservatively more often compared to male patients and received significantly less frequently aspirin (92% vs 88%, p = 0.002) or dual antiplatelet therapy (DAPT) (67% vs 58%, p = 0.001) at discharge. Median DAPT duration was also shorter (3 vs 9 months, p = 0.001). Kaplan-Meier analysis revealed no sex differences in death, MACE or bleeding during a median follow-up duration of 37 months, although male patients did experience acute coronary syndrome (ACS) more often during follow-up (15% vs 10%, p = 0.015). CONCLUSIONS: These CAAR findings showed a comparable high-risk cardiovascular risk profile for both sexes. Female patients were treated conservatively more often and received DAPT less often at discharge, with a shorter DAPT duration. ACS was more prevalent among male patients; however, overall clinical outcome was not different between male and female patients during follow-up.

Cardiology/Cardiovascular Research

Chugh Y, Khatri JJ, Shishehbor MH, Banerjee S, Croce K, **Alaswad K**, Murad B, Garcia S, Burke MN, and Brilakis ES. Adverse Events With Intravascular Lithotripsy After Peripheral and Off-Label Coronary Use: A Report From the FDA MAUDE Database. *J Invasive Cardiol* 2021; 33(12):E974-E977. PMID: Not assigned. Request Article

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Background. Currently only the peripheral intravascular lithotripsy (IVL) device is approved for use in the United States. We queried the United States Food and Drug Administration's Manufacturer and User Facility Device Experience (MAUDE) database from January 1, 2016 to December 14, 2020 for all reports of adverse events and modes of failure related to the peripheral IVL device, when used for on- and off-label indications. There were 20 reports of use in peripheral artery disease interventions and 3 reports of off-label use in coronary interventions. Device malfunction in 13 of 23 patients (56.5%) was the most common adverse event reported. Partial balloon or catheter dislodgment was the most common mode of IVL device failure in 12 of 20 patients (60%), followed by balloon rupture in 3 of 20 patients (15%). Coronary use was rare, and associated with balloon perforation in 1 of 3 patients, bradycardia in 1 of 3

patients, and aortocoronary dissection in 1 of 3 patients. In summary, IVL use carries risk of complications; hence, continued vigilance and postmarketing monitoring are warranted.

Cardiology/Cardiovascular Research

Kerrigan DJ, **Cowger JA**, and **Keteyian SJ**. Exercise in patients with left ventricular devices: The interaction between the device and the patient. *Prog Cardiovasc Dis* 2021; Epub ahead of print. PMID: 34921848. Full Text

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Advances in the engineering of surgically implanted, durable left ventricular assist devices (LVAD) has led to improvements in the two-year survival of patients on LVAD support, which is now comparable to that of heart transplant (HT) recipients. And with the advent of magnetic levitation technology, both the survival rate and average time on LVAD support are expected to improve even further. However, despite these advances, the functional capacity of patients on LVAD support remains reduced compared to those who received a HT. A few small clinical trials have shown improvement in functional capacity with exercise training. Peak oxygen uptake improves modestly (10%-20%) with exercise training, suggesting a possible celling-effect linked to the ability of the LVAD to increase flow during exercise. This paper reviews both (a) the effect of the LVAD on the cardiorespiratory responses during a single, acute bout of exercise up to maximum and (b) the central and peripheral adaptations that occur among patients with an LVAD who undergo an exercise training regimen. We also address the tenets of the exercise prescription that are unique to patients with a durable LVAD.

Cardiology/Cardiovascular Research

Lala A, Shah P, Khalatbari S, Yosef M, Mountis MM, Robinson SW, **Lanfear DE**, Estep JD, Jeffries N, Taddei-Peters WC, Stevenson LW, Richards B, Mann DL, Mancini DM, Stewart GC, and Aaronson KD. Frailty Measures of Patient-reported Activity and Fatigue May Predict 1-year Outcomes in Ambulatory Advanced Heart Failure: A Report From the REVIVAL Registry. *J Card Fail* 2021; Epub ahead of print. PMID: 34961663. Full Text

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BACKGROUND: The Fried Frailty Phenotype predicts adverse outcomes in geriatric populations, but has not been well-studied in advanced heart failure (HF). The Registry Evaluation of Vital Information for Ventricular Assist Devices (VADs) in Ambulatory Life (REVIVAL) study prospectively collected frailty measures in patients with advanced HF to determine relevant assessments and their impact on clinical outcomes. METHODS AND RESULTS: HF-Fried Frailty was defined by 5 baseline components (1 point each): (1) weakness: hand grip strength less than 25% of body weight; (2) slowness based on time to

walk 15 feet; (3) weight loss of more than 10 lbs in the past year; (4) inactivity; and (5) exhaustion, both assessed by the Kansas City Cardiomyopathy Questionnaire. A score of 0 or 1 was deemed nonfrail, 2 prefrail, and 3 or greater was considered frail. The primary composite outcome was durable mechanical circulatory support implantation, cardiac transplant or death at 1 year. Event-free survival for each group was determined by the Kaplan-Meier method and the hazard of prefrailty and frailty were compared with nonfrailty with proportional hazards modeling. Among 345 patients with all 5 frailty domains assessed, frailty was present in 17%, prefrailty in 40%, and 43% were nonfrail, with 67% (n = 232) meeting the criteria based on inactivity and 54% (n = 186) for exhaustion. Frail patients had an increased risk of the primary composite outcome (unadjusted hazard ratio [HR] 2.82, 95% confidence interval [CI] 1.52-5.24; adjusted HR 3.41, 95% CI 1.79-6.52), as did prefrail patients (unadjusted HR 1.97, 95% CI 1.14-3.41; adjusted HR 2.11, 95% CI 1.21-3.66) compared with nonfrail patients, however, the predictive value of HF-Fried Frailty criteria was modest (Harrel's C-statistic of 0.603, P = .004). CONCLUSIONS: The HF-Fried Frailty criteria had only modest predictive power in identifying ambulatory patients with advanced HF at high risk for durable mechanical circulatory support, transplant, or death within 1 year, driven primarily by assessments of inactivity and exhaustion. Focus on these patient-reported measures may better inform clinical trajectories in this population.

Cardiology/Cardiovascular Research

Lemor A, Dehkordi SHH, **Alrayes H**, **Cowger J**, Naidu SS, **Villablanca PA**, **Basir MB**, and **O'Neill W**. Outcomes, Temporal Trends, and Resource Utilization in Ischemic vs Non-Ischemic Cardiogenic Shock. *Crit Pathw Cardiol* 2021; Epub ahead of print. PMID: 34907938. Full Text

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Cardiogenic shock (CS) is associated with significant morbidity and mortality. Differentiating the etiologic factors driving CS has epidemiological significance and aids in optimization of therapeutic strategies, prognostication and resource utilization. The aim herein is to investigate the epidemiology and clinical outcomes of cardiogenic shock in those with ischemic and non-ischemic CS etiologies. Using International Classification of Diseases (ICD) codes, we queried the National Inpatient Sample for cardiogenic shock hospitalization from 2007 to 2018 and divided the study sample into cohorts of ischemic (I-CS) and nonischemic cardiogenic shock. (NI-CS). We then compared the primary outcome of in-hospital mortality between these two cohorts. Two groups of secondary outcomes (clinical and procedural) were also assessed between the two cohorts. CS was present in 557,860 hospitalizations; 84% of these were I-CS and 15.8% NI-CS. Patients with I-CS were older, more commonly males, with more risk factors for coronary artery disease ($p<0.05$). NI-CS had higher prevalence of pre-existing systolic heart failure and atrial fibrillation. The in-hospital mortality was significantly higher in patients with I-CS (32.2% vs 29.5%, adjOR 1.10, $p<0.001$). Frequencies of acute ischemic stroke, mechanical ventilation, ventricular arrhythmias, and vascular complications were higher in I-CS vs NI-CS, while AKI and acute liver failure were more common in NI-CS ($p<0.05$). The use of mechanical circulatory support devices was higher in the I-CS group. In conclusion, patients with I-CS comprise the vast majority of CS, and are associated with higher mortality and higher resource utilization. Conversely, patients with NI-CS appear to have higher survival but with a higher prevalence of end-organ dysfunction.

Cardiology/Cardiovascular Research

McKinnon JE, **Wang DD**, **Zervos M**, **Saval M**, **Marshall-Nightengale L**, **Kilgore P**, **Pabla P**, **Szandzik E**, **Maksimowicz-McKinnon K**, and **O'Neill WW**. Safety and Tolerability of Hydroxychloroquine in healthcare workers and first responders for the prevention of COVID-19: WHIP COVID-19 Study. *Int J Infect Dis* 2021; Epub ahead of print. PMID: 34954095. Full Text

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BACKGROUND: Healthcare workers (HCW) are among the highest risk groups for acquisition of COVID-19 due to occupational exposures. The WHIP COVID-19 study aimed to evaluate the safety and efficacy of hydroxychloroquine (HCQ) as chemoprophylaxis for SARS-CoV-2 infection in this population. METHODS: HCW, first responders and other occupationally high-risk participants were enrolled in a randomized, placebo-controlled clinical study of HCQ from April-October 2020. The trial compared daily versus weekly HCQ to placebo and to a prospective cohort on HCQ for autoimmune diseases. Participants were followed for 8 weeks. Serology or a positive PCR test were used to determine laboratory confirmed clinical cases. RESULTS: 624 participants were randomized to placebo (n=200), weekly HCQ (n=201), daily HCQ (n=197). For the primary safety endpoint, 279 (44.7%) participants experienced AE level II or lower (total AEs n=589), similar rates in all randomized groups (p=0.188) with no hospitalizations or interventions required. Only 4 laboratory confirmed COVID-19 cases occurred, with 2 in the placebo arm and one in each HCQ randomized arm. CONCLUSIONS: This randomized placebo-controlled trial was able to demonstrate the safety of HCQ outpatient chemoprophylaxis in high-risk groups against COVID-19. Future studies of chemoprophylaxis for SARS-CoV-2 are needed as the epidemic continues worldwide.

Cardiology/Cardiovascular Research

Megaly M, **Basir MB**, Brilakis E, and **Alaswad K**. Wire Entrapment and Unraveling in the Aorta: Snaring Technique for the Nonvisible Filament. *JACC Cardiovasc Interv* 2021; Epub ahead of print. PMID: 34973909. Full Text

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Cardiology/Cardiovascular Research

Ranka S, Lahan S, Chhatriwalla AK, Allen KB, **Chiang M**, **O'Neill B**, **Verma S**, **Wang DD**, **Lee J**, **Frisoli T**, Eng M, Bagur R, **O'Neill W**, and **Villablanca P**. Network meta-analysis comparing the short and long-term outcomes of alternative access for transcatheter aortic valve replacement. *Cardiovasc Revasc Med* 2021; Epub ahead of print. PMID: 34972667. Full Text

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BACKGROUND: Several studies have pair-wise compared access sites for transcatheter aortic valve replacement (TAVR) but pooled estimate of overall comparative efficacy and safety outcomes are not well known. We sought to compare short- and long-term outcomes following various alternative access routes for TAVR. METHODS: Thirty-four studies with a pooled sample size of 32,756 patients were selected by searching PubMed and Cochrane library databases from inception through 11th June 2021 for patients

undergoing TAVR via 1 of 6 different access sites: Transfemoral (TF), Transaortic (TAO), Transapical (TA), Transcarotid (TC), Transaxillary/Subclavian (TSA), and Transcaval (TCV). Data were extracted to conduct a frequentist network meta-analysis with a random-effects model using TF access as a reference group. RESULTS: Compared with TF, both TAO [RR 1.91, 95% CI (1.46-2.50)] and TA access [RR 2.12, 95% CI (1.84-2.46)] were associated with an increased risk of 30-day mortality. No significant difference was observed for stroke, myocardial infarction, major bleeding, conversion to open surgery, and major adverse cardiovascular or cerebrovascular events at 30 days between different accesses. Major vascular complications were lower in TA [RR 0.43, (95% CI, 0.28-0.67)] and TC [RR 0.51, 95% CI (0.35-0.73)] access compared to TF. The 1-year mortality was higher in TAO [RR of 1.35, (95% CI, 1.01-1.81)] and TA [RR 1.44, (95% CI, 1.14-1.81)] groups. CONCLUSION: Non-thoracic alternative access site utilization for TAVR implantation (TC, TSA and TCV) is associated with outcomes similar to conventional TF access. Thoracic TAVR access (TAO and TA) translates into increased short and long-term mortality.

Cardiology/Cardiovascular Research

Singh-Kucukarslan G, **Raad M**, **Al-Darzi W**, **Cowger J**, **Brice L**, **Basir MB**, **O'Neill WW**, **Alaswaad K**, and Eng MH. Hemodynamic Effects of Left-Atrial Venous Arterial Extra-Corporeal Membrane Oxygenation (LAVA-ECMO). *Asaio j* 2021; Epub ahead of print. PMID: 34967778. Full Text

From the Department of Medicine, Henry Ford Health System, Detroit, Michigan; Division of Cardiology, Henry Ford Health System, Detroit, Michigan; Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan; Division of Cardiology, Banner University Medical Center, Phoenix, Arizona.

We report a case of a 59-year-old male in post-myocardial infarction cardiogenic shock undergoing left atrial venous arterial extracorporeal membrane oxygenation (LAVA-ECMO) as a bridge to transplantation. The unique feature of this ECMO configuration is use of a single trans-septal cannula to provide biventricular unloading and use of a single arterial access.

Cardiology/Cardiovascular Research

Wagner CM, Clark MJ, Theurer PF, Lall SC, **Nemeh HW**, Downey RS, Martin DE, Dabir RR, Asfaw ZE, Robinson PL, **Harrington SD**, Gandhi DB, Waljee JF, Englesbe MJ, Brummett CM, Prager RL, Likosky DS, Kim KM, Lagisetty KH, and Brescia AA. Predictors of Discharge Home Without Opioids After Cardiac Surgery: A Multicenter Analysis. *Ann Thorac Surg* 2021; Epub ahead of print. PMID: 34924190. Full Text

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BACKGROUND: Whether all patients will require an opioid prescription after cardiac surgery is unknown. We performed a multicenter analysis to identify patient predictors of not receiving an opioid prescription at the time of discharge home after cardiac surgery. METHODS: Opioid-naïve patients undergoing coronary artery bypass grafting and/or valve surgery through a sternotomy at 10 centers from January to December 2019 were identified retrospectively from a prospectively maintained data set. Opioid-naïve was defined as not taking opioids at the time of admission. The primary outcome was discharge without an opioid prescription. Mixed-effects logistic regression was performed to identify predictors of discharge without an opioid prescription, and postdischarge opioid prescribing was monitored to assess patient tolerance of discharge without an opioid prescription. RESULTS: Among 1924 eligible opioid-naïve patients, mean age was 64 ± 11 years, and 25% were women. In total, 28% of all patients were discharged without an opioid prescription. On multivariable analysis, older age, longer length of hospital stay, and undergoing surgery during the last 3 months of the study were independent predictors of discharge without an opioid prescription, whereas depression, non-Black and non-White race, and using more opioid pills on the day before discharge were independent predictors of receiving an opioid prescription. Among patients discharged without an opioid prescription, 1.8% (10 of 547) were subsequently prescribed an opioid. CONCLUSIONS: Discharging select patients without an opioid prescription after cardiac surgery appears well tolerated, with a low incidence of postdischarge opioid prescriptions. Increasing the number of patients discharged without an opioid prescription may be an area for quality improvement.

Cardiology/Cardiovascular Research

Xiao S, **Sahasrabudhe N**, **Hochstadt S**, **Cabral W**, **Simons S**, **Yang M**, **Lanfear DE**, and **Williams LK**. Predicting death from COVID-19 using pre-existing conditions: implications for vaccination triage. *BMJ Open Respir Res* 2021; 8(1). PMID: 34949575. Full Text

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INTRODUCTION: Global shortages in the supply of SARS-CoV-2 vaccines have resulted in campaigns to first inoculate individuals at highest risk for death from COVID-19. Here, we develop a predictive model of COVID-19-related death using longitudinal clinical data from patients in metropolitan Detroit. METHODS: All individuals included in the analysis had a laboratory-confirmed SARS-CoV-2 infection. Thirty-six pre-existing conditions with a false discovery rate $p<0.05$ were combined with other demographic variables to develop a parsimonious prediction model using least absolute shrinkage and selection operator regression. The model was then prospectively validated in a separate set of individuals with confirmed COVID-19. RESULTS: The study population consisted of 15 502 individuals with laboratory-confirmed SARS-CoV-2. The main prediction model was developed using data from 11 635 individuals with 709 reported deaths (case fatality ratio 6.1%). The final prediction model consisted of 14 variables with 11 comorbidities. This model was then prospectively assessed among the remaining 3867 individuals (185 deaths; case fatality ratio 4.8%). When compared with using an age threshold of 65 years, the 14-variable model detected 6% more of the individuals who would die from COVID-19. However, below age 45 years and its risk equivalent, there was no benefit to using the prediction model over age alone. DISCUSSION: Using a prediction model, such as the one described here, may help identify individuals who would most benefit from COVID-19 inoculation, and thereby may produce more dramatic initial drops in deaths through targeted vaccination.

Cardiology/Cardiovascular Research

Zaidan M, Alkhalil M, and **Alaswad K**. Calcium Modifications Therapies in Contemporary Percutaneous Coronary Intervention. *Curr Cardiol Rev* 2021; Epub ahead of print. PMID: 34963434. Request Article

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Coronary artery calcifications (CAC) has been known to be associated with worse Percutaneous Coronary Intervention (PCI) short- and long-term outcomes. Nowadays with the increased prevalence of the risk factors leading to CAC in the population and also more PCI procedures done in older patients and with the growing number of higher risk cases of chronic total occlusion (CTO) PCI and PCI after coronary artery bypass grafting(CABG), severe cases of CAC are now encountered on a daily basis in the catheterization lab and remain a big challenge to the interventional community, making it crucial to identify cases of severe CAC and plan a CAC PCI modification strategy upfront. Improved CAC detection with intravascular imaging helped identifying more of these severe CAC cases and predicting response to therapy and stent expansion based on CAC distribution in the vessel. Multiple available therapies for CAC modification has evolved over the years, familiarity with the specifics and special considerations and limitations of each of these tools is essential in the choice and application of these therapies when used in severe CAC treatment. In this review we discuss CAC pathophysiology, modes of detection, and different available therapies for CAC modification.

Center for Health Policy and Health Services Research

Bal VH, **Maye M**, Salzman E, Huerta M, Pepa L, Risi S, and Lord C. Correction to: The Adapted ADOS: A New Module Set for the Assessment of Minimally Verbal Adolescents and Adults. *J Autism Dev Disord* 2021; 51(12):4504-4505. PMID: 33515418. Full Text

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Center for Health Policy and Health Services Research

Glance LG, **Nerenz DR**, Joynt Maddox KE, Hall BL, and Dick AW. Reproducibility of Hospital Rankings Based on Centers for Medicare & Medicaid Services Hospital Compare Measures as a Function of Measure Reliability. *JAMA Netw Open* 2021; 4(12):e2137647. PMID: 34874402. Full Text

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IMPORTANCE: Unreliable performance measures can mask poor-quality care and distort financial incentives in value-based purchasing. OBJECTIVE: To examine the association between test-retest reliability and the reproducibility of hospital rankings. DESIGN, SETTING, AND PARTICIPANTS: In a cross-sectional design, Centers for Medicare & Medicaid Services Hospital Compare data were analyzed for the 2017 (based on 2014-2017 data) and 2018 (based on 2015-2018 data) reporting periods. The study was conducted from December 13, 2020, to September 30, 2021. This analysis was based on 28 measures, including mortality (acute myocardial infarction, congestive heart failure, pneumonia, and coronary artery bypass grafting), readmissions (acute myocardial infarction, congestive heart failure, pneumonia, and coronary artery bypass grafting), and surgical complications (postoperative acute kidney failure, postoperative respiratory failure, postoperative sepsis, and failure to rescue). EXPOSURES: Measure reliability based on test-retest reliability testing. MAIN OUTCOMES AND MEASURES: The reproducibility of hospital rankings was quantified by calculating the reclassification rate across the 2017 and 2018 reporting periods after categorizing the hospitals into terciles, quartiles, deciles, and statistical outliers. Linear regression analysis was used to examine the association between the reclassification rate and the intraclass correlation coefficient for each of the classification systems. RESULTS: The analytic cohort consisted of 28 measures from 4452 hospitals with a median of 2927 (IQR, 2378-3160) hospitals contributing data for each measure. The hospitals participating in the Inpatient Prospective Payment System (n = 3195) had a median bed size of 141 (IQR, 69-261), average daily census of 70 (IQR, 24-155) patients, and a median disproportionate share hospital percentage of 38.2% (IQR, 18.7%-36.6%). The median intraclass correlation coefficient was 0.78 (IQR, 0.72-0.81), ranging between 0.50 and 0.85. The median reclassification rate was 70% (IQR, 62%-71%) when hospitals were ranked by deciles, 43% (IQR, 39%-45%) when ranked by quartiles, 34% (IQR, 31%-36%) when ranked by terciles, and 3.8% (IQR, 2.0%-6.2%) when ranked by outlier status. Increases in measure reliability were not associated with decreases in the reclassification rate. Each 0.1-point increase in the intraclass correlation coefficient was associated with a 6.80 (95% CI, 2.28-11.30; P = .005) percentage-point increase in the reclassification rate when hospitals were ranked into performance deciles, 4.15 (95% CI, 1.16-7.14; P = .008) when ranked into performance quartiles, 1.47 (95% CI, 1.84, 4.77; P = .37) when ranked into performance terciles, and 3.70 (95% CI, 1.30-6.09; P = .004) when ranked by outlier status. CONCLUSIONS AND RELEVANCE: In this study, more reliable measures were not associated with lower rates of reclassifying hospitals using test-retest reliability testing. These findings suggest that measure reliability should not be assessed with test-retest reliability testing.

Center for Health Policy and Health Services Research

Hamilton T, **Macki M**, Oh SY, **Bazydlo M**, **Schultz L**, **Zakaria HM**, Khalil JG, Perez-Cruet M, Aleem I, Park P, Easton R, **Nerenz DR**, **Schwalb J**, **Abdulhak M**, and **Chang V**. The association of patient education level with outcomes after elective lumbar surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2021; 1-9. Epub ahead of print. PMID: 34891131. Full Text

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OBJECTIVE: Socioeconomic factors have been shown to impact a host of healthcare-related outcomes. Level of education is a marker of socioeconomic status. This study aimed to investigate the relationship between patient education level and outcomes after elective lumbar surgery and to characterize any education-related disparities. METHODS: The Michigan Spine Surgery Improvement Collaborative registry was queried for all lumbar spine operations. Primary outcomes included patient satisfaction determined by the North American Spine Society patient satisfaction index, and reaching the minimum clinically important difference of Patient-Reported Outcomes Measurement Information System Physical Function score and return to work up to 2 years after surgery. Multivariate Poisson generalized estimating

equation models reported adjusted risk ratios. RESULTS: A total of 26,229 lumbar spine patients had data available for inclusion in this study. On multivariate generalized estimating equation analysis all comparisons were done versus the high school (HS)/general equivalency development (GED)-level cohort. For North American Spine Society satisfaction scores after surgery the authors observed the following: at 90 days the likelihood of satisfaction significantly decreased by 11% ($p < 0.001$) among < HS, but increased by 1% ($p = 0.52$) among college-educated and 3% ($p = 0.011$) among postcollege-educated cohorts compared to the HS/GED cohort; at 1 year there was a decrease of 9% ($p = 0.02$) among < HS and increases of 3% ($p = 0.02$) among college-educated and 9% ($p < 0.001$) among postcollege-educated patients; and at 2 years, there was an increase of 5% ($p = 0.001$) among postcollege-educated patients compared to the < HS group. The likelihood of reaching a minimum clinically important difference of Patient-Reported Outcomes Measurement Information System Physical Function score at 90 days increased by 5% ($p = 0.005$) among college-educated and 9% ($p < 0.001$) among postcollege-educated cohorts; at 1 year, all comparison cohorts demonstrated significance, with a decrease of 12% ($p = 0.007$) among < HS, but an increase by 6% ($p < 0.001$) among college-educated patients and 14% ($p < 0.001$) among postcollege-educated compared to the HS/GED cohort; at 2 years, there was a significant decrease by 19% ($p = 0.003$) among the < HS cohort, an increase by 8% ($p = 0.001$) among the college-educated group, and an increase by 16% ($p < 0.001$) among the postcollege-educated group. For return to work, a significant increase was demonstrated at 90 days and 1 year when comparing the HS or less group with college or postcollege cohorts. CONCLUSIONS: This study demonstrated negative associations on all primary outcomes with lower levels of education. This finding suggests a potential disparity linked to education in elective spine surgery.

Center for Health Policy and Health Services Research

Jesse MT, Clifton E, **Kim DY**, **Nicholson D**, **Patil R**, **Bhavsar S**, **Desai S**, **Gartrelle K**, **Eshelman A**, **Fleagle E**, **Ahmedani B**, Carlozzi NE, **Tang A**, and **Patel A**. Prerenal Transplant Education and Evaluation Positively Impacts Outcomes. *Prog Transplant* 2021; Epub ahead of print. PMID: 34860614.
Full Text

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Introduction: An outstanding question in kidney transplantation is how to prepare candidates and their social supports for optimal posttransplant outcomes. Project Aims: This program evaluation assessed whether a pretransplant quality improvement clinic improved clinical outcomes in the year posttransplant compared to recipients receiving standard of care. Design: The Countdown to Transplant Clinic was implemented with kidney transplant candidates expected to receive a transplant within the next few months. The clinic included an enhanced education session on posttransplant lifestyle management, confirmation of support (≥2 adults), and evaluations by transplant social work, psychology, and nephrology. Results: Seventy-five patients participated in the clinic and underwent a transplant. A retrospective chart review of posttransplant laboratory values, rehospitalizations (within 3-months posttransplant), biopsy-confirmed graft failure, and mortality (within 1-year posttransplant) were collected from both groups. Univariate and multivariate propensity score-weighted linear or logistic regression models were used to evaluate the association between clinic participation and outcomes. In models adjusting for relevant covariates, participation in The Countdown to Transplant Clinic (vs standard care) was associated with a lower coefficient of variation of serum tacrolimus (all values collected 3-12 months posttransplant), 30-day posttransplant white blood cell counts (but not 90-day), 90-day posttransplant potassium, and 30 and 31 to 90 days rehospitalizations. Clinic participation did not predict serum glucose

levels at 30- or 90-days posttransplant. Due to low rates of rejection and mortality, meaningful comparisons were not possible. Conclusion: Participation in a pretransplant, multicomponent clinic may improve certain outcomes of interest posttransplantation. Pilot testing for feasibility for randomized controlled trials is a necessary next step.

Center for Health Policy and Health Services Research
Rossom RC, Yarborough BJ, Boggs JM, Coleman KJ, **Ahmedani BK**, Lynch FL, Daida Y, and Simon GE. Prediction of suicidal behavior using self-reported suicidal ideation among patients with bipolar disorder. *J Affect Disord* 2021; 295:410-415. PMID: 34507220. Full Text

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BACKGROUND: People with bipolar disorder have elevated suicide risk. We estimated the ability of the Patient Health Questionnaire (PHQ9) to predict suicide outcomes for outpatients with bipolar disorder. METHODS: Visits by adults with bipolar disorder who completed a PHQ9 were identified using electronic health record (EHR) data. Bipolar diagnoses and suicide attempts were ascertained from EHR and claims data, and suicide deaths from state and federal records. Depression severity was assessed via the first eight items of the PHQ9, while suicidal ideation was assessed by the ninth item. RESULTS: 37,243 patients made 126,483 visits. Patients reported at least moderate symptoms of depression in 49% and suicidal ideation in 30% of visits. Risk of suicide attempt was 4.21% in the subsequent 90 days for those reporting nearly daily suicidal ideation compared to 0.74% in those reporting none. Patients with nearly daily suicidal ideation were 3.85 (95% CI 3.32-4.47) times more likely to attempt suicide and 13.78 (95% CI 6.56-28.94) times more likely to die by suicide in the subsequent 90 days than patients reporting none. Patients with self-harm in the last year were 8.86 (95% 7.84-10.02) times more likely to attempt suicide in the subsequent 90 days than those without. LIMITATIONS: Our sample was limited to patients completing the PHQ9 and did not include data on some important social risk or protective factors. CONCLUSIONS: The PHQ9 was a robust predictor of suicide. Suicidal ideation reported on the PHQ9 should be considered a strong indicator of suicide risk and prompt further evaluation.

Center for Health Policy and Health Services Research
Vance AJ, Malin KJ, Benjamin A, Shuman CJ, Moore TA, and Costa DK. Pandemic visitor policies: Parent reactions and policy implications. *Acta Paediatr* 2021; Epub ahead of print. PMID: 34874577. Full Text

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Center for Health Policy and Health Services Research
Zhou Y, **Li J**, **Gordon SC**, **Trudeau S**, **Rupp LB**, Boscarino JA, Daida YG, Schmidt MA, and **Lu M**. Laboratory monitoring and antiviral treatment for chronic hepatitis B among routine care patients in the United States. *J Viral Hepat* 2021; Epub ahead of print. PMID: 34905259. Full Text

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We investigated factors associated with rates of recommended monitoring of chronic hepatitis B (HBV) patients for viral DNA and alanine aminotransferase (ALT), and initiation of antiviral treatment among eligible patients, in a US cohort of patients under routine care. Patients were categorised by treatment indication: definite, equivocal or ineligible. Baseline covariates included demographics, clinical characteristics and specialist care status. 'Recommended monitoring' was defined ≥1 ALT or HBV DNA test per year. Logit models, univariate then multivariable, were used to evaluate factors associated with monitoring and treatment. Among 3,830 patients, treatment was received by 67.5% (788/1168 patients) in the 'definite' category, and 34.1% (208/610 patients) in the 'equivocal' category, of whom 109 moved up to 'definite' status at some point during follow-up. Sex, age and specialist care were independently associated with receipt of treatment in 'definite' patients. Routine monitoring rates were high prior to treatment in 'definite/ treated' patients (ALT: 77%; DNA: 85%) but declined afterwards (ALT 63%; DNA 36%). Rates of monitoring were lower in 'definite/ untreated' patients (ALT: 48%; DNA: 32%). Among 'equivocal/ treated' patients, lower age and comorbidity scores were associated with receipt of treatment; ALT monitoring rates were similar before and after treatment initiation (41% and 46%, respectively), while rates of DNA monitoring declined (55% and 29%). Monitoring among 'treatment ineligible' patients was similar to those in the 'equivocal' and untreated 'definite' groups. A large proportion of US HBV patients under routine care did not receive recommended annual laboratory monitoring, especially after initiation of antiviral treatment, and nearly one-third of patients with 'definite' indications for antiviral therapy remained untreated.

Center for Individualized and Genomic Medicine Research
Xiao S, **Sahasrabudhe N**, **Hochstadt S**, **Cabral W**, **Simons S**, **Yang M**, **Lanfear DE**, and **Williams LK**. Predicting death from COVID-19 using pre-existing conditions: implications for vaccination triage. *BMJ Open Respir Res* 2021; 8(1). PMID: 34949575. Full Text

Center for Individualized and Genomic Medicine Research (CIGMA), Henry Ford Health System, Detroit, Michigan, USA.
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INTRODUCTION: Global shortages in the supply of SARS-CoV-2 vaccines have resulted in campaigns to first inoculate individuals at highest risk for death from COVID-19. Here, we develop a predictive model of COVID-19-related death using longitudinal clinical data from patients in metropolitan Detroit. METHODS: All individuals included in the analysis had a laboratory-confirmed SARS-CoV-2 infection. Thirty-six pre-existing conditions with a false discovery rate $p<0.05$ were combined with other demographic variables to develop a parsimonious prediction model using least absolute shrinkage and selection operator regression. The model was then prospectively validated in a separate set of individuals with confirmed COVID-19. RESULTS: The study population consisted of 15 502 individuals with laboratory-confirmed SARS-CoV-2. The main prediction model was developed using data from 11 635 individuals with 709 reported deaths (case fatality ratio 6.1%). The final prediction model consisted of 14 variables with 11 comorbidities. This model was then prospectively assessed among the remaining 3867 individuals (185 deaths; case fatality ratio 4.8%). When compared with using an age threshold of 65 years, the 14-variable model detected 6% more of the individuals who would die from COVID-19. However, below age 45 years and its risk equivalent, there was no benefit to using the prediction model over age alone. DISCUSSION: Using a prediction model, such as the one described here, may help identify individuals who would most benefit from COVID-19 inoculation, and thereby may produce more dramatic initial drops in deaths through targeted vaccination.

Dermatology

Arora H, **Boothby-Shoemaker W**, **Braunberger T**, **Lim HW**, and **Veenstra J**. Safety of conventional immunosuppressive therapies for patients with dermatological conditions and coronavirus disease 2019: A review of current evidence. *J Dermatol* 2021; Epub ahead of print. PMID: 34962304. Full Text

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The effect of coronavirus disease 2019 (COVID-19) on patients receiving conventional immunosuppressive (IS) therapy has yet to be fully determined; however, research on using IS therapy for treating COVID-19 in acutely ill patients is increasing. While some believe that IS therapy may be protective, others argue that these agents may make patients more susceptible to COVID-19 infection and morbidity and advocate for a more cautious, individualized approach to determining continuation, reduction, or discontinuation of therapy. In this review, we aim to provide an overview of COVID-19 risk in dermatological patients who are receiving conventional IS therapies, including mycophenolate mofetil, methotrexate, cyclosporine, azathioprine, apremilast, JAK inhibitors, and systemic steroids. Additionally, we provide recommendations for management of these medications for dermatological patients during the COVID-19 pandemic. Treatment of dermatological disease during the COVID-19 pandemic should involve shared decision-making between the patient and provider, with consideration of each patient's comorbidities and the severity of the patient's dermatological disease.

Dermatology

Buechler CR, **Sagher E**, **Tisack A**, **Jacobsen G**, **Lim HW**, **McHargue C**, **Friedman BJ**, **Mi QS**, **Ozog DM**, and **Veenstra J**. Contribution of Socioeconomic Risk Factors within a Diverse Mycosis Fungoides Cohort from Detroit, MI. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34920029. Full Text

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Dermatology

Grada A, Del Rosso JQ, Graber E, Bunick CG, **Stein Gold L**, Moore AY, Baldwin H, Obagi Z, Damiani G, Carrothers T, McNamee B, and Hanze E. Sarecycline treatment for acne vulgaris: Rationale for weight-based dosing and limited impact of food intake on clinical efficacy. *Dermatol Ther* 2021; e15275. Epub ahead of print. PMID: 34923732. Full Text

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Tetracycline-class antibiotics are frequently prescribed by dermatologists, commonly for acne vulgaris. Gastrointestinal absorption of first and second-generation tetracycline-class antibiotics, including doxycycline and minocycline, may be reduced by co-administration with food, resulting in potentially lower

clinical efficacy. Development of novel compounds and formulations that are not impacted by diet could improve compliance, absorption, and effectiveness among patients. The objective of this study is to investigate weight-based dosing protocols and the impact of food intake, including high-fat meals, on the absorption, and clinical efficacy of sarecycline, a novel oral narrow-spectrum third-generation tetracycline-class antibiotic approved by the Food and Drug Administration for acne vulgaris treatment. Data from 12 clinical studies were analyzed using population pharmacokinetic modeling, exposure-response modeling and pharmacodynamics to evaluate sarecycline dosing recommendations. The extent of exposure is estimated to decrease by 21.7% following co-administration of a sarecycline tablet with a high-fat meal. Based on the PopPK-PD model, this is equivalent to a decrease in efficacy of 0.9 inflammatory lesions, which is not clinically meaningful. Sarecycline can be administered using weight-based dosing with or without food. Co-administration with high-fat food has a limited impact on clinical efficacy. The pharmacokinetics of oral sarecycline may provide added convenience and support ease of use and improved compliance for acne vulgaris patients.

Dermatology

Krueger L, Saizan AL, Meehan SA, Ezzedine K, **Hamzavi I**, and Elbuluk N. Seborrheic macular hypopigmentation: a case series proposing a new pigmentary disorder. *J Eur Acad Dermatol Venereol* 2021; Epub ahead of print. PMID: 34927764. Full Text

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Dermatology

Kwa MC, and **Lim HW**. Commentary on: "Oxybenzone and pregnancy: Time for more research and patient education". *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34920030. Full Text

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Dermatology

Layton A, Alexis A, Baldwin H, Beissert S, Bettoli V, Del Rosso J, Dréno B, **Gold LS**, Harper J, Lynde C, Thiboutot D, Weiss J, and Tan J. Identifying gaps and providing recommendations to address shortcomings in the investigation of acne sequelae by the Personalising Acne: Consensus of Experts panel. *JAAD Int* 2021; 5:41-48. PMID: 34816133. Full Text

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BACKGROUND: The physical sequelae of acne include erythema, hyperpigmentation, and scarring, which are highly burdensome for patients. Early, effective treatment can potentially limit and prevent sequelae development, but there is a need for guidance for and evidence of prevention-oriented management to improve patient outcomes. OBJECTIVE: To identify unmet needs of acne sequelae and generate expert recommendations to address gaps in clinical guidance. METHODS: The Personalizing Acne: Consensus of Experts panel of 13 dermatologists used a modified Delphi approach to achieve a consensus on the clinical aspects of acne sequelae. A consensus was defined as ≥75% of the dermatologists voting "agree" or "strongly agree." All voting was electronic and blinded. RESULTS: The panel identified gaps in current guidance and made recommendations related to acne sequelae. These included identification and classification of sequelae, pertinent points to consider for patient consultations, and management aimed at reducing the development of sequelae. LIMITATIONS: The recommendations are based on expert opinion and made in the absence of high-quality evidence. CONCLUSIONS: The identified gaps should help inform future research and guideline development for acne sequelae. The consensus-based recommendations should also support the process of consultations throughout the patient journey, helping to reduce the development and burden of acne sequelae through improved risk factor recognition, early discussion, and appropriate management.

Dermatology

Lebwohl MG, **Stein Gold L**, Strober B, Papp KA, Armstrong AW, Bagel J, Kircik L, Ehst B, Hong HC, Soung J, Fromowitz J, Guenthner S, Piscitelli SC, Rubenstein DS, Brown PM, Tallman AM, and Bissonnette R. Phase 3 Trials of Tapinarof Cream for Plaque Psoriasis. *N Engl J Med* 2021; 385(24):2219-2229. PMID: 34879448. Full Text

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BACKGROUND: Tapinarof cream is a topical aryl hydrocarbon receptor-modulating agent under investigation for the treatment of psoriasis. Tapinarof modulates the expression of interleukin-17 and the skin-barrier proteins filaggrin and loricrin. METHODS: We conducted two identical phase 3 randomized trials of tapinarof in patients with mild-to-severe plaque psoriasis. Adults with a baseline Physician's Global Assessment (PGA) score of 2 (mild) to 4 (severe) (on a scale from 0 to 4, with higher scores indicating more severe psoriasis) and a percent of total body-surface area affected of 3 to 20% were randomly assigned in a 2:1 ratio to use tapinarof 1% cream or vehicle cream once daily for 12 weeks. The primary end point, PGA response, was a PGA score of 0 (clear) or 1 (almost clear) and a decrease from baseline of at least 2 points at week 12. Secondary efficacy end points at week 12 were a reduction of at least 75% in the Psoriasis Area and Severity Index (PASI) score, a PGA score of 0 or 1, the mean change from baseline in the percent of body-surface area affected, and a reduction of at least 90% in the PASI score. Patient-reported outcomes were the mean changes from baseline to week 12 in the proportion of patients who had a decrease of at least 4 points in the Peak Pruritus Numeric Rating Scale (PP-NRS) score (range, 0 [no itch] to 10 [worst imaginable itch]), the PP-NRS total score, the Dermatology Life Quality Index total score, and the Psoriasis Symptom Diary score. RESULTS: In trials 1 and 2, a total of 692 and 674 patients, respectively, were screened, with 510 and 515 patients being enrolled. A PGA response occurred in 35.4% of the patients in the tapinarof group and in 6.0% of those in the vehicle group in trial 1 and in 40.2% and 6.3%, respectively, in trial 2 ($P<0.001$ for both comparisons). Results for secondary end points and patient-reported outcomes were generally in the same direction as

those for the primary end point. Adverse events with tapinarof cream included folliculitis, nasopharyngitis, contact dermatitis, headache, upper respiratory tract infection, and pruritus. CONCLUSIONS: Tapinarof 1% cream once daily was superior to vehicle control in reducing the severity of plaque psoriasis over a period of 12 weeks but was associated with local adverse events and headache. Larger and longer trials are needed to evaluate the efficacy and safety of tapinarof cream as compared with existing treatments for psoriasis. (Funded by Dermavant Sciences; PSOARING 1 and 2 ClinicalTrials.gov numbers, NCT03956355 and NCT03983980, respectively.).

Dermatology

Lim HW, **Kohli I**, Ruvolo E, Kolbe L, and **Hamzavi IH**. Impact of visible light on skin health: The role of antioxidants and free radical quenchers in skin protection. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34942294. Full Text

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Until recently, the primary focus of photobiology has centered on the impact of UV radiation on skin health, including DNA damage and oncogenesis; however, the significant effects of visible light (VL) on skin remain grossly underreported. VL has been reported to cause erythema in individuals with light skin (Fitzpatrick skin types [FSTs] I-III) and pigmentary changes in individuals with dark skin types (FSTs IV-VI). These effects have importance in dermatologic diseases and potentially play a role in conditions aggravated by sun exposure, including phototoxicity in patients with FSTs I to III and post-inflammatory hyperpigmentation and melasma in patients with FSTs IV to VI. The induction of free radicals, leading to the generation of reactive species, is one driving mechanism of VL-induced skin pathologies, leading to the induction of melanogenesis and hyperpigmentation. Initial clinical studies have demonstrated the effectiveness of topical sunscreen with antioxidant combinations in inhibiting VL + UV-A1-induced erythema in FSTs I to III and reducing pigmentation in FSTs IV to VI. Antioxidants may help prevent the worsening of pigmentary disorders and can be incorporated into photoprotective strategies. It is essential that dermatologists and the public are aware of the impact of VL on skin, especially in patients with skin of color, and understand the available options for VL protection.

Dermatology

Maghfour J, Rietcheck H, Szeto MD, Rundle CW, Sivesind TE, Dellavalle RP, Lio P, Dunnick CA, Fernandez J, and Yardley H. Tolerability profile of topical cannabidiol and palmitoylethanolamide: a compilation of single-centre randomized evaluator-blinded clinical and in vitro studies in normal skin. *Clin Exp Dermatol* 2021; 46(8):1518-1529. PMID: 34022073. Full Text

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BACKGROUND: An increasing number of studies have investigated the adverse effect profile of oral cannabinoids; however, few studies have provided sufficient data on the tolerability of topical cannabinoids in human participants. AIM: To assess the tolerability profile of several commercial topical formulations containing cannabidiol (CBD) and palmitoylethanolamide (PEA) on the skin of healthy human participants. METHODS: Three human clinical trials and one in vitro study were conducted. The potential for skin irritation, sensitization and phototoxicity of several products, were assessed via patch testing on healthy human skin. The products assessed included two formulations containing CBD and PEA, one containing hemp seed oil and four concentrations of CBD alone. Ocular toxicity was tested using a traditional hen's egg chorioallantoic membrane model with three CBD, PEA and hemp seed oil formulations. RESULTS: There was no irritation or sensitization of the products evident via patch testing on healthy participants. Additionally, mild phototoxicity of a hemp seed oil product was found at the 48-h

time point compared with the negative control. The in vitro experiment demonstrated comparable effects of cannabinoid products with historically nonirritating products. CONCLUSION: These specific formulations of CBD- and PEA-containing products are nonirritating and nonsensitizing in healthy adults, and further encourage similar research assessing their long-term safety and efficacy in human participants with dermatological diseases. There are some limitations to the study: (i) external validity may be limited as formulations from a single manufacturer were used for this study, while vast heterogeneity exists across unregulated, commercial CBD products on the market; and (ii) products were assessed only on normal, nondiseased human skin, and therefore extrapolation to those with dermatological diseases cannot be assumed.

Dermatology
Osto M, **Edriss M**, and **Hamzavi I**. Prospective Protocol Registration Should Be Required for Systematic Reviews in Dermatology Literature. *Clin Dermatol* 2021; Epub ahead of print. PMID: 34915149. Full Text

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Dermatology
Rehman R, Saad M, Suhrawardy A, and **Kerr H**. Contact Dermatitis and TikTok: A Cross-sectional Analysis of Trending Content. *Dermatitis* 2021; Epub ahead of print. PMID: 34967771. Full Text

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Dermatology
Rigel D, **Lim HW**, Draelos Z, Weber TM, and Taylor S. PHOTOPROTECTION FOR ALL: CURRENT GAPS AND OPPORTUNITIES. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34942298. Full Text

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The effects of solar radiation on human skin differ based on skin phototype, the presence or absence of photodermatoses, biological capacity to repair DNA damage, wavelength, intensity of sun exposure, geographic latitude, and other factors, underscoring the need for a more tailored approach to photoprotection. To date, the focus of photoprotection guidelines has been to prevent sunburn and DNA damage induced by ultraviolet (UV) radiation, both UVB and UVA; however, several recent studies have shown that visible light (VL) also generates reactive oxygen and nitrogen species that can contribute to skin damage and pigmentation on the skin, particularly in people of color. Therefore, dark-skinned individuals, while naturally better protected against UVB radiation by virtue of high eumelanin content in melanocytes, may need additional protection from VL-induced skin damage. The current options for photoprotection products need to expand, and potential strategies against VL include the addition of iron oxide, titanium dioxide, and biologically relevant antioxidants to sunscreen formulations, as well as supplementation with orally active antioxidants.

Dermatology
Rigel DS, Taylor SC, **Lim HW**, Alexis AF, Armstrong AW, Chiesa Fuxench ZC, Draelos ZD, and Hamzavi IH. Photoprotection for skin of all color: Consensus and clinical guidance from an expert panel. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34942296. Full Text

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The negative effects of sun exposure have become better accepted among health care professionals and the lay public over recent decades. Most attention has been focused on the effects of UV light, particularly UVB wavelengths (290-320 nm). Accordingly, products to protect skin from sunlight-associated harm (sunscreens) have been developed to minimize UVB exposure. The effects of longer wavelengths, including UVA (320-400 nm) and visible light (VL, 400-700 nm), are increasingly appreciated. VL accounts for approximately half of the solar radiation that reaches the earth's surface and understanding of its effects on the skin is improving. Studies have shown that VL can induce hyperpigmentation in individuals with dark skin types (Fitzpatrick skin types IV-VI). In addition, VL can contribute to the exacerbation of pigmentary disorders, including melasma. Because these findings are relatively new, there are gaps in understanding the needs for photoprotection and guidance for clinicians. A panel of dermatologists and photobiologists was convened to develop consensus recommendations and clinical guidance about sunscreen use relevant to the current understanding of risks associated with sun exposure using a modified Delphi method.

Dermatology
Tan J, Alexis A, Baldwin H, Beissert S, Bettoli V, Del Rosso J, Dréno B, **Gold LS**, Harper J, Lynde C, Thiboutot D, Weiss J, and Layton AM. The Personalised Acne Care Pathway-Recommendations to guide longitudinal management from the Personalising Acne: Consensus of Experts. *JAAD Int* 2021; 5:101-111. PMID: 34816135. Full Text

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BACKGROUND: Acne is a chronic disease with a varying presentation that requires long-term management. Despite this, the clinical guidelines for acne offer limited guidance to facilitate personalized or longitudinal management of patients. OBJECTIVES: To generate recommendations to support comprehensive, personalized, long-term patient management that address all presentations of acne and its current and potential future burden. METHODS: The Personalising Acne: Consensus of Experts panel consisted of 13 dermatologists who used a modified Delphi approach to reach consensus on statements related to longitudinal acne management. The consensus was defined as ≥75% voting "agree" or

"strongly agree." All voting was electronic and blinded. RESULTS: Key management domains, consisting of distinct considerations, points to discuss with patients, and "pivot points" were identified and incorporated into the Personalised Acne Care Pathway. Long-term treatment goals and expectations and risk of (or fears about) sequelae are highlighted as particularly important to discuss frequently with patients. LIMITATIONS: Recommendations are based on expert opinion, which could potentially differ from patients' perspectives. Regional variations in health care systems may not have been captured. CONCLUSIONS: The Personalised Acne Care Pathway provides practical recommendations to facilitate the longitudinal management of acne, which can be used by health care professionals to optimize and personalize care throughout the patient journey.

Dermatology
Tan J, Alexis A, Baldwin H, Beissert S, Bettoli V, Del Rosso J, Dréno B, **Gold LS**, Harper J, Lynde C, Thiboutot D, Weiss J, and Layton AM. Gaps and recommendations for clinical management of truncal acne from the Personalising Acne: Consensus of Experts panel. *JAAD Int* 2021; 5:33-40. PMID: 34816132. Full Text

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BACKGROUND: Truncal acne is common and burdensome for patients; however, there is paucity of evidence and guidance for the management of truncal acne. Currently, clinical practice guidelines provide very little guidance on the assessment or management of truncal acne. OBJECTIVES: To identify unmet needs in truncal acne and make recommendations to address clinical and management gaps using an international consensus. METHODS: The Personalising Acne: Consensus of Experts panel consisted of 13 dermatologists, who used a modified Delphi approach to reach a consensus on statements related to clinically relevant aspects of truncal acne evaluation and management. A consensus was defined as ≥75% of the panelists voting "agree" or "strongly agree." The voting was electronic and blinded. RESULTS: The panel identified gaps and made recommendations related to truncal acne identification, assessment, and grading; the evaluation of the impact on patients; and treatment goals and factors to be considered for its management. LIMITATIONS: The recommendations are based on expert opinion, in the absence of high-quality evidence. CONCLUSIONS: We highlighted addressing not just facial acne but also truncal acne during patient consultations. The recommendations made herein may help facilitate the care of patients who present with truncal acne, with or without facial acne.

Dermatology
Taylor SC, Alexis AF, Armstrong AW, Chiesa Fuxench ZC, and **Lim HW**. Misconceptions of photoprotection in skin of color. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34942293. Full Text

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Terrestrial sunlight is the portion of electromagnetic radiation that is emitted by the sun and reaches Earth's surface. It encompasses 3 major components: UV radiation (290-400 nm), visible light (400-700 nm), and infrared radiation. The deleterious effects of UV radiation have been appreciated for decades, particularly among those with light skin tones (Fitzpatrick skin types I-II) who primarily manifest with burns of varying degrees of severity with sun exposure. In recent years, studies have increasingly shown the negative impact of visible light on skin health, particularly in individuals with skin of color (Fitzpatrick skin types IV-VI), including the exacerbation of hyperpigmentation disorders such as melasma and post-inflammatory hyperpigmentation, as well as induction of the former. Recommendations from medical societies and the US Food and Drug Administration for photoprotection have been evolving along with the knowledge base. Yet, misconceptions about skin damage related to sunlight and the benefits of photoprotection (particularly among those with Fitzpatrick skin types V-VI) are still prevalent among both clinicians and patients. Among patients with skin of color, disorders of hyperpigmentation and other consequences from sun exposure have been associated with impaired skin health and negative burden on quality of life. This review summarizes currently available evidence of the impact of both UV and visible wavelengths and the low utilization of photoprotection measures among people with skin of color, with the goal of providing recommendations to help educate patients.

Dermatology
Torres AE, **Awosika O**, **Maghfour J**, Taylor S, and **Lim HW**. Practical Guide to Tinted Sunscreens. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34973975. Full Text

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Dermatology
Trinidad J, Gabel CK, Bonomo L, Cartron A, Chand S, Coburn W, Daveluy S, Davis M, DeNiro KL, Guggina LM, Han JJ, Hennessy K, Hoffman M, Katz K, Keller JJ, Kim SJ, **Konda S**, Lake E, Lincoln FN, Lo JA, Markova A, Marvin EK, Micheletti RG, Newman S, Nutan F, Nguyen CV, Pahalyants V, Patel J, Rahnama-Moghadam S, **Rambhatla PV**, Riegert M, Reingold RE, Robinson DB, Rrapi R, Sartori-Valinotti JC, Seminario-Vidal L, Sharif-Sidi Z, Smogorzewski J, Spaccarelli N, Stewart JR, Tuttle SD, Ulrich MN, Wanat KA, Xia FD, Kaffenberger B, and Kroshinsky D. Telemedicine and Dermatology Hospital Consultations During The COVID-19 Pandemic: A Multi-Center Observational Study on Resource Utilization and Conversion to In-Person Consultations During the COVID-19 Pandemic. *J Eur Acad Dermatol Venereol* 2021; Epub ahead of print. PMID: 34932237. Full Text

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Dermatology

Vickers C, **Maghfour J**, **Kohli I**, **Lim HW**, and **Hamzavi IH**. Validation of a dermatologic surface area smartphone application: EZBSA. *Skin Res Technol* 2021; Epub ahead of print. PMID: 34923672. Full Text

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Diagnostic Radiology

Khalil LS, **Jildeh TR**, **Abbas MJ**, **Klochko CL**, **Scher C**, **Van Holsbeeck M**, **Muh SJ**, **Makhni EC**, **Moutzouros V**, and Okoroha KR. Elbow Torque May be Predictive of Anatomic Adaptations to the Elbow After a Season of Collegiate Pitching: A Dynamic Ultrasound Study. *Arthrosc Sports Med Rehabil* 2021; 3(6):e1843-e1851. PMID: 34977639. Full Text

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PURPOSE: To determine whether elbow torque was associated with anatomic adaptations of the medial elbow following a season of competitive pitching. METHODS: Pitchers from 3 collegiate baseball teams were recruited during the preseason for participation. Before the season, pitchers were recorded throwing 5 "game-speed" fastball pitches from a standard distance off a mound while wearing a wearable sensor baseball compression sleeve that calculates elbow torque, arm speed, arm slot, and arm rotation. Participants subsequently underwent dynamic ultrasound imaging of the medial elbow, including measurements of the ulnar collateral ligament (UCL) and ulnohumeral joint space to assess elbow laxity. Following a full season of competitive pitching, all testing was repeated, and statistical analysis comparing preseason to postseason sonographic findings was performed. RESULTS: Twenty-eight collegiate pitchers underwent preseason sonographic and kinematic testing. Nineteen pitchers were available for postseason testing. The average age (standard deviation) and playing experience was 19.9 (1.2) and 14.7 (1.5) years. Compared with preseason, there were significant increases in postseason UCL thickness (1.92 ± 0.09 vs 1.56 ± 0.09 mm, P < .01) and elbow laxity (1.77 ± 0.23 vs 1.15 ± 0.22 mm, P = .028) after a season of pitching. No significant changes in pitching kinematic measurements were observed between preseason and postseason testing. Preseason pitching kinematic measurements were significantly associated with increased UCL thickness (arm slot: beta estimate -0.03 ± 0.01, P = .011) and reduction in elbow laxity (elbow torque: beta estimate -0.03 ± 0.01, P = .04) after a season of pitching.

Pitchers with increased body weight and arm length demonstrated reduced medial elbow torque during pitching (P < .05). CONCLUSIONS: After a season of competitive pitching, adaptive changes of the medial elbow were demonstrated on dynamic ultrasound. However, the influence of pitching kinematic measurements on these adaptations are of small magnitude and unknown clinical significance. Although wearable sensor technology may have value in trending individual pitcher kinematics, no discrete threshold appears to predict the development of adaptive changes at the elbow. LEVEL OF EVIDENCE: Level II, prospective observational study.

Emergency Medicine

Carpenter CR, Abrams S, Courtney DM, Dorner SC, Dyne P, Elia T, **Jourdan DN**, Kaji AH, Martin IBK, Mills AM, Nagasawa K, Pillow M, Reznek M, Starnes A, Temin E, Wolfe R, and Chekijian S. Advanced practice providers in academic emergency medicine: A national survey of chairs and program directors. *Acad Emerg Med* 2021; Epub ahead of print. PMID: 34860436. Full Text

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BACKGROUND: The Society for Academic Emergency Medicine Board of Directors convened a task force to elucidate the current state of workforce, operational, and educational issues being faced by academic medical centers related to advanced practice providers (APPs). The task force surveyed academic emergency department (ED) chairs and residency program directors (PDs). METHODS: The survey was distributed to the Association of Academic Chairs of Emergency Medicine (AACEM)-member chairs and their respective residency PDs in 2021. We surveyed 125 chairs with their self-identified PDs. The survey sampled hiring, state-independent practice laws, scope of practice, teaching and supervision, training opportunities, delegation of procedures between physician learners and APPs, and perceptions of the impact on resident and medical student education. RESULTS: Of the AACEM-member chairs identified, 73% responded and 47% of PDs responded. Most (98%) employ either physician assistants or nurse practitioners. Among responding departments, 86% report APPs working in fast-track settings, 80% work in the main ED, and 54% work in the waiting room. In 44% of departments, APPs and residents evaluate patients concurrently, and 2% of respondents reported that APPs manage high-acuity patients without attending involvement. Two-thirds of chairs believe that APPs contribute positively to the quality of patient care, while 44% believe that APPs contribute to the academic environment. One-third of PDs believe that the presence of APPs interferes with resident education. Although 75% of PDs believe that

residents require training to work effectively with APPs in the ED, almost half (49%) report zero hours of training around APP supervision or collaborative skills. CONCLUSIONS: APPs are ubiquitous across academic EDs. Future research is required for academic ED leaders to balance physician and APP deployment across the academic ED within the context of patient care, resident education, institutional resources, professional development opportunities for APP staff, and standardization of APP EM training.

Emergency Medicine

Jaffe IS, **Jaehne AK**, Quackenbush E, Ko ER, Rivers EP, McClain MT, Ginsburg GS, Woods CW, and Tsalik EL. Comparing the Diagnostic Accuracy of Clinician Judgment to a Novel Host Response Diagnostic for Acute Respiratory Illness. *Open Forum Infect Dis* 2021; 8(12):ofab564. PMID: 34888402. Full Text

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BACKGROUND: Difficulty discriminating bacterial from viral infections drives antibacterial misuse. Host gene expression tests discriminate bacterial and viral etiologies, but their clinical utility has not been evaluated. METHODS: Host gene expression and procalcitonin levels were measured in 582 emergency department participants with suspected infection. We also recorded clinician diagnosis and clinician-recommended treatment. These 4 diagnostic strategies were compared with clinical adjudication as the reference. To estimate the clinical impact of host gene expression, we calculated the change in overall Net Benefit (ΔNB; the difference in Net Benefit comparing 1 diagnostic strategy with a reference) across a range of prevalence estimates while factoring in the clinical significance of false-positive and -negative errors. RESULTS: Gene expression correctly classified bacterial, viral, or noninfectious illness in 74.1% of subjects, similar to the other strategies. Clinical diagnosis and clinician-recommended treatment revealed a bias toward overdiagnosis of bacterial infection resulting in high sensitivity (92.6% and 94.5%, respectively) but poor specificity (67.2% and 58.8%, respectively), resulting in a 33.3% rate of inappropriate antibacterial use. Gene expression offered a more balanced sensitivity (79.0%) and specificity (80.7%), which corresponded to a statistically significant improvement in average weighted accuracy (79.9% vs 71.5% for procalcitonin and 76.3% for clinician-recommended treatment; P<.0001 for both). Consequently, host gene expression had greater Net Benefit in diagnosing bacterial infection than clinician-recommended treatment (ΔNB=6.4%) and procalcitonin (ΔNB=17.4%). CONCLUSIONS: Host gene expression-based tests to distinguish bacterial and viral infection can facilitate appropriate treatment, improving patient outcomes and mitigating the antibacterial resistance crisis.

Emergency Medicine

Miller J, Chaudhry F, **Tirgari S**, Calo S, Walker AP, Thompson R, Nahab B, **Lewandowski C**, and Levy P. Cardiac Stroke Volume Index Is Associated With Early Neurological Improvement in Acute Ischemic Stroke Patients. *Front Physiol* 2021; 12:689278. PMID: 34867433. Full Text

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Early neurological improvement as assessed with the NIH stroke scale (NIHSS) at 24 h has been associated with improved long-term functional outcomes following acute ischemic stroke (AIS). Cardiac dysfunction is often present in AIS, but its association with outcomes is incompletely defined. We performed a pilot study to evaluate the association between non-invasively measured cardiac parameters and 24-h neurological improvement in prospectively enrolled patients with suspected AIS who presented within 12 h of symptom-onset and had an initial systolic blood pressure>140 mm Hg. Patients receiving thrombolytic therapy or mechanical thrombectomy were excluded. Non-invasive pulse contour analysis was used to measure mean arterial blood pressure (MAP), cardiac stroke volume index (cSVI), cardiac output (CO) and cardiac index (CI). Transcranial Doppler recorded mean middle cerebral artery flow velocity (MFV). We defined a decrease of 4 NIHSS points or NIHSS ≤ 1 at 24-h as neurological improvement. Of 75 suspected, 38 had confirmed AIS and did not receive reperfusion therapy. Of these, 7/38 (18.4%) had neurological improvement over 24 h. MAP was greater in those without improvement (108, IQR 96-123 mm Hg) vs. those with (89, IQR 73-104 mm Hg). cSVI, CO, and MFV were similar between those without and with improvement: 37.4 (IQR 30.9-47.7) vs. 44.7 (IQR 42.3-55.3) ml/m(2); 5.2 (IQR 4.2-6.6) vs. 5.3 (IQR 4.7-6.7) mL/min; and 39.9 (IQR 32.1-45.7) vs. 34.4 (IQR 27.1-49.2) cm/s, respectively. Multivariate analysis found MAP and cSVI as predictors for improvement (OR 0.93, 95%CI 0.85-0.98 and 1.14, 95%CI 1.03-1.31). In this pilot study, cSVI and MAP were associated with 24-h neurological improvement in AIS.

Family Medicine

Ranka S, Lahan S, Chhatriwalla AK, Allen KB, **Chiang M**, **O'Neill B**, **Verma S**, **Wang DD**, **Lee J**, **Frisoli T**, Eng M, Bagur R, **O'Neill W**, and **Villablanca P**. Network meta-analysis comparing the short and long-term outcomes of alternative access for transcatheter aortic valve replacement. *Cardiovasc Revasc Med* 2021; Epub ahead of print. PMID: 34972667. Full Text

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BACKGROUND: Several studies have pair-wise compared access sites for transcatheter aortic valve replacement (TAVR) but pooled estimate of overall comparative efficacy and safety outcomes are not well known. We sought to compare short- and long-term outcomes following various alternative access routes for TAVR. METHODS: Thirty-four studies with a pooled sample size of 32,756 patients were selected by searching PubMed and Cochrane library databases from inception through 11th June 2021 for patients undergoing TAVR via 1 of 6 different access sites: Transfemoral (TF), Transaortic (TAO), Transapical (TA), Transcarotid (TC), Transaxillary/Subclavian (TSA), and Transcaval (TCV). Data were extracted to conduct a frequentist network meta-analysis with a random-effects model using TF access as a reference group. RESULTS: Compared with TF, both TAO [RR 1.91, 95% CI (1.46-2.50)] and TA access [RR 2.12, 95% CI (1.84-2.46)] were associated with an increased risk of 30-day mortality. No significant difference was observed for stroke, myocardial infarction, major bleeding, conversion to open surgery, and major adverse cardiovascular or cerebrovascular events at 30 days between different accesses. Major vascular complications were lower in TA [RR 0.43, (95% CI, 0.28-0.67)] and TC [RR 0.51, 95% CI (0.35-0.73)] access compared to TF. The 1-year mortality was higher in TAO [RR of 1.35, (95% CI, 1.01-1.81)] and TA [RR 1.44, (95% CI, 1.14-1.81)] groups. CONCLUSION: Non-thoracic alternative access site utilization for

TAVR implantation (TC, TSA and TCV) is associated with outcomes similar to conventional TF access. Thoracic TAVR access (TAO and TA) translates into increased short and long-term mortality.

Family Medicine

White Perkins D, **Milan P**, **Miazek K**, **Havstad S**, and **Wegienka G**. Identifying factors affecting diabetes education program participation within a metro Detroit integrated health system. *Prev Med Rep* 2021; 24:101646. PMID: 34976695. Full Text

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Diabetes self-management education and support (DSMES) can help people achieve optimal disease control, yet these services often remain underutilized. People referred to these programs by their provider can become disengaged in the program at several key steps. This study applies Classification and Regression Tree analysis to 3796 people with diabetes at a single health system based in the Detroit metropolitan area who were referred for DSMES provided by the health system to determine demographic patterns of those who were successfully contacted to schedule program intake appointments, those who did not attend their intake appointment, and those who began but did not complete their personalized DSMES program. White people > 43 years of age, those with a prior A1C value > 8.9 and those with Medicaid insurance had the highest rate of not being successfully contacted for their intake appointment. Those who did not attend their intake appointment tended to have Medicaid insurance, be younger than 48 years, and have A1C > 8.1. Within the Medicare or private insurance groups, those who did not attend were more likely to be female, of Black race and not partnered. Older males with a lower A1C (≤8.3%) had the lowest rate (34.0%) of failing to complete their DSMES plan. The data showed that almost half of those referred were not successfully contacted. The overall low completion rate of 13.2% confirms the need to examine factors predictive of participation and completion. This study highlights process improvement changes to improve personalization of outreach and engagement.

Gastroenterology

Dang DT, **Suresh S**, **Vance B**, **Singla S**, **Javia S**, **Watson A**, **Chathadi KV**, **Katakuri V**, **Pompa R**, Stidham RW, **Zuchelli T**, and **Piraka C**. Outcomes of cold snare piecemeal endoscopic mucosal resection for nonampullary small-bowel adenomas larger than 1 centimeter: a retrospective study. *Gastrointest Endosc* 2021; Epub ahead of print. PMID: 34971667. Full Text

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BACKGROUND AND AIMS: Nonampullary small-bowel adenomas ≥10 mm are typically resected using cautery-based polypectomy, which is associated with significant adverse events. Studies have demonstrated the safety and efficacy of piecemeal cold snare endoscopic mucosal resection (EMR) for removing large colon polyps. Our aim was to assess the safety and efficacy of cold snare EMR for removal of large adenomas in the small bowel. METHODS: A retrospective study of patients who underwent lift and piecemeal cold snare EMR of small-bowel adenomas ≥1 cm between January 2014 and March 2019 was conducted at a tertiary care medical center. Polyp characteristics at time of index and surveillance endoscopy were collected. Primary outcomes included residual or recurrent adenoma (RRA) seen on surveillance endoscopy, polyp eradication rate, and number of endoscopic procedures required for eradication. Adverse events including immediate and delayed bleeding, perforation, stricture, pancreatitis, and postpolypectomy syndrome were assessed. RESULTS: Of 43 patients who underwent piecemeal cold snare EMR, 39 had follow-up endoscopy. Polyps ranged in size from 10 to 70 mm, mean 26.5 mm. RRA was found in 18 patients (46%), with increased polyp size correlating with higher

recurrence (P < 0.001). Polyp eradication was observed in 35 patients (89%), requiring a median of 2 (range 1-6) endoscopic procedures. Only 1 patient (2.3%) had immediate postprocedural bleeding. No cases of perforation or postpolypectomy syndrome were seen. CONCLUSIONS: Piecemeal cold snare EMR may be a feasible, safe, and efficacious technique for small-bowel polyps >10 mm. Prospective, randomized studies are needed to assess how outcomes compare with traditional cautery-based polypectomy.

Gastroenterology
Naffouj S, **Al-Shammari M**, and **Salgia R**. Treatment of colonic varices with a superior mesenteric venous stent: a case report describing a unique approach. *Gastroenterol Rep (Oxf)* 2021; 9(6):597-600. PMID: 34925858. Full Text

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Gastroenterology
Zhou Y, **Li J**, **Gordon SC**, **Trudeau S**, **Rupp LB**, Boscarino JA, Daida YG, Schmidt MA, and **Lu M**. Laboratory monitoring and antiviral treatment for chronic hepatitis B among routine care patients in the United States. *J Viral Hepat* 2021; Epub ahead of print. PMID: 34905259. Full Text

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We investigated factors associated with rates of recommended monitoring of chronic hepatitis B (HBV) patients for viral DNA and alanine aminotransferase (ALT), and initiation of antiviral treatment among eligible patients, in a US cohort of patients under routine care. Patients were categorised by treatment indication: definite, equivocal or ineligible. Baseline covariates included demographics, clinical characteristics and specialist care status. 'Recommended monitoring' was defined ≥1 ALT or HBV DNA test per year. Logit models, univariate then multivariable, were used to evaluate factors associated with monitoring and treatment. Among 3,830 patients, treatment was received by 67.5% (788/1168 patients) in the 'definite' category, and 34.1% (208/610 patients) in the 'equivocal' category, of whom 109 moved up to 'definite' status at some point during follow-up. Sex, age and specialist care were independently associated with receipt of treatment in 'definite' patients. Routine monitoring rates were high prior to treatment in 'definite/ treated' patients (ALT: 77%; DNA: 85%) but declined afterwards (ALT 63%; DNA 36%). Rates of monitoring were lower in 'definite/ untreated' patients (ALT: 48%; DNA: 32%). Among 'equivocal/ treated' patients, lower age and comorbidity scores were associated with receipt of treatment; ALT monitoring rates were similar before and after treatment initiation (41% and 46%, respectively), while rates of DNA monitoring declined (55% and 29%). Monitoring among 'treatment ineligible' patients was similar to those in the 'equivocal' and untreated 'definite' groups. A large proportion of US HBV patients under routine care did not receive recommended annual laboratory monitoring, especially after initiation of antiviral treatment, and nearly one-third of patients with 'definite' indications for antiviral therapy remained untreated.

Graduate Medical Education
Gifford L, **Johnson CC**, **Haque N**, **Passalacqua KD**, **Swiderek J**, and **Kalkanis S**. COVID-19 in the hotspot of Metropolitan Detroit: A multi-faceted health system experience. *Int J Health Plann Manage* 2021; Epub ahead of print. PMID: 34859491. Full Text

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Health systems were abruptly plunged into a crisis as SARS-CoV-2 exploded into a pandemic in spring 2020. In March-April 2020, Metropolitan Detroit was a US "hotspot." As a large health system with five hospitals and two behavioural health inpatient facilities, a health insurance company, a medical group and physician network, and 41 ambulatory clinics normally hosting over 10,000 daily patient encounters, the Henry Ford Health System deployed numerous strategies in the management of this upheaval. As hospitals and Emergency Departments were inundated with COVID-19 patients, other services and activities needed to shut down as state-mandated policies were promulgated, new internal and external communication networks established, and management of employees and resources such as ventilators, ICU beds, personal protective equipment, and laboratory supplies became critical challenges. We describe herein the system-wide strategies implemented and lessons learned in the operation of a health system in the initial throes of a global pandemic.

Hematology-Oncology

Bayard S, Fasano G, **Chen Y**, Davis M, Drotman M, **Bensenhaver J**, Swistel A, Simmons R, Marti J, and Newman L. Screening mammography mitigates breast cancer disparities through early detection of triple negative breast cancer. *Clin Imaging* 2021; 80:430-437. PMID: 34543867. Full Text

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PURPOSE: Screening mammography improves breast cancer survival through early detection, but Triple Negative Breast Cancer (TNBC) is more difficult to detect on mammography and has lower survival compared to non-TNBC, even when detected at early stages. TNBC is twice as common among African American (AA) compared to White American (WA) women, thereby contributing to the 40% higher breast cancer mortality rates observed in AA women. The role of screening mammography in addressing breast cancer disparities is therefore worthy of study. METHODS: Outcomes were evaluated for TNBC patients treated in the prospectively-maintained databases of academic cancer programs in two metropolitan cities of the Northeast and Midwest, 1998-2018. RESULTS: Of 756 TNBC cases, 301 (39.8%) were mammographically screen-detected. 46% of 189 AA and 38.5% of 460 WA patients had screen-detected TNBC ($p = 0.16$). 25.3% of 257 TNBC cases ≤50 years old had screen-detected disease compared to 47.3% of 499 TNBC cases >50 years old ($p < 0.0001$). 220/301 (73.1%) screen-detected TNBC cases were T1 lesions versus 118/359 (32.9%) non-screen-detected cases ($p < 0.0001$). Screen-detected TNBC was more likely to be node-negative (51.9% v. 40.4%; $p < 0.0001$). Five-year overall survival was better in screen-detected TNBC compared to nonscreen-detected TNBC (92.8% v. 81.5%; $p < 0.0001$) in the entire cohort. The magnitude of this effect was most significant among AA patients (Fig. 1). Screening-related survival patterns were similar among AA and WA patients in both cities. CONCLUSION: Data from two different cities demonstrates the value of screening mammography to mitigate breast cancer disparities in AA women through the early detection of TNBC.

Hematology-Oncology

Gregory GP, Kumar SK, **Wang D**, Mahadevan D, Walker PA, Wagner-Johnston ND, Escobar C, Bannerji R, Bhutani D, Chang JE, Hernandez-Ilizaliturri FJ, Klein A, Pagel JM, Rybka W, Yee AJ, Mohrbacher A, Huang M, Farooqui MZH, Marinello P, and Quach H. Pembrolizumab plus dinaciclib in patients with hematologic malignancies: the phase 1b KEYNOTE-155 study. *Blood Adv* 2021; Epub ahead of print. PMID: 34972202. Full Text

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Preclinical data demonstrated that combining an anti-programmed cell death 1 (PD-1) inhibitor with a CDK9 inhibitor provided enhanced antitumor activity with no significant toxicities, suggesting this combination may be a potential therapeutic option. The multicohort, phase 1 KEYNOTE-155 study evaluated the safety and antitumor activity of the PD-1 inhibitor pembrolizumab plus the CDK9 inhibitor dinaciclib in patients with relapsed or refractory (rr) chronic lymphocytic leukemia (CLL), diffuse large B-cell lymphoma (DLBCL) and multiple myeloma (MM). Patients enrolled were ≥18 years of age with a confirmed diagnosis of CLL, DLBCL, or MM. The study included 2 phases: a dose-evaluation phase to determine dose-limiting toxicities and a signal-detection phase. Patients received pembrolizumab 200 mg every 3 weeks plus dinaciclib 7 mg/m2 on day 1 and 10 mg/m2 on day 8 of cycle 1 and 14 mg/m2 on days 1 and 8 of cycles 2 and later. Primary endpoint was safety, and a key secondary endpoint was objective response rate (ORR), Seventy-two patients were enrolled and received ≥1 dose of study treatment (CLL, n = 17; DLBCL, n = 38; MM, n = 17). Pembrolizumab plus dinaciclib was generally well tolerated and produced no unexpected toxicities. The ORRs were 29.4% (5/17, rrCLL), 21.1% (8/38, rrDLBCL), and 0% (0/17, rrMM), respectively. At data cutoff, all 72 patients had discontinued treatment, 38 (52.8%) because of progressive disease. These findings demonstrate activity with combination pembrolizumab plus dinaciclib and suggest that a careful and comprehensive approach to explore anti-PD-1 and CDK9 inhibitor combinations is warranted. Clinical trial registration: ClinicalTrials.gov, NCT02684617.

Hematology-Oncology

Monga J, **Adrianto I**, **Rogers C**, **Gadgeel S**, **Chitale D**, Alumkal JJ, Beltran H, Zoubeidi A, and **Ghosh J**. Tribbles 2 pseudokinase confers enzalutamide resistance in prostate cancer by promoting lineage plasticity. *J Biol Chem* 2021; 101556. Epub ahead of print. PMID: 34973338. Full Text

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Enzalutamide (Xtandi), a second-generation anti-androgen, is commonly prescribed for therapy of advanced prostate cancer, but enzalutamide-resistant, lethal or incurable disease invariably develops. To understand the molecular mechanism(s) behind enzalutamide resistance, here we comprehensively analyzed a range of prostate tumors and clinically relevant models by gene expression array, immunohistochemistry, and Western blot, which revealed that enzalutamide resistant prostate cancer cells and tumors overexpress the pseudokinase, Tribbles 2 (TRIB2). Inhibition of TRIB2 decreases the viability of enzalutamide-resistant prostate cancer cells, suggesting a critical role of TRIB2 in these cells. Moreover, overexpression of TRIB2 confers resistance in prostate cancer cells to clinically relevant doses of enzalutamide, and this resistance is lost upon inhibition of TRIB2. Interestingly, we found that TRIB2 downregulates the luminal markers AR (androgen receptor) and CK8 (cytokeratin 8) in prostate cancer cells but upregulates the neuronal transcription factor BRN2 (Brain-2) and the stemness factor SOX2 (SRY-box 2) to induce neuroendocrine characteristics. Finally, we show that inhibition of either TRIB2 or its downstream targets, BRN2 or SOX2, re-sensitizes resistant prostate cancer cells to enzalutamide. Thus, TRIB2 emerges as a potential new regulator of trans-differentiation that confers enzalutamide-resistance in prostate cancer cells via a mechanism involving increased cellular plasticity and lineage switching.

Hematology-Oncology

Schmidt AL, Labaki C, Hsu CY, Bakouny Z, **Balanchivadze N**, Berg SA, Blau S, Daher A, El Zarif T, Friese CR, Griffiths EA, Hawley JE, Hayes-Lattin B, Karivedu V, Latif T, Mavromatis BH, McKay RR, Nagaraj G, Nguyen RH, Panagiotou OA, Portuguese AJ, Puc M, Dutra MS, Schroeder BA, Thakkar A, Wulff-Burchfield EM, Mishra S, Farmakiotis D, Shyr Y, Warner JL, and Choueiri TK. COVID-19 Vaccination and Breakthrough Infections in Patients with Cancer. *Ann Oncol* 2021; Epub ahead of print. PMID: 34958894. Request Article

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BACKGROUND: Vaccination is an important preventive health measure to protect against symptomatic and severe COVID-19. Impaired immunity secondary to an underlying malignancy or recent receipt of anti-neoplastic systemic therapies can result in less robust antibody titres following vaccination and possible risk of breakthrough infection. As clinical trials evaluating COVID-19 vaccines largely excluded patients with a history of cancer and those on active immunosuppression (including chemotherapy), limited evidence is available to inform the clinical efficacy of COVID-19 vaccination across the spectrum of patients with cancer. PATIENTS AND METHODS: We describe the clinical features of patients with cancer who developed symptomatic COVID-19 following vaccination and compare weighted outcomes to those of contemporary unvaccinated patients, after adjustment for confounders, using data from the multi-institutional COVID-19 and Cancer Consortium (CCC19; ClinicalTrials.gov number, NCT04354701). RESULTS: Patients with cancer who develop COVID-19 following vaccination have substantial comorbidities and can present with severe and even lethal infection. Patients harboring hematologic malignancies are over-represented among vaccinated patients with cancer who develop symptomatic COVID-19. CONCLUSIONS: Vaccination against COVID-19 remains an essential strategy in protecting vulnerable populations, including patients with cancer. However, patients with cancer who develop breakthrough infection despite full vaccination remain at risk of severe outcomes. A multilayered public health mitigation approach that includes vaccination of close contacts, boosters, social distancing, and mask-wearing should be continued for the foreseeable future.

Hospital Medicine

Burnett AE, Ragheb B, and **Kaatz S**. Perioperative consultative hematology: can you clear my patient for a procedure? *Hematology Am Soc Hematol Educ Program* 2021; 2021(1):521-528. PMID: 34889442. Full Text

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Periprocedural management of antithrombotics is a common but challenging clinical scenario that renders patients vulnerable to potential adverse events such as bleeding and thrombosis. Over the past decade, periprocedural antithrombotic approaches have changed considerably with the advent of direct oral anticoagulants (DOACs), as well as a paradigm shift away from bridging in many warfarin patients. Successfully navigating this high-risk period relies on a number of individualized patient assessments conducted within a framework of standardized, systematic approaches. It also requires a thorough understanding of antithrombotic pharmacokinetics, multidisciplinary coordination of care, and comprehensive patient education and empowerment. In this article, we provide clinicians with a practical, stepwise approach to periprocedural management of antithrombotic agents through case-based examples of relevant clinical scenarios.

Hospital Medicine

Thilagar B, **Beidoun M**, Rhoades R, and **Kaatz S**. COVID-19 and thrombosis: searching for evidence. *Hematology Am Soc Hematol Educ Program* 2021; 2021(1):621-627. PMID: 34889411. Full Text

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Early in the pandemic, COVID-19-related increases in rates of venous and arterial thromboembolism were seen. Many observational studies suggested a benefit of prophylactic anticoagulation for hospitalized patients using various dosing strategies. Randomized trials were initiated to compare the efficacy of these different options in acutely ill and critically ill inpatients as the concept of immune-mediated inflammatory microthrombosis emerged. We present a case-based review of how we approach thromboembolic prophylaxis in COVID-19 and briefly discuss the epidemiology, the pathophysiology, and the rare occurrence of vaccine-induced thrombotic thrombocytopenia.

Hypertension and Vascular Research

Fonseca W, Asai N, Yagi K, Malinczak CA, **Savickas G**, **Johnson CC**, **Murray S**, **Zoratti EM**, Lukacs NW, **Li J**, and Schuler Iv CF. COVID-19 Modulates Inflammatory and Renal Markers That May Predict Hospital Outcomes among African American Males. *Viruses* 2021; 13(12). PMID: 34960684. Full Text

Department of Pathology, University of Michigan, Ann Arbor, MI 48109, USA.
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BACKGROUND AND OBJECTIVES: African Americans and males have elevated risks of infection, hospitalization, and death from SARS-CoV-2 in comparison with other populations. We report immune responses and renal injury markers in African American male patients hospitalized for COVID-19. METHODS: This was a single-center, retrospective study of 56 COVID-19 infected hospitalized African American males 50+ years of age selected from among non-intensive care unit (ICU) and ICU status patients. Demographics, hospitalization-related variables, and medical history were collected from electronic medical records. Plasma samples collected close to admission (≤2 days) were evaluated for cytokines and renal markers; results were compared to a control group (n = 31) and related to COVID-19 in-hospital mortality. RESULTS: Among COVID-19 patients, eight (14.2%) suffered in-hospital mortality; seven (23.3%) in the ICU and one (3.8%) among non-ICU patients. Interleukin (IL)-18 and IL-33 were elevated at admission in COVID-19 patients in comparison with controls. IL-6, IL-18, MCP-1/CCL2, MIP-1α/CCL3, IL-33, GST, and osteopontin were upregulated at admission in ICU patients in comparison with controls. In addition to clinical factors, MCP-1 and GST may provide incremental value for risk prediction of COVID-19 in-hospital mortality. CONCLUSIONS: Qualitatively similar inflammatory responses were observed in comparison to other populations reported in the literature, suggesting non-immunologic factors may account for outcome differences. Further, we provide initial evidence for cytokine and renal toxicity markers as prognostic factors for COVID-19 in-hospital mortality among African American males.

Infectious Diseases

Joshi S, **Shallal A**, and **Zervos M**. Vancomycin-Resistant Enterococci: Epidemiology, Infection Prevention, and Control. *Infect Dis Clin North Am* 2021; 35(4):953-968. PMID: 34752227. Full Text

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Vancomycin-resistant enterococcus (VRE) is a pathogen of growing concern due to increasing development of antibiotic resistance, increasing length of hospitalizations and excess mortality. The utility of some infection control practices are debatable, as newer developments in infection prevention strategies continued to be discovered. This article summarizes the significance of VRE and VRE transmission, along with highlighting key changes in infection control practices within the past 5 years.

Infectious Diseases

McKinnon JE, **Wang DD**, **Zervos M**, **Saval M**, **Marshall-Nightengale L**, **Kilgore P**, **Pabla P**, **Szandzik E**, **Maksimowicz-McKinnon K**, and **O'Neill WW**. Safety and Tolerability of Hydroxychloroquine in healthcare workers and first responders for the prevention of COVID-19: WHIP COVID-19 Study. *Int J Infect Dis* 2021; Epub ahead of print. PMID: 34954095. Full Text

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BACKGROUND: Healthcare workers (HCW) are among the highest risk groups for acquisition of COVID-19 due to occupational exposures. The WHIP COVID-19 study aimed to evaluate the safety and efficacy of hydroxychloroquine (HCQ) as chemoprophylaxis for SARS-CoV-2 infection in this population. METHODS: HCW, first responders and other occupationally high-risk participants were enrolled in a randomized, placebo-controlled clinical study of HCQ from April-October 2020. The trial compared daily versus weekly HCQ to placebo and to a prospective cohort on HCQ for autoimmune diseases. Participants were followed for 8 weeks. Serology or a positive PCR test were used to determine laboratory confirmed clinical cases. RESULTS: 624 participants were randomized to placebo (n=200), weekly HCQ (n=201), daily HCQ (n=197). For the primary safety endpoint, 279 (44.7%) participants experienced AE level II or lower (total AEs n=589), similar rates in all randomized groups (p=0.188) with no hospitalizations or interventions required. Only 4 laboratory confirmed COVID-19 cases occurred, with 2 in the placebo arm and one in each HCQ randomized arm. CONCLUSIONS: This randomized placebo-controlled trial was able to demonstrate the safety of HCQ outpatient chemoprophylaxis in high-risk groups against COVID-19. Future studies of chemoprophylaxis for SARS-CoV-2 are needed as the epidemic continues worldwide.

Infectious Diseases

Suleyman G, and **Alangaden GJ**. Nosocomial Fungal Infections: Epidemiology, Infection Control, and Prevention. *Infect Dis Clin North Am* 2021; 35(4):1027-1053. PMID: 34752219. Full Text

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Invasive fungal infections are an important cause of morbidity and mortality in hospitalized patients and in the immunocompromised population. This article reviews the current epidemiology of nosocomial fungal infections in adult patients, with an emphasis on invasive candidiasis (IC) and invasive aspergillosis (IA). Included are descriptions of nosocomial infections caused by Candida auris, an emerging pathogen, and IC- and IA-associated with coronavirus disease 2019. The characteristics and availability of newer nonculture-based tests for identification of nosocomial fungal pathogens are discussed. Recently published recommendations and guidelines for the control and prevention of these nosocomial fungal infections are summarized.

Internal Medicine

Fonseca W, Asai N, Yagi K, Malinczak CA, **Savickas G**, **Johnson CC**, **Murray S**, **Zoratti EM**, Lukacs NW, **Li J**, and Schuler Iv CF. COVID-19 Modulates Inflammatory and Renal Markers That May Predict Hospital Outcomes among African American Males. *Viruses* 2021; 13(12). PMID: 34960684. Full Text

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BACKGROUND AND OBJECTIVES: African Americans and males have elevated risks of infection, hospitalization, and death from SARS-CoV-2 in comparison with other populations. We report immune responses and renal injury markers in African American male patients hospitalized for COVID-19. METHODS: This was a single-center, retrospective study of 56 COVID-19 infected hospitalized African American males 50+ years of age selected from among non-intensive care unit (ICU) and ICU status patients. Demographics, hospitalization-related variables, and medical history were collected from electronic medical records. Plasma samples collected close to admission (≤2 days) were evaluated for cytokines and renal markers; results were compared to a control group (n = 31) and related to COVID-19 in-hospital mortality. RESULTS: Among COVID-19 patients, eight (14.2%) suffered in-hospital mortality; seven (23.3%) in the ICU and one (3.8%) among non-ICU patients. Interleukin (IL)-18 and IL-33 were elevated at admission in COVID-19 patients in comparison with controls. IL-6, IL-18, MCP-1/CCL2, MIP-1α/CCL3, IL-33, GST, and osteopontin were upregulated at admission in ICU patients in comparison with controls. In addition to clinical factors, MCP-1 and GST may provide incremental value for risk prediction of COVID-19 in-hospital mortality. CONCLUSIONS: Qualitatively similar inflammatory responses were observed in comparison to other populations reported in the literature, suggesting non-immunologic factors may account for outcome differences. Further, we provide initial evidence for cytokine and renal toxicity markers as prognostic factors for COVID-19 in-hospital mortality among African American males.

Internal Medicine

Gupta K, Nagalli S, Kalra R, Gupta R, Mahmood S, Jain V, Zhou W, Prabhu SD, and Bajaj NS. Sleep duration, baseline cardiovascular risk, inflammation and incident cardiovascular mortality in ambulatory U.S. Adults: National health and nutrition examination survey. *Am J Prev Cardiol* 2021; 8:100246. PMID: 34485966. Full Text

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Department of Psychiatry, State University of New York Downstate Medical Center, Brooklyn, NY, U.S.A.
Department of Internal Medicine, Cleveland Clinic, Cleveland, OH, U.S.A.
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Division of Molecular Imaging and Therapeutics, Department of Radiology, University of Alabama at Birmingham, AL, U.S.A.

INTRODUCTION: The interplay between sleep duration and inflammation on the baseline and incident cardiovascular (CV) risk is unknown. We sought to evaluate the association between sleep duration, C-reactive protein (CRP), baseline CV risk, and incident CV mortality. METHODS: We used data from the National Health and Nutrition Examination Survey 2005-2010 linked with the cause of death data from the

National Center for Health Statistics for adults aged ≥18 years. The associations between self-reported sleep duration and CRP, 10-year atherosclerotic CV disease risk score (ASCVD) and CV mortality were assessed using Linear, Poisson and Cox proportional hazard modeling as appropriate. RESULTS: There were 17,635 eligible participants with a median age of 46 years (interquartile range [IQR] 31, 63). Among them, 51.3% were women and 46.9% were non-Hispanic Whites. Over a median follow-up of 7.5 years (IQR 6.0, 9.1), 350 CV deaths occurred at an incident rate of 2.7 per 1000-person years (IQR 2.4, 3.0). We observed a U-shaped associations between sleep duration and incident CV mortality rate (P-trend=0.011), sleep duration and 10-year ASCVD risk (P-trend <0.001), as well as sleep duration and CRP (P-trend <0.001). A self-reported sleep duration of 6-7 hours appeared most optimal. We observed that those participants who reported <6 or >7 hours of sleep had higher risk of CV death attributable to inflammation after accounting for confounders. CONCLUSIONS: There was a U-shaped relationship of incident CV mortality, 10-year ASCVD risk, and CRP with sleep duration. These findings suggest an interplay between sleep duration, inflammation, and CV risk.

Internal Medicine
Naffouj S, **Al-Shammari M**, and **Salgia R**. Treatment of colonic varices with a superior mesenteric venous stent: a case report describing a unique approach. *Gastroenterol Rep (Oxf)* 2021; 9(6):597-600. PMID: 34925858. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, USA.
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Internal Medicine
Thilagar B, **Beidoun M**, Rhoades R, and **Kaatz S**. COVID-19 and thrombosis: searching for evidence. *Hematology Am Soc Hematol Educ Program* 2021; 2021(1):621-627. PMID: 34889411. Full Text

Division of Hospital Medicine, Henry Ford Health System, Detroit, MI.
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Division of Hematology, Thomas Jefferson University, Philadelphia, PA.

Early in the pandemic, COVID-19-related increases in rates of venous and arterial thromboembolism were seen. Many observational studies suggested a benefit of prophylactic anticoagulation for hospitalized patients using various dosing strategies. Randomized trials were initiated to compare the efficacy of these different options in acutely ill and critically ill inpatients as the concept of immune-mediated inflammatory microthrombosis emerged. We present a case-based review of how we approach thromboembolic prophylaxis in COVID-19 and briefly discuss the epidemiology, the pathophysiology, and the rare occurrence of vaccine-induced thrombotic thrombocytopenia.

Nephrology
Jesse MT, Clifton E, **Kim DY**, **Nicholson D**, **Patil R**, **Bhavsar S**, **Desai S**, **Gartrelle K**, **Eshelman A**, **Fleagle E**, **Ahmedani B**, Carlozzi NE, **Tang A**, and **Patel A**. Prerenal Transplant Education and Evaluation Positively Impacts Outcomes. *Prog Transplant* 2021; Epub ahead of print. PMID: 34860614. Full Text

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Department of Surgery, Wayne State School of Medicine, Detroit, MI, USA.
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Introduction: An outstanding question in kidney transplantation is how to prepare candidates and their social supports for optimal posttransplant outcomes. Project Aims: This program evaluation assessed whether a pretransplant quality improvement clinic improved clinical outcomes in the year posttransplant compared to recipients receiving standard of care. Design: The Countdown to Transplant Clinic was implemented with kidney transplant candidates expected to receive a transplant within the next few months. The clinic included an enhanced education session on posttransplant lifestyle management, confirmation of support (≥2 adults), and evaluations by transplant social work, psychology, and nephrology. Results: Seventy-five patients participated in the clinic and underwent a transplant. A retrospective chart review of posttransplant laboratory values, rehospitalizations (within 3-months posttransplant), biopsy-confirmed graft failure, and mortality (within 1-year posttransplant) were collected from both groups. Univariate and multivariate propensity score-weighted linear or logistic regression models were used to evaluate the association between clinic participation and outcomes. In models adjusting for relevant covariates, participation in The Countdown to Transplant Clinic (vs standard care) was associated with a lower coefficient of variation of serum tacrolimus (all values collected 3-12 months posttransplant), 30-day posttransplant white blood cell counts (but not 90-day), 90-day posttransplant potassium, and 30 and 31 to 90 days rehospitalizations. Clinic participation did not predict serum glucose levels at 30- or 90-days posttransplant. Due to low rates of rejection and mortality, meaningful comparisons were not possible. Conclusion: Participation in a pretransplant, multicomponent clinic may improve certain outcomes of interest posttransplantation. Pilot testing for feasibility for randomized controlled trials is a necessary next step.

Neurology

Alhajala H, **Ramadan AR**, Suneja A, **Schultz L**, and **Zaman IF**. Single-centre study surveying neurology trainees' and faculty's perceptions of the impact of the COVID-19 pandemic on residents' medical education. *BMJ Neurol Open* 2021; 3(2):e000184. PMID: 34934946. Full Text

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OBJECTIVE: To assess perceptions of our neurology residents and faculty regarding training experience and medical education during the early COVID-19 pandemic. METHODS: We distributed two online, voluntary and anonymous surveys to trainees and teaching faculty of our Neurology Department at Henry Ford Hospital. Surveys inquired about trainees' stress, well-being, clinical experience and satisfaction with medical education and available support resources during the first wave of the COVID-19 pandemic in Michigan (mid-March to June 2020). RESULTS: A total of 17/31 trainees and 25/42 faculty responded to the surveys. Eight (47%) trainees reported high stress levels. Nine (57%) were redeployed to cover COVID-19 units. Compared with non-redeployed trainees, redeployed residents reported augmented medical knowledge (89% vs 38%, p=0.05). There was no difference in the two groups regarding overall satisfaction with residency experience, stress levels and didactics attendance. Twenty-one (84%) faculty felt that the redeployment interfered with trainees education but was appropriate, while 10 (59%) trainees described a positive experience overall. Both trainees and faculty believed the pandemic positively impacted trainees' experience by increasing maturity level, teamwork, empathy, and medical knowledge, while both agreed that increased stress and anxiety levels were negative outcomes of the pandemic. Twelve (70%) trainees and 13 (52%) faculty were interested in pursuing more virtual didactics in the future. CONCLUSION: Our findings provide an objective assessment of residents' experience during the COVID-19 pandemic and can guide teaching programmes in their medical education response in the face of future global crises.

Neurology

Wardrope A, Dworetzky BA, **Barkley GL**, Baslet G, Buchhalter J, Doss J, Goldstein LH, Hallett M, Kozlowska K, LaFrance WC, Jr., McGonigal A, Mildon B, Oto M, Perez DL, Riker E, Roberts NA, Stone J, Tolchin B, and Reuber M. How to do things with words: Two seminars on the naming of functional (psychogenic, non-epileptic, dissociative, conversion, …) seizures. *Seizure* 2021; 93:102-110. PMID: 34740139. Full Text

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King's College London Department of Psychology, Institute of Psychiatry, Psychology and Neuroscience, London, United Kingdom.
Human Motor Control Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, United States.
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Aix Marseille Univ, Inserm, INS, Institut de Neurosciences des Systèmes, Marseille, France; APHM, Timone Hospital, Clinical Neurophysiology, Marseille, France.
FND Hope International, Salmon, ID, United States.
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Departments of Neurology and Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States.
National Association of Epilepsy Centers, Washington, DC, United States.
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Amongst the most important conditions in the differential diagnosis of epilepsy is the one that manifests as paroxysms of altered behaviour, awareness, sensation or sense of bodily control in ways that often resemble epileptic seizures, but without the abnormal excessive or synchronous electrical activity in the brain that defines these. Despite this importance, there remains little agreement - and frequent debate - on what to call this condition, known inter alia as psychogenic non-epileptic seizures (PNES), dissociative seizures (DS), functional seizures (FS), non-epileptic attack disorder (NEAD), pseudoseizures, conversion disorder with seizures, and by many other labels besides. This choice of terminology is not merely academic - it affects patients' response to and understanding of their diagnosis, and their ability to navigate health care systems.This paper summarises two recent discussions hosted by the American Epilepsy Society and Functional Neurological Disorders Society on the naming of this condition. These discussions are conceptualised as the initial step of an exploration of whether it might be possible to build consensus for a new diagnostic label.

Neurosurgery

Asmaro K, **Yoo F**, Yassin-Kassab A, **Bazydlo M**, **Robin AM**, **Rock JP**, and **Craig JR**. Sinonasal Packing is Not a Requisite for Successful Cerebrospinal Fluid Leak Repair. *J Neurol Surg B Skull Base*:9. PMID: Not assigned. Request Article

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Background Numerous methods have been described to repair nasal cerebrospinal fluid (CSF) leaks. Most studies have focused on optimizing CSF leak repair success, leading to closure rates of 90 to 95%. Objective This study aimed to determine if excellent reconstruction rates could be achieved without using sinonasal packing. Methods A prospective case series of 73 consecutive patients with various CSF leak etiologies and skull base defects was conducted to evaluate reconstruction success without sinonasal packing. The primary outcome measure was postoperative CSF leak. Secondary outcome measures were postoperative epistaxis requiring intervention in operating room or emergency department, infectious sinusitis, and 22-item sinonasal outcome test (SNOT-22) changes. Results Mean age was 54.5 years and 64% were female. Multilayered reconstructions were performed in 55.3% of cases, with collagen or bone epidural inlay grafts, and nasal mucosal grafts or nasoseptal flaps for onlay layers. Onlay-only reconstructions with mucosal grafts or nasoseptal flaps were performed in 44.7% of cases. Tissue sealants were used in all cases, and lumbar drains were used in 40.8% of cases. There were two initial failures (97.4% initial success), but both resolved with lumbar drains alone (no revision surgeries). There were no instances of postoperative epistaxis requiring intervention in the operating room or emergency department. Infectious sinusitis occurred in 2.7% of patients in the first 3 months postoperatively. SNOT-22 did not change significantly from preoperatively to first postoperative visits, then improved over time. Conclusion Nasal CSF leaks from various etiologies and defect sites were successfully repaired without using sinonasal packing, and patients experienced minimal sinonasal morbidity.

Neurosurgery

Brodie S, **Lee HK**, **Jiang W**, **Cazacu S**, **Xiang C**, **Poisson LM**, **Datta I**, **Kalkanis S**, Ginsberg D, and **Brodie C**. Correction: The novel long non-coding RNA TALNEC2, regulates tumor cell growth and the stemness and radiation response of glioma stem cells. *Oncotarget* 2021; 12(26):2546-2547. PMID: 34966487. Full Text

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[This corrects the article DOI: 10.18632/oncotarget.15991.].

Neurosurgery

Gifford L, **Johnson CC**, **Haque N**, **Passalacqua KD**, **Swiderek J**, and **Kalkanis S**. COVID-19 in the hotspot of Metropolitan Detroit: A multi-faceted health system experience. *Int J Health Plann Manage* 2021; Epub ahead of print. PMID: 34859491. Full Text

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Health systems were abruptly plunged into a crisis as SARS-CoV-2 exploded into a pandemic in spring 2020. In March-April 2020, Metropolitan Detroit was a US "hotspot." As a large health system with five hospitals and two behavioural health inpatient facilities, a health insurance company, a medical group and physician network, and 41 ambulatory clinics normally hosting over 10,000 daily patient encounters, the Henry Ford Health System deployed numerous strategies in the management of this upheaval. As

hospitals and Emergency Departments were inundated with COVID-19 patients, other services and activities needed to shut down as state-mandated policies were promulgated, new internal and external communication networks established, and management of employees and resources such as ventilators, ICU beds, personal protective equipment, and laboratory supplies became critical challenges. We describe herein the system-wide strategies implemented and lessons learned in the operation of a health system in the initial throes of a global pandemic.

Neurosurgery

Hamilton T, **Macki M**, Oh SY, **Bazydlo M**, **Schultz L**, **Zakaria HM**, Khalil JG, Perez-Cruet M, Aleem I, Park P, Easton R, **Nerenz DR**, **Schwalb J**, **Abdulhak M**, and **Chang V**. The association of patient education level with outcomes after elective lumbar surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2021; 1-9. Epub ahead of print. PMID: 34891131. Full Text

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OBJECTIVE: Socioeconomic factors have been shown to impact a host of healthcare-related outcomes. Level of education is a marker of socioeconomic status. This study aimed to investigate the relationship between patient education level and outcomes after elective lumbar surgery and to characterize any education-related disparities. METHODS: The Michigan Spine Surgery Improvement Collaborative registry was queried for all lumbar spine operations. Primary outcomes included patient satisfaction determined by the North American Spine Society patient satisfaction index, and reaching the minimum clinically important difference of Patient-Reported Outcomes Measurement Information System Physical Function score and return to work up to 2 years after surgery. Multivariate Poisson generalized estimating equation models reported adjusted risk ratios. RESULTS: A total of 26,229 lumbar spine patients had data available for inclusion in this study. On multivariate generalized estimating equation analysis all comparisons were done versus the high school (HS)/general equivalency development (GED)-level cohort. For North American Spine Society satisfaction scores after surgery the authors observed the following: at 90 days the likelihood of satisfaction significantly decreased by 11% ($p < 0.001$) among < HS, but increased by 1% ($p = 0.52$) among college-educated and 3% ($p = 0.011$) among postcollege-educated cohorts compared to the HS/GED cohort; at 1 year there was a decrease of 9% ($p = 0.02$) among < HS and increases of 3% ($p = 0.02$) among college-educated and 9% ($p < 0.001$) among postcollege-educated patients; and at 2 years, there was an increase of 5% ($p = 0.001$) among postcollege-educated patients compared to the < HS group. The likelihood of reaching a minimum clinically important difference of Patient-Reported Outcomes Measurement Information System Physical Function score at 90 days increased by 5% ($p = 0.005$) among college-educated and 9% ($p < 0.001$) among postcollege-educated cohorts; at 1 year, all comparison cohorts demonstrated significance, with a decrease of 12% ($p = 0.007$) among < HS, but an increase by 6% ($p < 0.001$) among college-educated patients and 14% ($p < 0.001$) among postcollege-educated compared to the HS/GED cohort; at 2 years, there was a significant decrease by 19% ($p = 0.003$) among the < HS cohort, an increase by 8% ($p = 0.001$) among the college-educated group, and an increase by 16% ($p < 0.001$) among the postcollege-educated group. For return to work, a significant increase was demonstrated at 90 days and 1 year when comparing the HS or less group with college or postcollege cohorts. CONCLUSIONS: This study demonstrated negative associations on all primary outcomes with lower levels of education. This finding suggests a potential disparity linked to education in elective spine surgery.

Nursing

Wojack CA, VanBlarcom AG, and Casida J. Ambulatory Extracorporeal Membrane Oxygenation: Times Are Changing. *AACN Adv Crit Care* 2021; 32(4):434-442. PMID: 34879137. Request Article

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During the past century, medical technology has evolved to enhance quality and quantity of life. Medications, surgeries, and implantable devices have been developed and enhanced to reduce complications and improve patient outcomes. The use of extracorporeal membrane oxygenation is one of the most substantial advances in life-saving modalities. Extracorporeal membrane oxygenation has been widely used for patients with heart or lung failure across the lifespan. Expansion and simplifications of extracorporeal membrane oxygenation circuit designs have informed changes in patient treatment (from bed confinement to ambulatory) and shifted many clinical staffing structures (from cardiovascular perfusionist to nurse-managed care). Highly skilled registered nurses and advanced practice registered nurses are increasingly involved in managing extracorporeal membrane oxygenation in the critical care setting. The purpose of this article is to highlight the technological evolution of extracorporeal membrane oxygenation and the corresponding patient care that bedside registered nurses and advanced practice registered nurses provide.

Obstetrics, Gynecology and Women's Health Services

Cook AE, **Aref I**, **Burmeister C**, **Hijaz M**, and **Elshaikh MA**. Quantification of recurrence risk based on number of adverse prognostic factors in women with stage I uterine endometrioid carcinoma. *J Turk Ger Gynecol Assoc* 2021; 22(4):262-267. PMID: 34866366. Full Text

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OBJECTIVE: The goal was to develop an updated model to predict the risk of recurrence, based on the number of adverse pathologic features in women with International Federation of Gynecology and Obstetrics stage I uterine endometrioid carcinoma, who did not undergo any adjuvant treatment. MATERIAL AND METHODS: Women at a single center who underwent surgical staging without adjuvant therapy between January 1990 and December 2019 were included. Cox proportional hazards model was used to identify independent predictors of relapse free survival (RFS). Prognostic groups were then created based on the number of independent predictors of recurrence that were identified (0, 1, or 2-3 risk factors). Overall survival (OS) and disease specific survival (DSS) were also calculated for each group. RESULTS: In total 1133 women were eligible for inclusion. Median follow-up was 84 months. Independent prognostic factors of recurrence included: age ≥60; grade 2 or 3 differentiation; and presence of lymphovascular space invasion (LVSI). Due to the small number of patients with either 2 or 3 risk factors, these groups were combined into one (group 2/3). Isolated vaginal cuff recurrence was the most common site of recurrence in all study groups (2%, 7%, and 17% for groups 0, 1, and 2/3, respectively). Five-year RFS rates were 96%, 85%, and 57% for groups 0, 1, and 2/3 ($p<0.01$), respectively. Five-year DSS rates were 99%, 96%, and 85% and 5-year OS rates were 94%, 85%, and 62% ($p<0.01$), respectively. CONCLUSION: We identified older age, high grade, and presence of LVSI as independent predictors of recurrence for women with stage I uterine endometrioid carcinoma. Using these prognostic factors, recurrence risk can be quantified for individual patients, and these factors can be used in deciding the appropriate adjuvant management course.

Obstetrics, Gynecology and Women's Health Services

White KM, Dunietz GL, **Pitts DS**, **Kalmbach DA**, Lucchini M, and O'Brien LM. Burden of sleep disturbance in non-Hispanic Black pregnant women. *J Clin Sleep Med* 2021; Epub ahead of print. PMID: 34964433. Full Text

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STUDY OBJECTIVES: Non-Hispanic Black pregnant women disproportionately experience poor perinatal outcomes compared to other racial/ethnic groups. Sleep disruption has emerged as a risk factor for adverse pregnancy outcomes but there are limited data in minority pregnant women. We examined the prevalence of habitual snoring and its timing of onset with several key sleep-wake disturbances and their associations with perinatal outcomes in a cohort of non-Hispanic Black pregnant women. METHODS: Third trimester non-Hispanic Black pregnant women were recruited from a large, academic medical center and screened for habitual snoring - and its timing relative to pregnancy - sleep quality, symptoms of insomnia, excessive daytime sleepiness, as well as daytime function. Clinical diagnoses of hypertensive disorders of pregnancy were obtained along with delivery outcomes. RESULTS: In 235 women the vast majority (80%) reported three or more sleep-wake disturbances, and almost half had at least five disturbances. Sixteen percent endorsed pre-pregnancy snoring and 20% pregnancy-onset snoring. Women with pregnancy-onset snoring had significantly increased odds of poor sleep quality aOR 8.2, trouble staying asleep aOR 3.6, waking up too early aOR 2.7, excessive daytime sleepiness aOR 2.3, and poor daytime function aOR 8.7 but no relationship with perinatal outcomes. In contrast, pre-pregnancy snoring was related to chronic hypertension, pre-term delivery and fetal growth restriction; aOR 2.6, aOR 2.8, and aOR 5.1 respectively. CONCLUSIONS: Sleep-wake disturbances confer a significant burden to pregnant non-Hispanic Black women, an infrequently studied yet disproportionately affected population. Contributions of maternal sleep to racial disparities in perinatal health should be a priority for public health research.

Ophthalmology and Eye Care Services

Jin ML, Brown MM, Patwa D, Nirmalan A, and **Edwards PA**. Telemedicine, telementoring, and telesurgery for surgical practices. *Curr Probl Surg* 2021; 58(12):100986. PMID: 34895561. Full Text

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Ophthalmology and Eye Care Services

Jin ML, Brown MM, Patwa D, Nirmalan A, and **Edwards PA**. In Brief. *Curr Prob Surg* 2021; 58(12):3. PMID: Not assigned. Full Text

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Orthopedics/Bone and Joint Center

Abbas MJ, **Jildeh TR**, **Khalil LS**, **Buckley P**, Mumuni SP, Washington KJ, and Okoroha KR. Social Media Use Continues to Increase Among Orthopaedic Residency Programs in the United States. *Arthrosc Sports Med Rehabil* 2021; 3(6):e1761-e1767. PMID: 34977631. Full Text

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PURPOSE: To evaluate the social media usage of orthopaedic residency programs, program directors (PDs), and department chairs across Instagram, Facebook, and Twitter and to determine which types of social media posts are indicative of increased user following. METHODS: A systematic online search strategy was performed in October 2020 to identify all allopathic orthopaedic surgery residency program accounts on Instagram, Facebook, and Twitter. Instagram posts were further analyzed to evaluate the type of post that significantly correlated with increased follower counts. RESULTS: Of 158 orthopaedic surgery programs, 69 (43.7%) had Instagram accounts, 52 (32.9%) had Facebook accounts, and 54 (34.2%) had Twitter accounts. Program presence on Instagram and Twitter continued to grow exponentially (R (2) = 0.99 and R (2) = 0.95, respectively). Regarding program leadership, a total of 151 PDs and 156 chairs were identified. Of these, 21 PDs (14%) and 8 chairs (5.1%) had Instagram accounts. The number of posts and the numbers of educational, social, program information, and operative posts (P < .01) significantly correlated with increased followers on Instagram. CONCLUSIONS: Fewer than one-half of orthopaedic surgery residency programs and fewer than one-quarter of PDs and department chairs have a social media presence. However, the number of residency programs on social media continues to rise year-over-year. The total number of posts; the amount of educational, social, and program information; and the number of operative posts significantly correlated with increased followers on Instagram. CLINICAL RELEVANCE: With the growing prevalence of social media, orthopaedic surgery residency programs have the opportunity to connect with future applicants and disseminate informational content regarding their programs.

Orthopedics/Bone and Joint Center

Carrier J, and Colorado B. Isolated Anterior Interosseous Neuropathy Affecting Only the Flexor Digitorum Profundus to the Index Finger After Shoulder Arthroscopy: A Case Report and Review of the Literature. *Am J Phys Med Rehabil* 2021; 100(12):e188-e190. PMID: 34793377. Full Text

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Anterior interosseous nerve neuropathy is an uncommon neuropathy with multiple potential etiologies. We present a rare case of anterior interosseous nerve neuropathy affecting only the flexor digitorum profundus to the index finger and occurring after shoulder arthroscopy. This unique presentation used a combination of both electrodiagnostic testing and neuromuscular ultrasound to obtain an accurate diagnosis and highlights the importance of these complementary tests in the evaluation of nerve disorders. To our knowledge, anterior interosseous nerve neuropathy after shoulder arthroscopy affecting only the flexor digitorum profundus to the index finger has not been previously described in the literature.

Orthopedics/Bone and Joint Center

Castle JP, **Jildeh TR**, **Buckley PJ**, **Abbas MJ**, Mumuni S, and Okoroha KR. Older, Heavier, Arthritic, Psychiatrically Disordered, and Opioid-Familiar Patients Are at Risk for Opioid Use After Medial Patellofemoral Ligament Reconstruction. *Arthrosc Sports Med Rehabil* 2021; 3(6):e2025-e2031. PMID: 34977662. Full Text

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PURPOSE: To investigate which factors predispose patients for prolonged opioid use after medial patellofemoral ligament (MPFL) reconstruction. METHODS: A retrospective review of all patients who underwent MPFL reconstruction at a single institution between January 2013 and June 2020 was conducted. Opioid consumption before and after surgery was recorded and confirmed using Michigan Automated Prescriptions System monitoring program. Patients were classified into preoperative opioid users and nonusers. Risk factors for continued opioid use were assessed by collecting patient demographic variables, psychiatric history, number of previous patellar dislocations, and operative factors. RESULTS: A total of 102 patients were included during the time frame of interest. Patients were on average 21.6 ± 8.5 years old with a mean body mass index of 28.2 ± 7.9. Thirty patients (29.0%) sustained >10 dislocations preoperatively. Preoperative opioid use was present in 13 (12.7%) patients. Greater than 10 dislocations (odds ratio [OR] 5.00, 95% confidence interval [CI] 1.12-20.92) and psychiatric history (OR 3.33, 95% CI, 1.2-9.1; P = .016) significantly predicted opioid refills the first month after surgery. Risk factors for opioid refills at 2 to 12 months postoperatively included smoking (OR 4.50, 95% CI 1.13-17.96), preoperative opioid use (OR 7.32, 95% CI 1.88-28.47), psychiatric disorder (OR 3.77, 95% CI 2.3-6.2; P < .001), age >30 years (OR 7.03, 95% CI 3.63-13.61; P < .001), and obesity (OR 2.68, 95% CI 1.40-5.14; P = .002). Compared with Outerbridge 0, a greater percentage of patients with Outerbridge 1 or 2 and 3 or 4 continued using opioids 2 to 12 months after surgery (OR 3.06, 95% CI 1.33-7.02; P = .006 and OR 2.86, 95% CI 1.24-6.59; P = .010, respectively). CONCLUSIONS: For patients undergoing MPFL reconstruction, preoperative opioid use, cartilage damage, age >30 years, smoking history, body mass index >30, and history of psychiatric disorder were found to be significantly associated with prolonged opioid use after surgery. Postoperative opioid refills in this cohort declined after 1 month. LEVEL OF EVIDENCE: Level III, retrospective cohort study.

Orthopedics/Bone and Joint Center

Figueiredo L, **Makhni EC**, Dierks M, Ferreira FC, and Finkelstein S. Early cost estimating model for new bioabsorbable orthopedic implant candidates: A theoretical study. *J Mech Behav Biomed Mater* 2021; 124:104731. PMID: 34500353. Request Article

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An early health technology assessment (HTA) study was performed to assess the need for developing a new bioabsorbable implant for the treatment of specific orthopedic injuries. The Anterior Cruciate Ligament Reconstruction (ACLR) procedure was selected based on the need and potential impact of bioabsorbable implants in the treatment of ACL injuries. The economic model considers the possible health events after an ACLR (failures and other complications such as stiffness and pain). A decision tree approach was used, and several sensitivity analyses were performed using a Monte Carlo simulation. A cost estimating model was applied comparatively for currently available metal and bioabsorbable implants against a potential new bioabsorbable implant with improved performance. A reduction in stiffness and pain symptoms were considered as targets for these new implants performance, with reduced inflammation resulting from the use of materials with appropriate biological and mechanical properties. The current study estimates that, under the assumptions made, the introduction of a new bioabsorbable implant in ACLR surgeries may generate yearly cost savings. The model estimates positive cost-benefits of the new implant when it reduces the probability of failure by more than 30%, or reduces at least 14%

the probability of complications of an inflammatory nature. The development of a new bioabsorbable orthopedic implant for ACLR is encouraged by this study identifying the need for new bioabsorbable implants with improved biological and mechanical performance. The results of this early HTA have made it possible to anticipate design needs and objectives for the research and development of new orthopedic bioabsorbable implants.

Orthopedics/Bone and Joint Center
Guo EW, **Yedulla NR**, **Cross AG**, **Hessburg LT**, **Elhage KG**, **Koolmees DS**, and **Makhni EC**. Older, Male Orthopaedic Surgeons From Southern Geographies Prescribe Higher Doses of Post-Operative Narcotics Than do their Counterparts: A Medicare Population Study. *Arthrosc Sports Med Rehabil* 2021; 3(6):e1577-e1583. PMID: 34977609. Full Text

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PURPOSE: We wanted to evaluate opioid prescribing patterns among orthopaedic surgeons and to identify demographics that may be associated with more extensive opioid prescribing habits that could be candidates for targeted education policies. METHODS: Medicare Part D prescriber and prescription information for the most recent available year, 2017, was accessed via a publicly available database offered by the Centers for Medicare and Medicaid. Number of total prescriptions, number of opioid prescriptions, and the total days' supply of opioids prescribed were analyzed for each of 19,219 orthopaedic surgeons. Demographics and board certification status were also recorded. RESULTS: Orthopaedic surgeons who wrote the most opioid prescriptions (>400 per year) also wrote the longest prescription durations (14.1 days/prescription, $P < .05$ for all comparisons). Surgeons with more than 30 years of experience wrote the longest prescriptions (11.8 days/prescription; $P < .001$). Male surgeons wrote more opioid prescriptions than female surgeons (151 vs 95, respectively; $P < .001$). However, female surgeons wrote longer prescriptions than male surgeons (7.5 days/prescription vs 6.1 days/prescription, respectively; $P = .01$). Surgeons from southern states wrote the most opioid prescriptions (1,386,897) and the longest prescriptions, with an average of 13.0 days per prescription, whereas western states wrote the shortest prescriptions at 10.4 days per prescription ($P = .004$). CONCLUSION: There are demographic correlations between orthopaedic surgeons and opioid prescribing patterns. In particular, male, older southern surgeons prescribe the highest volumes of opioids. This provides an opportunity for targeted education versus overarching, general policies. Potential directions for future investigation can focus on assessing recent trends in opioid prescriptions among orthopaedic providers. LEVEL OF EVIDENCE: Level III, retrospective cohort study.

Orthopedics/Bone and Joint Center
Khalil LS, **Jildeh TR**, **Abbas MJ**, **Klochko CL**, **Scher C**, **Van Holsbeeck M**, **Muh SJ**, **Makhni EC**, **Moutzouros V**, and Okoroha KR. Elbow Torque May be Predictive of Anatomic Adaptations to the Elbow After a Season of Collegiate Pitching: A Dynamic Ultrasound Study. *Arthrosc Sports Med Rehabil* 2021; 3(6):e1843-e1851. PMID: 34977639. Full Text

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PURPOSE: To determine whether elbow torque was associated with anatomic adaptations of the medial elbow following a season of competitive pitching. METHODS: Pitchers from 3 collegiate baseball teams were recruited during the preseason for participation. Before the season, pitchers were recorded throwing 5 "game-speed" fastball pitches from a standard distance off a mound while wearing a wearable sensor baseball compression sleeve that calculates elbow torque, arm speed, arm slot, and arm rotation. Participants subsequently underwent dynamic ultrasound imaging of the medial elbow, including measurements of the ulnar collateral ligament (UCL) and ulnohumeral joint space to assess elbow laxity. Following a full season of competitive pitching, all testing was repeated, and statistical analysis comparing preseason to postseason sonographic findings was performed. RESULTS: Twenty-eight collegiate pitchers underwent preseason sonographic and kinematic testing. Nineteen pitchers were

available for postseason testing. The average age (standard deviation) and playing experience was 19.9 (1.2) and 14.7 (1.5) years. Compared with preseason, there were significant increases in postseason UCL thickness (1.92 ± 0.09 vs 1.56 ± 0.09 mm, P < .01) and elbow laxity (1.77 ± 0.23 vs 1.15 ± 0.22 mm, P = .028) after a season of pitching. No significant changes in pitching kinematic measurements were observed between preseason and postseason testing. Preseason pitching kinematic measurements were significantly associated with increased UCL thickness (arm slot: beta estimate -0.03 ± 0.01, P = .011) and reduction in elbow laxity (elbow torque: beta estimate -0.03 ± 0.01, P = .04) after a season of pitching. Pitchers with increased body weight and arm length demonstrated reduced medial elbow torque during pitching (P < .05). CONCLUSIONS: After a season of competitive pitching, adaptive changes of the medial elbow were demonstrated on dynamic ultrasound. However, the influence of pitching kinematic measurements on these adaptations are of small magnitude and unknown clinical significance. Although wearable sensor technology may have value in trending individual pitcher kinematics, no discrete threshold appears to predict the development of adaptive changes at the elbow. LEVEL OF EVIDENCE: Level II, prospective observational study.

Orthopedics/Bone and Joint Center
Lawrence RL, Ludewig PM, and Ward SR. An Integrated Approach to Musculoskeletal Performance, Disease, and Recovery. *Phys Ther* 2021; 101(12). PMID: 34636897. Full Text

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Orthopedics/Bone and Joint Center
Mobasheri A, Kapoor M, **Ali SA**, Lang A, and Madry H. The future of deep phenotyping in osteoarthritis: How can high throughput omics technologies advance our understanding of the cellular and molecular taxonomy of the disease? *Osteoarthr Cartil Open* 2021; 3(4). PMID: Not assigned. Request Article

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Osteoarthritis (OA) is the most common form of musculoskeletal disease with significant healthcare costs and unmet needs in terms of early diagnosis and treatment. Many of the drugs that have been developed to treat OA failed in phase 2 and phase 3 clinical trials or produced inconclusive and ambiguous results. High throughput omics technologies are a powerful tool to better understand the mechanisms of the development of OA and other arthritic diseases. In this paper we outline the strategic reasons for increasingly applying deep phenotyping in OA for the benefit of gaining a better understanding of disease mechanisms and developing targeted treatments. This editorial is intended to launch a special themed issue of Osteoarthritis and Cartilage Open addressing the timely topic of “Advances in omics technologies for deep phenotyping in osteoarthritis”. High throughput omics technologies are increasingly being applied in mechanistic studies of OA and other arthritic diseases. Applying multi-omics approaches in OA is a high priority and will allow us to gather new information on disease pathogenesis at the cellular level, and integrate data from diverse omics technology platforms to enable deep phenotyping. We anticipate that new knowledge in this area will allow us to harness the power of Big Data Analytics and resolve the extremely complex and overlapping clinical phenotypes into molecular endotypes, revealing new information about the cellular taxonomy of OA and “druggable pathways”, thus facilitating future drug development.

Orthopedics/Bone and Joint Center
Taylor K, **Warren JR**, **Jildeh T**, **Kuhlmann N**, **Pietroski AD**, **Beydoun R**, **Keinath C**, and **Muh SJ**. The Impact of External Beam Radiation Therapy on Shoulder Surgical Outcomes: A Case Series Study. *J Shoulder Elbow Surg* 2021; Epub ahead of print. PMID: 34902586. Full Text

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PURPOSE: External beam radiation therapy (XRT) is a commonly used treatment adjunct in patients with breast cancer, and is known to cause soft tissue dysfunction. However, data on XRT as a preoperative risk factor for shoulder surgery is limited. The purpose of this study is to assess whether prior history of breast cancer treated with XRT has an impact on surgical complications or outcomes. METHODS: A 20-year, retrospective chart review across one large, academic health care system was performed. Inclusion criteria comprised any patient with history of breast cancer of the upper-outer or axillary region treated with XRT. Patients also must have undergone a surgical procedure to the ipsilateral shoulder with at least 1-year postoperative follow-up. Patients were stratified by demographics, hand-dominance, and surgery type. Postoperative outcomes including range of motion (ROM) and visual analogue scale (VAS) for pain were also collected. RESULTS: Eighteen patients were identified (100% female) with an average age of 66.3 years (standard deviation 10.5 years). Ten shoulders underwent rotator cuff repair (RCR), four total shoulder arthroplasty (TSA), three Reverse Shoulder Arthroplasty (RSA) and one arthroscopic superior labrum anterior and posterior (SLAP) repair. Four patients treated with RCR (40%) experienced postoperative complications related to their procedure. These included scapular winging, adhesive capsulitis, stiffness, and one re-tear. Two patients treated with shoulder arthroplasty (28.6%) experienced postoperative complications which included lymphedema and peri-prosthetic fracture following a mechanical fall in one RSA patient and peri-prosthetic infection in one TSA patient. ROM across all groups improved, most significantly in forward flexion and internal rotation among RCR patients ($p<0.001$). Furthermore, a statistically significant improvement in VAS scores was achieved in each group (6.2 ± 2.14 preop, 1.06 ± 1.75 postop $p<0.001$). CONCLUSION: When compared to national averages, complication rates in our cohort were higher (40% vs. 10-17% in RCR patients and 28.6% vs. 4-14% in arthroplasty patients). Upon further scrutiny, many of these complications were independent of a history of XRT and many resolved with appropriate therapy. Most importantly, functional outcomes as measured by ROM and pain scores showed appropriate improvement consistent with normal populations without history of XRT. Thus, our results suggest that performing shoulder surgery after ipsilateral XRT for breast cancer is likely safe, may offer improved pain and improved ROM compared to forgoing surgery without necessarily increasing the risk for postoperative complication.

Orthopedics/Bone and Joint Center

Yedulla NR, **Tramer JS**, **Koolmees DS**, **Franovic S**, **Elhage KG**, **Moutzouros V**, and **Makhni EC**. Preoperative Patient-Reported Outcomes Measurement Information System Computerized Adaptive Testing (PROMIS CAT) Scores Predict Achievement of Minimum Clinically Important Difference Following Anterior Cruciate Ligament Reconstruction Using an Anchor-Based Methodology. *Arthrosc Sports Med Rehabil* 2021; 3(6):e1891-e1898. PMID: 34977645. Full Text

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PURPOSE: To determine the change in Patient-Reported Outcomes Measurement Information System Computerized Adaptive Testing (PROMIS CAT) scores for physical function, pain interference, and depression that constitute minimum clinically important difference (MCID) using an anchor-based technique and to identify pre-operative clinical thresholds in anchor-based MCID that predict likelihood of achieving MCID following anterior cruciate ligament (ACL) reconstruction. METHODS: Adult patients aged 18 years or older undergoing ACL reconstruction that completed both preoperative and postoperative PROMIS CAT assessments and an anchor-based questionnaire were identified over a 23-month period. Anchor-based MCID was determined for PROMIS CAT forms for physical function (PROMIS PF CAT), pain interference (PROMIS PI CAT), and depression (PROMIS D CAT). RESULTS: A total of 137 patients were included for statistical analysis, with pre-operative PROMIS CAT forms completed 27.9 ± 31.2 days before surgery and 492.5 ± 219.9 days postoperatively on average. Statistically significant improvements were observed for all PROMIS CAT domains. PROMIS PF CAT improved from 39.5 ± 8.2 to 55.0 ± 9.7 ($P < .0005$), PROMIS PI CAT from 59.8 ± 7.2 to 48.2 ± 8.3 ($P < .0005$), and PROMIS D CAT from 47.9 ± 8.8 to 41.5 ± 8.6 ($P < .0005$). Anchor-based MCID for each PROMIS CAT form was calculated to be +4.5, -5.4, and -4.1 for PROMIS PF CAT, PROMIS PI CAT, and

PROMIS D CAT, respectively. Mean difference between preoperative and postoperative PROMIS CAT scores exceeded MCID for all domains. The percentage of patients achieving MCID for PROMIS PF CAT, PROMIS PI CAT, and PROMIS D CAT was 85%, 72%, and 55%, respectively. After introduction of 95% specificity cutoffs, the percentage of patients achieving MCID for PROMIS PF CAT, PROMIS PI CAT, and PROMIS D CAT increased to 100% (<35.6 cutoff score), 92% (>65.7 cutoff score), and 83% (>57.5 cutoff score), respectively. CONCLUSIONS: According to anchor-based analysis of PROMIS CAT MCID, ACL reconstruction is effective in improving physical function, pain interference, and depression symptoms. In addition, preoperative PROMIS CAT scores can predict the likelihood of achieving MCID postoperatively. LEVEL OF EVIDENCE: Level IV, prognostic case series.

Otolaryngology – Head and Neck Surgery

Asmaro K, **Yoo F**, Yassin-Kassab A, **Bazydlo M**, **Robin AM**, **Rock JP**, and **Craig JR**. Sinonasal Packing is Not a Requisite for Successful Cerebrospinal Fluid Leak Repair. *J Neurol Surg B Skull Base*:9. PMID: Not assigned. Request Article

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Background Numerous methods have been described to repair nasal cerebrospinal fluid (CSF) leaks. Most studies have focused on optimizing CSF leak repair success, leading to closure rates of 90 to 95%. Objective This study aimed to determine if excellent reconstruction rates could be achieved without using sinonasal packing. Methods A prospective case series of 73 consecutive patients with various CSF leak etiologies and skull base defects was conducted to evaluate reconstruction success without sinonasal packing. The primary outcome measure was postoperative CSF leak. Secondary outcome measures were postoperative epistaxis requiring intervention in operating room or emergency department, infectious sinusitis, and 22-item sinonasal outcome test (SNOT-22) changes. Results Mean age was 54.5 years and 64% were female. Multilayered reconstructions were performed in 55.3% of cases, with collagen or bone epidural inlay grafts, and nasal mucosal grafts or nasoseptal flaps for onlay layers. Onlay-only reconstructions with mucosal grafts or nasoseptal flaps were performed in 44.7% of cases. Tissue sealants were used in all cases, and lumbar drains were used in 40.8% of cases. There were two initial failures (97.4% initial success), but both resolved with lumbar drains alone (no revision surgeries). There were no instances of postoperative epistaxis requiring intervention in the operating room or emergency department. Infectious sinusitis occurred in 2.7% of patients in the first 3 months postoperatively. SNOT-22 did not change significantly from preoperatively to first postoperative visits, then improved over time. Conclusion Nasal CSF leaks from various etiologies and defect sites were successfully repaired without using sinonasal packing, and patients experienced minimal sinonasal morbidity.

Otolaryngology – Head and Neck Surgery

Macias D, Hand BN, Pipkorn P, **Williams AM**, Chang SS, Zenga J, Nilsen ML, Rhoten BA, Huang AT, Osazuwa-Peters N, Maurer S, Balliet W, Li H, Ruggiero KJ, Sterba KR, and Graboyes EM. Association of Inventory to Measure and Assess imaGe Disturbance - Head and Neck Scores With Clinically Meaningful Body Image-Related Distress Among Head and Neck Cancer Survivors. *Front Psychol* 2021; 12:794038. PMID: 34956022. Full Text

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Objective: The Inventory to Measure and Assess imaGe disturbance - Head and Neck (IMAGE-HN) is a validated patient-reported outcome measure of head and neck cancer-related body image-related distress (BID). However, the IMAGE-HN score corresponding to clinically relevant BID is unknown. The study objective is to determine the IMAGE-HN cutoff score that identifies head and neck cancer patients with clinically relevant BID. Methods: We conducted a cross-sectional study at six academic medical centers. Individuals ≥18 years old with a history of head and neck cancer treated with definitive intent were included. The primary outcome measure was the IMAGE-HN. A Receiver Operating Characteristic curve analysis was performed to identify the IMAGE-HN score that maximized sensitivity and specificity relative to a Body Image Scale score of ≥10 (which indicates clinically relevant BID in a general oncology population). To confirm the validity of the IMAGE-HN cutoff score, we compared the severity of depressive [Patient Health Questionnaire-9 (PHQ-9)] and anxiety symptoms [Generalized Anxiety Disorder-7 (GAD-7)], and quality of life [University of Washington-QOL (UW-QOL)] in patients with IMAGE-HN scores above and below the cutoff. Results: Of the 250 patients, 70.4% were male and the mean age was 62.3 years. An IMAGE-HN score of ≥22 was the optimal cutoff score relative to a Body Image Scale score of ≥10 and represents a clinically relevant level of head and neck cancer-related BID. Relative to those with an IMAGE-HN score of <22, patients with IMAGE-HN scores of ≥22 had a clinically meaningful increase in symptoms of depression (mean PHQ-9 score difference = 5.8) and anxiety (mean GAD-7 score difference = 4.1) as well as worse physical (mean UW-QOL score difference = 18.9) and social-emotional QOL (mean UW-QOL score difference = 21.5). Using an IMAGE-HN cutoff score ≥22, 28% of patients had clinically relevant BID. Conclusion: An IMAGE-HN score of ≥22 identifies patients with clinically relevant head and neck cancer-related BID. This score may be used to detect patients who could benefit from strategies to manage their distress, select patients for studies evaluating interventions to manage head and neck cancer-related BID, and improve our understanding of the underlying epidemiology of the disorder.

Otolaryngology – Head and Neck Surgery
Orloff LA, Noel JE, Stack BC, Jr., Russell MD, Angelos P, Baek JH, Brumund KT, Chiang FY, Cunnane MB, Davies L, Frasoldati A, Feng AY, Hegedüs L, Iwata AJ, Kandil E, Kuo J, Lombardi C, Lupo M, Maia AL, McIver B, Na DG, Novizio R, Papini E, Patel KN, Rangel L, Russell JO, Shin J, Shindo M, Shonka DC, Jr., Karcioglu AS, Sinclair C, **Singer M**, Spiezia S, Steck JH, Steward D, Tae K, Tolley N, Valcavi R, Tufano RP, Tuttle RM, Volpi E, Wu CW, Abdelhamid Ahmed AH, and Randolph GW. Radiofrequency ablation and related ultrasound-guided ablation technologies for treatment of benign and malignant thyroid disease: An international multidisciplinary consensus statement of the American Head and Neck Society Endocrine Surgery Section with the Asia Pacific Society of Thyroid Surgery, Associazione Medici Endocrinologi, British Association of Endocrine and Thyroid Surgeons, European Thyroid Association, Italian Society of Endocrine Surgery Units, Korean Society of Thyroid Radiology, Latin American Thyroid Society, and Thyroid Nodules Therapies Association. *Head Neck* 2021; Epub ahead of print. PMID: 34939714. Full Text

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BACKGROUND: The use of ultrasound-guided ablation procedures to treat both benign and malignant thyroid conditions is gaining increasing interest. This document has been developed as an international interdisciplinary evidence-based statement with a primary focus on radiofrequency ablation and is intended to serve as a manual for best practice application of ablation technologies. METHODS: A comprehensive literature review was conducted to guide statement development and generation of best practice recommendations. Modified Delphi method was applied to assess whether statements met consensus among the entire author panel. RESULTS: A review of the current state of ultrasound-guided ablation procedures for the treatment of benign and malignant thyroid conditions is presented. Eighteen best practice recommendations in topic areas of preprocedural evaluation, technique, postprocedural management, efficacy, potential complications, and implementation are provided. CONCLUSIONS: As ultrasound-guided ablation procedures are increasingly utilized in benign and malignant thyroid disease, evidence-based and thoughtful application of best practices is warranted.

Otolaryngology – Head and Neck Surgery

Plawecki AM, **Keller CE**, and **Mayerhoff RM**. Glycogenic Acanthosis: An Unusual Cause of Vocal Fold Leukoplakia. *Laryngoscope* 2021; Epub ahead of print. PMID: 34913490. Full Text

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Glycogenic acanthosis is a common benign lesion of the esophagus; however, reports of extra-esophageal manifestations are exceedingly rare. This case represents the first report of laryngeal glycogenic acanthosis found in a living patient, presenting as vocal fold leukoplakia. Glycogenic acanthosis may be considered among the differential diagnoses of conditions presenting as vocal fold leukoplakia. Laryngoscope, 2021.

Pathology and Laboratory Medicine

Marzinke MA, Greene DN, Bossuyt PM, Chambliss AB, Cirrincione LR, McCudden CR, Melanson SEF, Noguez JH, Patel K, Radix AE, Takwoingi Y, **Winston-McPherson G**, Young BA, and Hoenig MP. Limited Evidence for Use of a Black Race Modifier in eGFR Calculations: A Systematic Review. *Clin Chem* 2021; Epub ahead of print. PMID: 34927677. Full Text

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BACKGROUND: Commonly used estimated glomerular filtration rate (eGFR) equations include a Black race modifier (BRM) that was incorporated during equation derivation. Race is a social construct, and a poorly characterized variable that is applied inconsistently in clinical settings. The BRM results in higher eGFR for any creatinine concentration, implying fundamental differences in creatinine production or excretion in Black individuals compared to other populations. Equations without inclusion of the BRM have the potential to detect kidney disease earlier in patients at the greatest risk of chronic kidney disease (CKD), but also has the potential to over-diagnose CKD or impact downstream clinical interventions. The purpose of this study was to use an evidence- based approach to systematically evaluate the literature relevant to the performance of the eGFR equations with and without the BRM and to examine the clinical impact of the use or removal. CONTENT: PubMed and Embase databases were searched for studies comparing measured GFR to eGFR in racially diverse adult populations using the Modification of Diet in Renal Disease or the 2009-Chronic Kidney Disease Epidemiology Collaboration-creatinine equations based on standardized creatinine measurements. Additionally, we searched for studies comparing clinical use of eGFR calculated with and without the BRM. 8,632 unique publications were identified; an additional 3 studies were added post-hoc. In total, 96 studies were subjected to further analysis and 44 studies were used to make a final assessment. SUMMARY: There is limited published evidence to support the use of a BRM in eGFR equations.

Pathology and Laboratory Medicine

Monga J, **Adrianto I**, **Rogers C**, **Gadgeel S**, **Chitale D**, Alumkal JJ, Beltran H, Zoubeidi A, and **Ghosh J**. Tribbles 2 pseudokinase confers enzalutamide resistance in prostate cancer by promoting lineage plasticity. *J Biol Chem* 2021; 101556. Epub ahead of print. PMID: 34973338. Full Text

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Enzalutamide (Xtandi), a second-generation anti-androgen, is commonly prescribed for therapy of advanced prostate cancer, but enzalutamide-resistant, lethal or incurable disease invariably develops. To understand the molecular mechanism(s) behind enzalutamide resistance, here we comprehensively analyzed a range of prostate tumors and clinically relevant models by gene expression array, immunohistochemistry, and Western blot, which revealed that enzalutamide resistant prostate cancer cells and tumors overexpress the pseudokinase, Tribbles 2 (TRIB2). Inhibition of TRIB2 decreases the viability of enzalutamide-resistant prostate cancer cells, suggesting a critical role of TRIB2 in these cells. Moreover, overexpression of TRIB2 confers resistance in prostate cancer cells to clinically relevant doses of enzalutamide, and this resistance is lost upon inhibition of TRIB2. Interestingly, we found that TRIB2 downregulates the luminal markers AR (androgen receptor) and CK8 (cytokeratin 8) in prostate cancer

cells but upregulates the neuronal transcription factor BRN2 (Brain-2) and the stemness factor SOX2 (SRY-box 2) to induce neuroendocrine characteristics. Finally, we show that inhibition of either TRIB2 or its downstream targets, BRN2 or SOX2, re-sensitizes resistant prostate cancer cells to enzalutamide. Thus, TRIB2 emerges as a potential new regulator of trans-differentiation that confers enzalutamide-resistance in prostate cancer cells via a mechanism involving increased cellular plasticity and lineage switching.

Pathology and Laboratory Medicine

Plawecki AM, **Keller CE**, and **Mayerhoff RM**. Glycogenic Acanthosis: An Unusual Cause of Vocal Fold Leukoplakia. *Laryngoscope* 2021; Epub ahead of print. PMID: 34913490. Full Text

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Glycogenic acanthosis is a common benign lesion of the esophagus; however, reports of extra-esophageal manifestations are exceedingly rare. This case represents the first report of laryngeal glycogenic acanthosis found in a living patient, presenting as vocal fold leukoplakia. Glycogenic acanthosis may be considered among the differential diagnoses of conditions presenting as vocal fold leukoplakia. Laryngoscope, 2021.

Pathology and Laboratory Medicine

Sood A, **Jeong W**, **Palma-Zamora I**, **Abdollah F**, **Butaney M**, **Corsi N**, **Wurst H**, **Arora S**, **Kachroo N**, **Hassan O**, **Gupta N**, Gorin MA, and **Menon M**. Description of Surgical Technique and Oncologic and Functional Outcomes of the Precision Prostatectomy Procedure (IDEAL Stage 1-2b Study). *Eur Urol* 2021; Epub ahead of print. PMID: 34872786. Full Text

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BACKGROUND: The existing treatment options for men with intermediate- or high-volume low-risk prostate cancer (PCa) are associated with a substantial risk of over- or undertreatment. The development of risk-adjusted therapies is an unmet need for these patients. OBJECTIVE: To describe our novel technique of precision prostatectomy, a form of surgical focal therapy that allows radical excision of the index PCa lesion along with >90% prostatic tissue extirpation while preserving the prostatic capsule and seminal vesicle/vas deferens complex on the side contralateral to the dominant cancer lesion, and to report on medium-term functional and oncologic outcomes in the first 88 consecutive men who underwent this procedure between December 2016 and January 2020. DESIGN, SETTING, AND PARTICIPANTS: Men with (1) prostate-specific antigen (PSA) ≤20 ng/ml, (2) clinical T stage ≤cT2, (3) a dominant unilateral lesion with Gleason ≤ 4 + 3 disease with any number or percentage of cores involved ipsilaterally on prostate biopsy, (4) no primary Gleason ≥4 lesion contralaterally, and (5) a preoperative Sexual Health Inventory of Men (SHIM) score of ≥17 (out of 25) with/without phosphodiesterase type-5 inhibitor use who consented to undergo precision prostatectomy were included in this single-arm, single-center, IDEAL stage 2b prospective development study. INTERVENTION: Robotic precision prostatectomy. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: The safety and urinary, sexual, and oncologic

outcomes of the precision prostatectomy technique were studied. Descriptive statistics and Kaplan-Meier analyses were used to assess 12-mo urinary continence (0-1 pad), 12-mo sexual potency (SHIM score ≥17), 36-mo freedom from clinically significant PCa (grade group ≥2), secondary treatments, metastatic disease, and mortality. RESULTS AND LIMITATIONS: At study entry, the median age, PSA, and SHIM score were 60.0 yr (interquartile range [IQR] 54.2-65.9), 5.7 ng/ml (IQR 4.2-7.1), and 22 points (IQR 19-24), respectively. The median follow-up was 25 mo (IQR 14-38). At 12 mo, all patients were continent (0-1 pads), with 90.9% of patients using 0 pads. The median time to urinary continence was 1 mo (IQR 1-4). At 12 mo, 85% of all-comers and 90.2% of the preoperatively potent men were potent. The median time to sexual potency was 4 mo (IQR 4-12). From an oncologic standpoint, at 36 mo an estimated 93.4% of the patients were free from clinically significant residual PCa and 91.7% had not undergone any additional treatment. All patients were alive and free of metastatic disease at 36 mo. CONCLUSIONS: Precision prostatectomy is technically safe and reproducible and offers excellent postoperative functional results. At 36-mo follow-up, the oncologic outcomes and secondary treatment rates appear to be superior to existing ablative focal therapy results. Pending long-term data, a risk-stratified surgical approach to PCa may avoid whole-gland therapy and preserve functional quality of life in men with localized PCa. PATIENT SUMMARY: Precision prostatectomy is a new form of focal therapy for intermediate-risk prostate cancer in which a 5-10-mm rim of prostate capsule is left on the opposite side of the gland to where the dominant cancer is located. The technique appears to be safe and efficacious and adds to the growing armamentarium of risk-adapted therapies for treatment of localized prostate cancer that avoid the adverse effects on urinary and erectile function of whole-gland treatments.

Pathology and Laboratory Medicine

Yuan S, and **Otrock ZK**. Platelet Transfusion: An Update on Indications and Guidelines. *Clin Lab Med* 2021; 41(4):621-634. PMID: 34689969. Full Text

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Platelets are commonly transfused either therapeutically or prophylactically to maintain hemostasis. Most platelet transfusions are used to manage patients with hematologic malignancies. Although platelet transfusion guidelines have been published, platelet transfusion practices are still heterogeneous. Platelet transfusion guidelines partly lack recommendations or differ in the platelet threshold recommendations in some clinical situations. This article reviews platelet transfusions focusing on transfusion guidelines and platelet thresholds in different clinical settings.

Pharmacy

McKinnon JE, **Wang DD**, **Zervos M**, **Saval M**, **Marshall-Nightengale L**, **Kilgore P**, **Pabla P**, **Szandzik E**, **Maksimowicz-McKinnon K**, and **O'Neill WW**. Safety and Tolerability of Hydroxychloroquine in healthcare workers and first responders for the prevention of COVID-19: WHIP COVID-19 Study. *Int J Infect Dis* 2021; Epub ahead of print. PMID: 34954095. Full Text

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BACKGROUND: Healthcare workers (HCW) are among the highest risk groups for acquisition of COVID-19 due to occupational exposures. The WHIP COVID-19 study aimed to evaluate the safety and efficacy of hydroxychloroquine (HCQ) as chemoprophylaxis for SARS-CoV-2 infection in this population. METHODS: HCW, first responders and other occupationally high-risk participants were enrolled in a

randomized, placebo-controlled clinical study of HCQ from April-October 2020. The trial compared daily versus weekly HCQ to placebo and to a prospective cohort on HCQ for autoimmune diseases. Participants were followed for 8 weeks. Serology or a positive PCR test were used to determine laboratory confirmed clinical cases. RESULTS: 624 participants were randomized to placebo (n=200), weekly HCQ (n=201), daily HCQ (n=197). For the primary safety endpoint, 279 (44.7%) participants experienced AE level II or lower (total AEs n=589), similar rates in all randomized groups (p=0.188) with no hospitalizations or interventions required. Only 4 laboratory confirmed COVID-19 cases occurred, with 2 in the placebo arm and one in each HCQ randomized arm. CONCLUSIONS: This randomized placebo-controlled trial was able to demonstrate the safety of HCQ outpatient chemoprophylaxis in high-risk groups against COVID-19. Future studies of chemoprophylaxis for SARS-CoV-2 are needed as the epidemic continues worldwide.

Public Health Sciences

Asmaro K, **Yoo F**, Yassin-Kassab A, **Bazydlo M**, **Robin AM**, **Rock JP**, and **Craig JR**. Sinonasal Packing is Not a Requisite for Successful Cerebrospinal Fluid Leak Repair. *J Neurol Surg B Skull Base*:9. PMID: Not assigned. Request Article

Background Numerous methods have been described to repair nasal cerebrospinal fluid (CSF) leaks. Most studies have focused on optimizing CSF leak repair success, leading to closure rates of 90 to 95%. Objective This study aimed to determine if excellent reconstruction rates could be achieved without using sinonasal packing. Methods A prospective case series of 73 consecutive patients with various CSF leak etiologies and skull base defects was conducted to evaluate reconstruction success without sinonasal packing. The primary outcome measure was postoperative CSF leak. Secondary outcome measures were postoperative epistaxis requiring intervention in operating room or emergency department, infectious sinusitis, and 22-item sinonasal outcome test (SNOT-22) changes. Results Mean age was 54.5 years and 64% were female. Multilayered reconstructions were performed in 55.3% of cases, with collagen or bone epidural inlay grafts, and nasal mucosal grafts or nasoseptal flaps for onlay layers. Onlay-only reconstructions with mucosal grafts or nasoseptal flaps were performed in 44.7% of cases. Tissue sealants were used in all cases, and lumbar drains were used in 40.8% of cases. There were two initial failures (97.4% initial success), but both resolved with lumbar drains alone (no revision surgeries). There were no instances of postoperative epistaxis requiring intervention in the operating room or emergency department. Infectious sinusitis occurred in 2.7% of patients in the first 3 months postoperatively. SNOT-22 did not change significantly from preoperatively to first postoperative visits, then improved over time. Conclusion Nasal CSF leaks from various etiologies and defect sites were successfully repaired without using sinonasal packing, and patients experienced minimal sinonasal morbidity.

Public Health Sciences

Bayard S, Fasano G, **Chen Y**, Davis M, Drotman M, **Bensenhaver J**, Swistel A, Simmons R, Marti J, and Newman L. Screening mammography mitigates breast cancer disparities through early detection of triple negative breast cancer. *Clin Imaging* 2021; 80:430-437. PMID: 34543867. Full Text

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PURPOSE: Screening mammography improves breast cancer survival through early detection, but Triple Negative Breast Cancer (TNBC) is more difficult to detect on mammography and has lower survival compared to non-TNBC, even when detected at early stages. TNBC is twice as common among African American (AA) compared to White American (WA) women, thereby contributing to the 40% higher breast cancer mortality rates observed in AA women. The role of screening mammography in addressing breast cancer disparities is therefore worthy of study. METHODS: Outcomes were evaluated for TNBC patients treated in the prospectively-maintained databases of academic cancer programs in two metropolitan cities of the Northeast and Midwest, 1998-2018. RESULTS: Of 756 TNBC cases, 301 (39.8%) were

mammographically screen-detected. 46% of 189 AA and 38.5% of 460 WA patients had screen-detected TNBC (p = 0.16). 25.3% of 257 TNBC cases ≤50 years old had screen-detected disease compared to 47.3% of 499 TNBC cases >50 years old (p < 0.0001). 220/301 (73.1%) screen-detected TNBC cases were T1 lesions versus 118/359 (32.9%) non-screen-detected cases (p < 0.0001). Screen-detected TNBC was more likely to be node-negative (51.9% v. 40.4%; p < 0.0001). Five-year overall survival was better in screen-detected TNBC compared to nonscreen-detected TNBC (92.8% v. 81.5%; p < 0.0001) in the entire cohort. The magnitude of this effect was most significant among AA patients (Fig. 1). Screening-related survival patterns were similar among AA and WA patients in both cities. CONCLUSION: Data from two different cities demonstrates the value of screening mammography to mitigate breast cancer disparities in AA women through the early detection of TNBC.

Public Health Sciences

Brodie S, **Lee HK**, **Jiang W**, **Cazacu S**, **Xiang C**, **Poisson LM**, **Datta I**, **Kalkanis S**, Ginsberg D, and **Brodie C**. Correction: The novel long non-coding RNA TALNEC2, regulates tumor cell growth and the stemness and radiation response of glioma stem cells. *Oncotarget* 2021; 12(26):2546-2547. PMID: 34966487. Full Text

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Public Health Sciences

Buechler CR, **Sagher E**, **Tisack A**, **Jacobsen G**, **Lim HW**, **McHargue C**, **Friedman BJ**, **Mi QS**, **Ozog DM**, and **Veenstra J**. Contribution of Socioeconomic Risk Factors within a Diverse Mycosis Fungoides Cohort from Detroit, MI. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34920029. Full Text

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Public Health Sciences

Cook AE, **Aref I**, **Burmeister C**, **Hijaz M**, and **Elshaikh MA**. Quantification of recurrence risk based on number of adverse prognostic factors in women with stage I uterine endometrioid carcinoma. *J Turk Ger Gynecol Assoc* 2021; 22(4):262-267. PMID: 34866366. Full Text

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OBJECTIVE: The goal was to develop an updated model to predict the risk of recurrence, based on the number of adverse pathologic features in women with International Federation of Gynecology and Obstetrics stage I uterine endometrioid carcinoma, who did not undergo any adjuvant treatment. MATERIAL AND METHODS: Women at a single center who underwent surgical staging without adjuvant therapy between January 1990 and December 2019 were included. Cox proportional hazards model was used to identify independent predictors of relapse free survival (RFS). Prognostic groups were then created based on the number of independent predictors of recurrence that were identified (0, 1, or 2-3 risk factors). Overall survival (OS) and disease specific survival (DSS) were also calculated for each group. RESULTS: In total 1133 women were eligible for inclusion. Median follow-up was 84 months. Independent prognostic factors of recurrence included: age ≥60; grade 2 or 3 differentiation; and presence of lymphovascular space invasion (LVSI). Due to the small number of patients with either 2 or 3

risk factors, these groups were combined into one (group 2/3). Isolated vaginal cuff recurrence was the most common site of recurrence in all study groups (2%, 7%, and 17% for groups 0, 1, and 2/3, respectively). Five-year RFS rates were 96%, 85%, and 57% for groups 0, 1, and 2/3 ($p<0.01$), respectively. Five-year DSS rates were 99%, 96%, and 85% and 5-year OS rates were 94%, 85%, and 62% ($p<0.01$), respectively. CONCLUSION: We identified older age, high grade, and presence of LVSI as independent predictors of recurrence for women with stage I uterine endometrioid carcinoma. Using these prognostic factors, recurrence risk can be quantified for individual patients, and these factors can be used in deciding the appropriate adjuvant management course.

Public Health Sciences

Fonseca W, Asai N, Yagi K, Malinczak CA, **Savickas G**, **Johnson CC**, **Murray S**, **Zoratti EM**, Lukacs NW, **Li J**, and Schuler Iv CF. COVID-19 Modulates Inflammatory and Renal Markers That May Predict Hospital Outcomes among African American Males. *Viruses* 2021; 13(12). PMID: 34960684. Full Text

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BACKGROUND AND OBJECTIVES: African Americans and males have elevated risks of infection, hospitalization, and death from SARS-CoV-2 in comparison with other populations. We report immune responses and renal injury markers in African American male patients hospitalized for COVID-19. METHODS: This was a single-center, retrospective study of 56 COVID-19 infected hospitalized African American males 50+ years of age selected from among non-intensive care unit (ICU) and ICU status patients. Demographics, hospitalization-related variables, and medical history were collected from electronic medical records. Plasma samples collected close to admission (≤2 days) were evaluated for cytokines and renal markers; results were compared to a control group (n = 31) and related to COVID-19 in-hospital mortality. RESULTS: Among COVID-19 patients, eight (14.2%) suffered in-hospital mortality; seven (23.3%) in the ICU and one (3.8%) among non-ICU patients. Interleukin (IL)-18 and IL-33 were elevated at admission in COVID-19 patients in comparison with controls. IL-6, IL-18, MCP-1/CCL2, MIP-1α/CCL3, IL-33, GST, and osteopontin were upregulated at admission in ICU patients in comparison with controls. In addition to clinical factors, MCP-1 and GST may provide incremental value for risk prediction of COVID-19 in-hospital mortality. CONCLUSIONS: Qualitatively similar inflammatory responses were observed in comparison to other populations reported in the literature, suggesting non-immunologic factors may account for outcome differences. Further, we provide initial evidence for cytokine and renal toxicity markers as prognostic factors for COVID-19 in-hospital mortality among African American males.

Public Health Sciences

Gifford L, **Johnson CC**, **Haque N**, **Passalacqua KD**, **Swiderek J**, and **Kalkanis S**. COVID-19 in the hotspot of Metropolitan Detroit: A multi-faceted health system experience. *Int J Health Plann Manage* 2021; Epub ahead of print. PMID: 34859491. Full Text

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Health systems were abruptly plunged into a crisis as SARS-CoV-2 exploded into a pandemic in spring 2020. In March-April 2020, Metropolitan Detroit was a US "hotspot." As a large health system with five

hospitals and two behavioural health inpatient facilities, a health insurance company, a medical group and physician network, and 41 ambulatory clinics normally hosting over 10,000 daily patient encounters, the Henry Ford Health System deployed numerous strategies in the management of this upheaval. As hospitals and Emergency Departments were inundated with COVID-19 patients, other services and activities needed to shut down as state-mandated policies were promulgated, new internal and external communication networks established, and management of employees and resources such as ventilators, ICU beds, personal protective equipment, and laboratory supplies became critical challenges. We describe herein the system-wide strategies implemented and lessons learned in the operation of a health system in the initial throes of a global pandemic.

Public Health Sciences

Hamilton T, **Macki M**, Oh SY, **Bazydlo M**, **Schultz L**, **Zakaria HM**, Khalil JG, Perez-Cruet M, Aleem I, Park P, Easton R, **Nerenz DR**, **Schwalb J**, **Abdulhak M**, and **Chang V**. The association of patient education level with outcomes after elective lumbar surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2021; 1-9. Epub ahead of print. PMID: 34891131. Full Text

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OBJECTIVE: Socioeconomic factors have been shown to impact a host of healthcare-related outcomes. Level of education is a marker of socioeconomic status. This study aimed to investigate the relationship between patient education level and outcomes after elective lumbar surgery and to characterize any education-related disparities. METHODS: The Michigan Spine Surgery Improvement Collaborative registry was queried for all lumbar spine operations. Primary outcomes included patient satisfaction determined by the North American Spine Society patient satisfaction index, and reaching the minimum clinically important difference of Patient-Reported Outcomes Measurement Information System Physical Function score and return to work up to 2 years after surgery. Multivariate Poisson generalized estimating equation models reported adjusted risk ratios. RESULTS: A total of 26,229 lumbar spine patients had data available for inclusion in this study. On multivariate generalized estimating equation analysis all comparisons were done versus the high school (HS)/general equivalency development (GED)-level cohort. For North American Spine Society satisfaction scores after surgery the authors observed the following: at 90 days the likelihood of satisfaction significantly decreased by 11% ($p < 0.001$) among < HS, but increased by 1% ($p = 0.52$) among college-educated and 3% ($p = 0.011$) among postcollege-educated cohorts compared to the HS/GED cohort; at 1 year there was a decrease of 9% ($p = 0.02$) among < HS and increases of 3% ($p = 0.02$) among college-educated and 9% ($p < 0.001$) among postcollege-educated patients; and at 2 years, there was an increase of 5% ($p = 0.001$) among postcollege-educated patients compared to the < HS group. The likelihood of reaching a minimum clinically important difference of Patient-Reported Outcomes Measurement Information System Physical Function score at 90 days increased by 5% ($p = 0.005$) among college-educated and 9% ($p < 0.001$) among postcollege-educated cohorts; at 1 year, all comparison cohorts demonstrated significance, with a decrease of 12% ($p = 0.007$) among < HS, but an increase by 6% ($p < 0.001$) among college-educated patients and 14% ($p < 0.001$) among postcollege-educated compared to the HS/GED cohort; at 2 years, there was a significant decrease by 19% ($p = 0.003$) among the < HS cohort, an increase by 8% ($p = 0.001$) among the college-educated group, and an increase by 16% ($p < 0.001$) among the postcollege-educated group. For return to work, a significant increase was demonstrated at 90 days and 1 year when comparing the HS or less group with college or postcollege cohorts. CONCLUSIONS: This study demonstrated negative associations on all primary outcomes with lower levels of education. This finding suggests a potential disparity linked to education in elective spine surgery.

Public Health Sciences

Jesse MT, Clifton E, **Kim DY**, **Nicholson D**, **Patil R**, **Bhavsar S**, **Desai S**, **Gartrelle K**, **Eshelman A**, **Fleagle E**, **Ahmedani B**, Carlozzi NE, **Tang A**, and **Patel A**. Prerenal Transplant Education and Evaluation Positively Impacts Outcomes. *Prog Transplant* 2021; Epub ahead of print. PMID: 34860614. Full Text

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Introduction: An outstanding question in kidney transplantation is how to prepare candidates and their social supports for optimal posttransplant outcomes. Project Aims: This program evaluation assessed whether a pretransplant quality improvement clinic improved clinical outcomes in the year posttransplant compared to recipients receiving standard of care. Design: The Countdown to Transplant Clinic was implemented with kidney transplant candidates expected to receive a transplant within the next few months. The clinic included an enhanced education session on posttransplant lifestyle management, confirmation of support (≥2 adults), and evaluations by transplant social work, psychology, and nephrology. Results: Seventy-five patients participated in the clinic and underwent a transplant. A retrospective chart review of posttransplant laboratory values, rehospitalizations (within 3-months posttransplant), biopsy-confirmed graft failure, and mortality (within 1-year posttransplant) were collected from both groups. Univariate and multivariate propensity score-weighted linear or logistic regression models were used to evaluate the association between clinic participation and outcomes. In models adjusting for relevant covariates, participation in The Countdown to Transplant Clinic (vs standard care) was associated with a lower coefficient of variation of serum tacrolimus (all values collected 3-12 months posttransplant), 30-day posttransplant white blood cell counts (but not 90-day), 90-day posttransplant potassium, and 30 and 31 to 90 days rehospitalizations. Clinic participation did not predict serum glucose levels at 30- or 90-days posttransplant. Due to low rates of rejection and mortality, meaningful comparisons were not possible. Conclusion: Participation in a pretransplant, multicomponent clinic may improve certain outcomes of interest posttransplantation. Pilot testing for feasibility for randomized controlled trials is a necessary next step.

Public Health Sciences

McAllister P, **Lamerato L**, Krasenbaum LJ, Cohen JM, Tangirala K, Thompson S, Driessen M, Casciano J, Dotiwala Z, and Mauskop A. Real-world impact of fremanezumab on migraine symptoms and resource utilization in the United States. *J Headache Pain* 2021; 22(1):156. PMID: 34930112. Full Text

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BACKGROUND: Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), is approved for migraine prevention in adults. Real-world

data on the effectiveness of fremanezumab are limited. This retrospective, observational cohort study assessed patient-reported migraine symptoms, health care resource utilization (HCRU), and direct medical costs before and after fremanezumab treatment initiation. METHODS: Data were extracted from September 2018 through June 2020 from the Midwest component of EMRClaims+®, an integrated health services database containing > 20 million medical records from national commercial insurance claims, Medicare claims, and regional electronic medical records. Patients included in the cohort analysis were aged ≥ 18 years and were administered fremanezumab, with enrollment or treatment history for ≥ 6 months prior (pre-index) to initiating fremanezumab (index date) and ≥ 1 month after the index date (post-index), and without pregnancy or pregnancy-related encounters during the study period. Patient-reported headache frequency, migraine pain intensity (MPI), composite migraine symptoms, and HCRU were assessed pre-index and ≥ 1 month after fremanezumab initiation. Wilcoxon signed-rank tests were used to compare means of migraine symptoms and outcomes and HCRU before and after fremanezumab initiation. RESULTS: Overall, 172 patients were eligible for analysis. Of patients who self-reported (n = 129), 83.7% reported improvement in headache frequency or symptoms after fremanezumab treatment. Specifically, headache frequency decreased by 63% after fremanezumab initiation: mean (standard deviation) headache frequency was 22.24 (9.29) days per month pre-index versus 8.24 (7.42) days per month post-index (P < 0.0001). Mean MPI also decreased by 18% after fremanezumab initiation: MPI was 5.47 (3.19) pre-index versus 4.51 (3.34) post-index (P = 0.014). Mean emergency room (ER) visits per month decreased from 0.72 to 0.54 (P = 0.003), and mean outpatient visits per month decreased from 1.04 to 0.81 (P < 0.001). Mean hospitalizations per month decreased, but the results did not reach statistical significance (P = 0.095). Hospitalization and ER costs decreased, while outpatient costs increased, from pre-index to post-index, but differences were not statistically significant (P ≥ 0.232). CONCLUSIONS: Significant reductions in headache frequency, MPI, and HCRU were observed after fremanezumab initiation in patients with migraine in a US real-world setting.

Public Health Sciences

McKinnon JE, **Wang DD**, **Zervos M**, **Saval M**, **Marshall-Nightengale L**, **Kilgore P**, **Pabla P**, **Szandzik E**, **Maksimowicz-McKinnon K**, and **O'Neill WW**. Safety and Tolerability of Hydroxychloroquine in healthcare workers and first responders for the prevention of COVID-19: WHIP COVID-19 Study. *Int J Infect Dis* 2021; Epub ahead of print. PMID: 34954095. Full Text

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BACKGROUND: Healthcare workers (HCW) are among the highest risk groups for acquisition of COVID-19 due to occupational exposures. The WHIP COVID-19 study aimed to evaluate the safety and efficacy of hydroxychloroquine (HCQ) as chemoprophylaxis for SARS-CoV-2 infection in this population. METHODS: HCW, first responders and other occupationally high-risk participants were enrolled in a randomized, placebo-controlled clinical study of HCQ from April-October 2020. The trial compared daily versus weekly HCQ to placebo and to a prospective cohort on HCQ for autoimmune diseases. Participants were followed for 8 weeks. Serology or a positive PCR test were used to determine laboratory confirmed clinical cases. RESULTS: 624 participants were randomized to placebo (n=200), weekly HCQ (n=201), daily HCQ (n=197). For the primary safety endpoint, 279 (44.7%) participants experienced AE level II or lower (total AEs n=589), similar rates in all randomized groups (p=0.188) with no hospitalizations or interventions required. Only 4 laboratory confirmed COVID-19 cases occurred, with 2 in the placebo arm and one in each HCQ randomized arm. CONCLUSIONS: This randomized placebo-controlled trial was able to demonstrate the safety of HCQ outpatient chemoprophylaxis in high-risk groups against COVID-19. Future studies of chemoprophylaxis for SARS-CoV-2 are needed as the epidemic continues worldwide.

Public Health Sciences

Monga J, **Adrianto I**, **Rogers C**, **Gadgeel S**, **Chitale D**, Alumkal JJ, Beltran H, Zoubeidi A, and **Ghosh J**. Tribbles 2 pseudokinase confers enzalutamide resistance in prostate cancer by promoting lineage plasticity. *J Biol Chem* 2021; 101556. Epub ahead of print. PMID: 34973338. Full Text

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Enzalutamide (Xtandi), a second-generation anti-androgen, is commonly prescribed for therapy of advanced prostate cancer, but enzalutamide-resistant, lethal or incurable disease invariably develops. To understand the molecular mechanism(s) behind enzalutamide resistance, here we comprehensively analyzed a range of prostate tumors and clinically relevant models by gene expression array, immunohistochemistry, and Western blot, which revealed that enzalutamide resistant prostate cancer cells and tumors overexpress the pseudokinase, Tribbles 2 (TRIB2). Inhibition of TRIB2 decreases the viability of enzalutamide-resistant prostate cancer cells, suggesting a critical role of TRIB2 in these cells. Moreover, overexpression of TRIB2 confers resistance in prostate cancer cells to clinically relevant doses of enzalutamide, and this resistance is lost upon inhibition of TRIB2. Interestingly, we found that TRIB2 downregulates the luminal markers AR (androgen receptor) and CK8 (cytokeratin 8) in prostate cancer cells but upregulates the neuronal transcription factor BRN2 (Brain-2) and the stemness factor SOX2 (SRY-box 2) to induce neuroendocrine characteristics. Finally, we show that inhibition of either TRIB2 or its downstream targets, BRN2 or SOX2, re-sensitizes resistant prostate cancer cells to enzalutamide. Thus, TRIB2 emerges as a potential new regulator of trans-differentiation that confers enzalutamide-resistance in prostate cancer cells via a mechanism involving increased cellular plasticity and lineage switching.

Public Health Sciences

White Perkins D, **Milan P**, **Miazek K**, **Havstad S**, and **Wegienka G**. Identifying factors affecting diabetes education program participation within a metro Detroit integrated health system. *Prev Med Rep* 2021; 24:101646. PMID: 34976695. Full Text

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Diabetes self-management education and support (DSMES) can help people achieve optimal disease control, yet these services often remain underutilized. People referred to these programs by their provider can become disengaged in the program at several key steps. This study applies Classification and Regression Tree analysis to 3796 people with diabetes at a single health system based in the Detroit metropolitan area who were referred for DSMES provided by the health system to determine demographic patterns of those who were successfully contacted to schedule program intake appointments, those who did not attend their intake appointment, and those who began but did not complete their personalized DSMES program. White people > 43 years of age, those with a prior A1C value > 8.9 and those with Medicaid insurance had the highest rate of not being successfully contacted for their intake appointment. Those who did not attend their intake appointment tended to have Medicaid

insurance, be younger than 48 years, and have A1C > 8.1. Within the Medicare or private insurance groups, those who did not attend were more likely to be female, of Black race and not partnered. Older males with a lower A1C (≤8.3%) had the lowest rate (34.0%) of failing to complete their DSMES plan. The data showed that almost half of those referred were not successfully contacted. The overall low completion rate of 13.2% confirms the need to examine factors predictive of participation and completion. This study highlights process improvement changes to improve personalization of outreach and engagement.

Public Health Sciences

Zhou Y, **Li J**, **Gordon SC**, **Trudeau S**, **Rupp LB**, Boscarino JA, Daida YG, Schmidt MA, and **Lu M**. Laboratory monitoring and antiviral treatment for chronic hepatitis B among routine care patients in the United States. *J Viral Hepat* 2021; Epub ahead of print. PMID: 34905259. Full Text

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We investigated factors associated with rates of recommended monitoring of chronic hepatitis B (HBV) patients for viral DNA and alanine aminotransferase (ALT), and initiation of antiviral treatment among eligible patients, in a US cohort of patients under routine care. Patients were categorised by treatment indication: definite, equivocal or ineligible. Baseline covariates included demographics, clinical characteristics and specialist care status. 'Recommended monitoring' was defined ≥1 ALT or HBV DNA test per year. Logit models, univariate then multivariable, were used to evaluate factors associated with monitoring and treatment. Among 3,830 patients, treatment was received by 67.5% (788/1168 patients) in the 'definite' category, and 34.1% (208/610 patients) in the 'equivocal' category, of whom 109 moved up to 'definite' status at some point during follow-up. Sex, age and specialist care were independently associated with receipt of treatment in 'definite' patients. Routine monitoring rates were high prior to treatment in 'definite/ treated' patients (ALT: 77%; DNA: 85%) but declined afterwards (ALT 63%; DNA 36%). Rates of monitoring were lower in 'definite/ untreated' patients (ALT: 48%; DNA: 32%). Among 'equivocal/ treated' patients, lower age and comorbidity scores were associated with receipt of treatment; ALT monitoring rates were similar before and after treatment initiation (41% and 46%, respectively), while rates of DNA monitoring declined (55% and 29%). Monitoring among 'treatment ineligible' patients was similar to those in the 'equivocal' and untreated 'definite' groups. A large proportion of US HBV patients under routine care did not receive recommended annual laboratory monitoring, especially after initiation of antiviral treatment, and nearly one-third of patients with 'definite' indications for antiviral therapy remained untreated.

Pulmonary and Critical Care Medicine

Baughman RP, Valeyre D, Korsten P, Mathioudakis AG, Wuyts WA, Wells A, Rottoli P, Nunes H, Lower EE, Judson MA, Israel-Biet D, Grutters JC, Drent M, Culver DA, Bonella F, Antoniou K, Martone F, Quadder B, Spitzer G, Nagavci B, Tonia T, Rigau D, and **Ouellette DR**. ERS clinical practice guidelines on treatment of sarcoidosis. *Eur Respir J* 2021; 58(6). PMID: 34140301. Full Text

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BACKGROUND: The major reasons to treat sarcoidosis are to lower the morbidity and mortality risk or to improve quality of life (QoL). The indication for treatment varies depending on which manifestation is the cause of symptoms: lungs, heart, brain, skin or other manifestations. While glucocorticoids remain the first choice for initial treatment of symptomatic disease, prolonged use is associated with significant toxicity. Glucocorticoid-sparing alternatives are available. The presented treatment guidelines aim to provide guidance to physicians treating the very heterogenous sarcoidosis manifestations. METHODS: A European Respiratory Society Task Force committee composed of clinicians, methodologists and patients with experience in sarcoidosis developed recommendations based on the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) methodology. The committee developed eight PICO (Patients, Intervention, Comparison, Outcomes) questions and these were used to make specific evidence-based recommendations. RESULTS: The Task Force committee delivered 12 recommendations for seven PICOs. These included treatment of pulmonary, cutaneous, cardiac and neurologic disease as well as fatigue. One PICO question regarding small-fibre neuropathy had insufficient evidence to support a recommendation. In addition to the recommendations, the committee provided information on how they use alternative treatments, when there was insufficient evidence to support a recommendation. CONCLUSIONS: There are many treatments available to treat sarcoidosis. Given the diverse nature of the disease, treatment decisions require an assessment of organ involvement, risk for significant morbidity, and impact on QoL of the disease and treatment.

Pulmonary and Critical Care Medicine

Gifford L, **Johnson CC**, **Haque N**, **Passalacqua KD**, **Swiderek J**, and **Kalkanis S**. COVID-19 in the hotspot of Metropolitan Detroit: A multi-faceted health system experience. *Int J Health Plann Manage* 2021; Epub ahead of print. PMID: 34859491. Full Text

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Health systems were abruptly plunged into a crisis as SARS-CoV-2 exploded into a pandemic in spring 2020. In March-April 2020, Metropolitan Detroit was a US "hotspot." As a large health system with five hospitals and two behavioural health inpatient facilities, a health insurance company, a medical group and physician network, and 41 ambulatory clinics normally hosting over 10,000 daily patient encounters, the Henry Ford Health System deployed numerous strategies in the management of this upheaval. As hospitals and Emergency Departments were inundated with COVID-19 patients, other services and activities needed to shut down as state-mandated policies were promulgated, new internal and external communication networks established, and management of employees and resources such as ventilators, ICU beds, personal protective equipment, and laboratory supplies became critical challenges. We describe herein the system-wide strategies implemented and lessons learned in the operation of a health system in the initial throes of a global pandemic.

Pulmonary and Critical Care Medicine

Husnain SMN, and Shojaee S. Hepatic Hydrothorax and Congestive Heart Failure Induced Pleural Effusion. *Clin Chest Med* 2021; 42(4):625-635. PMID: 34774170. Full Text

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Pleural effusions (PEs) are frequently encountered in routine clinical practice, affecting more than 3000 people per million population every year. Heart and liver failures are two of the most common causes of transudative PE. Because these effusions have nonmalignant etiologies, they are commonly referred to as benign effusions despite of the poor prognosis they foretell in their refractory stages. Like malignant effusions, symptom management is important and plays a significant role in palliation when these effusions become refractory to medical therapy.

Radiation Oncology

Cook AE, **Aref I**, **Burmeister C**, **Hijaz M**, and **Elshaikh MA**. Quantification of recurrence risk based on number of adverse prognostic factors in women with stage I uterine endometrioid carcinoma. *J Turk Ger Gynecol Assoc* 2021; 22(4):262-267. PMID: 34866366. Full Text

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OBJECTIVE: The goal was to develop an updated model to predict the risk of recurrence, based on the number of adverse pathologic features in women with International Federation of Gynecology and Obstetrics stage I uterine endometrioid carcinoma, who did not undergo any adjuvant treatment. MATERIAL AND METHODS: Women at a single center who underwent surgical staging without adjuvant therapy between January 1990 and December 2019 were included. Cox proportional hazards model was used to identify independent predictors of relapse free survival (RFS). Prognostic groups were then created based on the number of independent predictors of recurrence that were identified (0, 1, or 2-3 risk factors). Overall survival (OS) and disease specific survival (DSS) were also calculated for each group. RESULTS: In total 1133 women were eligible for inclusion. Median follow-up was 84 months. Independent prognostic factors of recurrence included: age ≥60; grade 2 or 3 differentiation; and presence of lymphovascular space invasion (LVSI). Due to the small number of patients with either 2 or 3 risk factors, these groups were combined into one (group 2/3). Isolated vaginal cuff recurrence was the most common site of recurrence in all study groups (2%, 7%, and 17% for groups 0, 1, and 2/3, respectively). Five-year RFS rates were 96%, 85%, and 57% for groups 0, 1, and 2/3 ($p<0.01$), respectively. Five-year DSS rates were 99%, 96%, and 85% and 5-year OS rates were 94%, 85%, and

62% (p<0.01), respectively. CONCLUSION: We identified older age, high grade, and presence of LVSI as independent predictors of recurrence for women with stage I uterine endometrioid carcinoma. Using these prognostic factors, recurrence risk can be quantified for individual patients, and these factors can be used in deciding the appropriate adjuvant management course.

Radiation Oncology

Willett G, Chang DT, Czito BG, Liauw SL, Wo JY, Klein PEE, Chen Z, Carlson DJ, and **Chetty IJ**. Reflections on Anthony Zietman From Gastrointestinal Cancer and Physics Editors. *Int J Radiat Oncol Biol Phys* 2021; 111(5):1114-1117. PMID: 34793734. Full Text

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Research Administration

Ebrahimzadeh E, Shams M, Seraji M, Sadjadi SM, Rajabion L, and **Soltanian-Zadeh H**. Localizing Epileptic Foci Using Simultaneous EEG-fMRI Recording: Template Component Cross-Correlation. *Front Neurol* 2021; 12:695997. PMID: 34867704. Full Text

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Conventional EEG-fMRI methods have been proven to be of limited use in the sense that they cannot reveal the information existing in between the spikes. To resolve this issue, the current study obtains the epileptic components time series detected on EEG and uses them to fit the Generalized Linear Model (GLM), as a substitution for classical regressors. This approach allows for a more precise localization, and equally importantly, the prediction of the future behavior of the epileptic generators. The proposed method approaches the localization process in the component domain, rather than the electrode domain (EEG), and localizes the generators through investigating the spatial correlation between the candidate components and the spike template, as well as the medical records of the patient. To evaluate the contribution of EEG-fMRI and concordance between fMRI and EEG, this method was applied on the data of 30 patients with refractory epilepsy. The results demonstrated the significant numbers of 29 and 24 for concordance and contribution, respectively, which mark improvement as compared to the existing literature. This study also shows that while conventional methods often fail to properly localize the epileptogenic zones in deep brain structures, the proposed method can be of particular use. For further evaluation, the concordance level between IED-related BOLD clusters and Seizure Onset Zone (SOZ) has been quantitatively investigated by measuring the distance between IED/SOZ locations and the BOLD clusters in all patients. The results showed the superiority of the proposed method in delineating the spike-generating network compared to conventional EEG-fMRI approaches. In all, the proposed method goes beyond the conventional methods by breaking the dependency on spikes and using the outside-the-scanner spike templates and the selected components, achieving an accuracy of 97%. Doing

so, this method contributes to improving the yield of EEG-fMRI and creates a more realistic perception of the neural behavior of epileptic generators which is almost without precedent in the literature.

Research Administration

Fonseca W, Asai N, Yagi K, Malinczak CA, **Savickas G**, **Johnson CC**, **Murray S**, **Zoratti EM**, Lukacs NW, **Li J**, and Schuler Iv CF. COVID-19 Modulates Inflammatory and Renal Markers That May Predict Hospital Outcomes among African American Males. *Viruses* 2021; 13(12). PMID: 34960684. Full Text

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BACKGROUND AND OBJECTIVES: African Americans and males have elevated risks of infection, hospitalization, and death from SARS-CoV-2 in comparison with other populations. We report immune responses and renal injury markers in African American male patients hospitalized for COVID-19. METHODS: This was a single-center, retrospective study of 56 COVID-19 infected hospitalized African American males 50+ years of age selected from among non-intensive care unit (ICU) and ICU status patients. Demographics, hospitalization-related variables, and medical history were collected from electronic medical records. Plasma samples collected close to admission (≤2 days) were evaluated for cytokines and renal markers; results were compared to a control group (n = 31) and related to COVID-19 in-hospital mortality. RESULTS: Among COVID-19 patients, eight (14.2%) suffered in-hospital mortality; seven (23.3%) in the ICU and one (3.8%) among non-ICU patients. Interleukin (IL)-18 and IL-33 were elevated at admission in COVID-19 patients in comparison with controls. IL-6, IL-18, MCP-1/CCL2, MIP-1α/CCL3, IL-33, GST, and osteopontin were upregulated at admission in ICU patients in comparison with controls. In addition to clinical factors, MCP-1 and GST may provide incremental value for risk prediction of COVID-19 in-hospital mortality. CONCLUSIONS: Qualitatively similar inflammatory responses were observed in comparison to other populations reported in the literature, suggesting non-immunologic factors may account for outcome differences. Further, we provide initial evidence for cytokine and renal toxicity markers as prognostic factors for COVID-19 in-hospital mortality among African American males.

Rheumatology

McKinnon JE, **Wang DD**, **Zervos M**, **Saval M**, **Marshall-Nightengale L**, **Kilgore P**, **Pabla P**, **Szandzik E**, **Maksimowicz-McKinnon K**, and **O'Neill WW**. Safety and Tolerability of Hydroxychloroquine in healthcare workers and first responders for the prevention of COVID-19: WHIP COVID-19 Study. *Int J Infect Dis* 2021; Epub ahead of print. PMID: 34954095. Full Text

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BACKGROUND: Healthcare workers (HCW) are among the highest risk groups for acquisition of COVID-19 due to occupational exposures. The WHIP COVID-19 study aimed to evaluate the safety and efficacy of hydroxychloroquine (HCQ) as chemoprophylaxis for SARS-CoV-2 infection in this population. METHODS: HCW, first responders and other occupationally high-risk participants were enrolled in a randomized, placebo-controlled clinical study of HCQ from April-October 2020. The trial compared daily versus weekly HCQ to placebo and to a prospective cohort on HCQ for autoimmune diseases.

Participants were followed for 8 weeks. Serology or a positive PCR test were used to determine laboratory confirmed clinical cases. RESULTS: 624 participants were randomized to placebo (n=200), weekly HCQ (n=201), daily HCQ (n=197). For the primary safety endpoint, 279 (44.7%) participants experienced AE level II or lower (total AEs n=589), similar rates in all randomized groups (p=0.188) with no hospitalizations or interventions required. Only 4 laboratory confirmed COVID-19 cases occurred, with 2 in the placebo arm and one in each HCQ randomized arm. CONCLUSIONS: This randomized placebo-controlled trial was able to demonstrate the safety of HCQ outpatient chemoprophylaxis in high-risk groups against COVID-19. Future studies of chemoprophylaxis for SARS-CoV-2 are needed as the epidemic continues worldwide.

Sleep Medicine
Collen J, Capaldi VF, Williams SG, Labra C, Assefa SZ, Abdelwadoud M, Mullins CD, Manber R, Mahoney A, Bevan J, **Drake CL**, Albrecht JS, Edwards H, Grandner MA, and Wickwire EM. Moving Beyond "Leaning In"-It Is Time to Reach Out and Partner to Solve the Military Sleep Problem. *Mil Med* 2021; Epub ahead of print. PMID: 34964479. Full Text

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Sleep Medicine
White KM, Dunietz GL, **Pitts DS**, **Kalmbach DA**, Lucchini M, and O'Brien LM. Burden of sleep disturbance in non-Hispanic Black pregnant women. *J Clin Sleep Med* 2021; Epub ahead of print. PMID: 34964433. Full Text

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STUDY OBJECTIVES: Non-Hispanic Black pregnant women disproportionately experience poor perinatal outcomes compared to other racial/ethnic groups. Sleep disruption has emerged as a risk factor for

adverse pregnancy outcomes but there are limited data in minority pregnant women. We examined the prevalence of habitual snoring and its timing of onset with several key sleep-wake disturbances and their associations with perinatal outcomes in a cohort of non-Hispanic Black pregnant women. METHODS: Third trimester non-Hispanic Black pregnant women were recruited from a large, academic medical center and screened for habitual snoring - and its timing relative to pregnancy - sleep quality, symptoms of insomnia, excessive daytime sleepiness, as well as daytime function. Clinical diagnoses of hypertensive disorders of pregnancy were obtained along with delivery outcomes. RESULTS: In 235 women the vast majority (80%) reported three or more sleep-wake disturbances, and almost half had at least five disturbances. Sixteen percent endorsed pre-pregnancy snoring and 20% pregnancy-onset snoring. Women with pregnancy-onset snoring had significantly increased odds of poor sleep quality aOR 8.2, trouble staying asleep aOR 3.6, waking up too early aOR 2.7, excessive daytime sleepiness aOR 2.3, and poor daytime function aOR 8.7 but no relationship with perinatal outcomes. In contrast, pre-pregnancy snoring was related to chronic hypertension, pre-term delivery and fetal growth restriction; aOR 2.6, aOR 2.8, and aOR 5.1 respectively. CONCLUSIONS: Sleep-wake disturbances confer a significant burden to pregnant non-Hispanic Black women, an infrequently studied yet disproportionately affected population. Contributions of maternal sleep to racial disparities in perinatal health should be a priority for public health research.

Surgery

Gangi A, and **Shah R**. The Landmark Series: Appendiceal Primary Peritoneal Surface Malignancy. *Ann Surg Oncol* 2021; Epub ahead of print. PMID: 34853944. Full Text

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Appendiceal primary peritoneal surface malignancies are rare and include a broad spectrum of pathologies ranging from indolent disease to aggressive disease. As such, the data that drive the management of appendiceal peritoneal surface malignancies is generally not based on prospective clinical trial data, but rather consists of level 1 data based on retrospective studies and high-volume institutional experiences. Complete surgical debulking typically offers the best chance for long-term survival. This review highlights the landmark articles on which management of primary appendiceal peritoneal surface malignancies are based.

Surgery

Goto T, **Ivanics T**, Cattral MS, Reichman T, Ghanekar A, Sapisochin G, McGilvray ID, Sayed B, Lilly L, Bhat M, Selzner M, and Selzner N. Superior long-term outcome of Adult Living Donor Liver Transplantation A cumulative single-center cohort study with 20 years follow-up. *Liver Transpl* 2021; Epub ahead of print. PMID: 34870890. Full Text

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Living donor liver transplantation (LDLT) is an attractive alternative to deceased donor liver transplantation (DDLT). Although both modalities have similar short-term outcomes, long-term outcomes are not well studied. Herein, we compared 20-year outcomes of 668 adults who received LDLT with1596 DDLT at the largest liver transplant (LT) program in Canada. Recipients of LDLT were significantly younger and more often male than DDLT ($p<0.001$). Autoimmune diseases were more frequent in LDLT, whereas viral hepatitis and alcohol-related liver disease in DDLT. LDLT recipients had lower MELD scores ($P=.008$), waited less ($p<0.001$), and were less often inpatient at the time of LT ($P<0.001$). In a non-adjusted analysis, 1-, 10-, and 20-year patient survival rates were significantly higher in LDLT (93%, 74%, and 56%) versus DDLT (91%, 67%, and 46%; log-rank $P = 0.02$), as were graft survival rates LDLT (91%, 67%, and 50%) versus (90%, 65%, and 44.3%, respectively, for DDLT; log-rank $P = 0.31$). After

multivariable adjustment, LDLT and DDLT were associated with a similar hazard of patient and graft survival. Our data of 20-years follow-up of LDLT from a single, large Western center demonstrates excellent long-term outcomes for recipients of LDLT.

Surgery
Ivanics T, Toso C, Ilyas SI, and Sapisochin G. Transplant Oncology in locally advanced intrahepatic cholangiocarcinoma: one more step on a long road. *Am J Transplant* 2021; Epub ahead of print. PMID: 34971482. Full Text

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Surgery
Jesse MT, Clifton E, **Kim DY**, **Nicholson D**, **Patil R**, **Bhavsar S**, **Desai S**, **Gartrelle K**, **Eshelman A**, **Fleagle E**, **Ahmedani B**, Carlozzi NE, **Tang A**, and **Patel A**. Prerenal Transplant Education and Evaluation Positively Impacts Outcomes. *Prog Transplant* 2021; Epub ahead of print. PMID: 34860614. Full Text

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Introduction: An outstanding question in kidney transplantation is how to prepare candidates and their social supports for optimal posttransplant outcomes. Project Aims: This program evaluation assessed whether a pretransplant quality improvement clinic improved clinical outcomes in the year posttransplant compared to recipients receiving standard of care. Design: The Countdown to Transplant Clinic was implemented with kidney transplant candidates expected to receive a transplant within the next few months. The clinic included an enhanced education session on posttransplant lifestyle management, confirmation of support (≥2 adults), and evaluations by transplant social work, psychology, and nephrology. Results: Seventy-five patients participated in the clinic and underwent a transplant. A retrospective chart review of posttransplant laboratory values, rehospitalizations (within 3-months posttransplant), biopsy-confirmed graft failure, and mortality (within 1-year posttransplant) were collected from both groups. Univariate and multivariate propensity score-weighted linear or logistic regression models were used to evaluate the association between clinic participation and outcomes. In models adjusting for relevant covariates, participation in The Countdown to Transplant Clinic (vs standard care) was associated with a lower coefficient of variation of serum tacrolimus (all values collected 3-12 months posttransplant), 30-day posttransplant white blood cell counts (but not 90-day), 90-day posttransplant potassium, and 30 and 31 to 90 days rehospitalizations. Clinic participation did not predict serum glucose levels at 30- or 90-days posttransplant. Due to low rates of rejection and mortality, meaningful comparisons were not possible. Conclusion: Participation in a pretransplant, multicomponent clinic may improve certain outcomes of interest posttransplantation. Pilot testing for feasibility for randomized controlled trials is a necessary next step.

Surgery

Natour AK, **Rteil A**, **Corcoran P**, **Weaver M**, **Ahsan S**, and **Kabbani L**. Socioeconomic status and clinical stage of patients presenting for treatment of chronic venous disease. *Ann Vasc Surg* 2021; Epub ahead of print. PMID: 34954041. Full Text

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OBJECTIVES: The association between socioeconomic status (SES) and chronic venous insufficiency has not been rigorously studied. This study aimed to determine the influence of SES on the clinical stage of patients presenting for chronic venous disease therapy. METHODS: We performed a retrospective study of a prospectively collected data from the Vascular Quality Initiative Varicose Vein Registry at our tertiary referral center. Medical records of patients who underwent therapy for chronic venous disease between January 2015 and June 2019 were queried. SES was quantified using the neighborhood deprivation index (NDI), which summarizes 8 domains of socioeconomic deprivation and is based on census tract data derived from the patients' addresses at the time of the treatment. High NDI scores correspond with lower SES. The association between SES and severity of vein disease at presentation was assessed with bivariate analysis of variance and linear regression analysis. RESULTS: A total of 449 patients with complete SES and clinical-etiology-anatomy-pathophysiology (CEAP) class data were included in the study. The mean age was 58 years, 67% were female, and 60% were White. CEAP classes were distributed as follows C2, 22%; C3, 50%; C4, 15%; C5, 5%; and C6, 8%. Patients with lower SES (higher NDI score) tended to have a higher CEAP class at presentation ($P < 0.05$). SES was not associated with history of deep venous thrombosis, use of compression therapy, or venous clinical severity score. CONCLUSIONS: At our institution, patients with more advanced venous disease tended to belong to a lower SES group. This may reflect that patients with a lower SES have a longer time to presentation due to delay in seeking medical help for venous disease.

Surgery

Okereke IC, Westra J, Tyler D, Klimberg S, Jupiter D, Venkatesan R, Brooks K, and Kuo YF. Disparities in esophageal cancer care based on race: a National Cancer Database analysis. *Dis Esophagus* 2021; Epub ahead of print. PMID: 34918057. Full Text

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Esophageal cancer is one of the most common cancer killers in our country. The effects of racial disparities on care for esophageal cancer patients are incompletely understood. Using the National Cancer Database, we investigated racial disparities in treatment and outcome of esophageal cancer patients. The National Cancer Database was queried from 2004 to 2017. Logistic regression and survival analysis were used to determine racial differences in access, treatment and outcome. A total of 127,098 patients were included. All minority groups were more likely to be diagnosed at advanced stages versus Caucasians after adjusting for covariates (African American OR-1.64 [95% confidence interval 1.53-1.76], Hispanic OR-1.19 [1.08-1.32], Asian OR-1.78 [1.55-2.06]). After adjustment, all minorities were less likely at every stage to receive surgery. Despite these disparities, Hispanics and Asians had improved survival compared with Caucasians. African Americans had worse survival. Racial disparities for receiving surgery were present in both academic and community institutions, and at high-volume and low-volume

institutions. Surgery partially mediated the survival difference between African Americans and Caucasians (HR-1.13 [1.10-1.16] and HR-1.04 [1.02-1.07], without and with adjustment of surgery).There are racial disparities in the treatment of esophageal cancer. Despite these disparities, Hispanics and Asians have improved overall survival versus Caucasians. African Americans have the worst overall survival. Racial disparities likely affect outcome in esophageal cancer. But other factors, such as epigenetics and tumor biology, may correlate more strongly with outcome for patients with esophageal cancer.

Surgery
Sapisochin G, **Ivanics T**, and Heimbach J. Liver Transplantation for intrahepatic cholangiocarcinoma: ready for prime time? *Hepatology* 2021; Epub ahead of print. PMID: 34859465. Full Text

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Cholangiocarcinoma (CCA) represents the second most common primary liver malignancy after hepatocellular carcinoma and has risen in incidence globally in the past decades. Intrahepatic cholangiocarcinoma (iCCA) comprises 20% of all CCAs, with the rest being extrahepatic (including perihilar [pCCA] and distal CCA). Though long representing an absolute contraindication for liver transplantation (LT), recent analyses of outcomes of LT for iCCA have suggested that iCCA may be a potentially feasible option for highly selected patients. This has been motivated both by successes seen in outcomes of LT for other malignancies such as HCC and perihilar CCA and by several retrospective reviews demonstrating favorable results with LT for a selected group of iCCA patients with small lesions. LT for iCCA is primarily relevant within two clinical scenarios. The first includes patients with very early disease (single tumor ≤2 cm) with cirrhosis and are not candidates for liver resection (LR). The second scenario is patients with locally advanced iCCA, but where the extent of LR would be too extensive to be feasible. Preliminary single-center reports have described LT in a selected group of patients with locally advanced tumors which have responded to neoadjuvant therapy and have a period of disease stability. Currently, there are three prospective trials underway that will help clarify the role of LT in iCCA. This review seeks to explore the available studies involving LT for iCCA, the challenges of ongoing trials, and opportunities for the future.

Surgery
Takahashi K, **Nagai S**, Gosho M, Kitajima T, Kim J, Oda T, and **Abouljoud M**. The Lactate-to-Platelet Ratio: A Novel Predictor for Short-Term Early Allograft Failure After Liver Transplantation. *Transplant Proc* 2021; 53(10):2993-2999. PMID: 34756715. Full Text

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BACKGROUND: Early allograft dysfunction (EAD) is a criterion to evaluate initial graft dysfunction associated with inferior graft survival and postoperative complications after liver transplantation (LT). This study defined the lactate-to-platelet ratio (LPR) as lactate level immediately post-LT/platelet count on postoperative day 1 and evaluated its association with EAD and short-term graft failure. MATERIALS AND METHODS: This study reviewed 434 deceased-donor LTs from individuals with confirmed brain death between January 2008 and December 2014. The area under the curve (AUC) was used to compare the predictive capacity for 3-month graft survival between EAD and the LPR. Along with LPR, the risk factors for 3-month graft failure were analyzed by multivariate analysis. RESULTS: EAD was

reported in 127 patients (31%). The LPR in patients with EAD was significantly higher than that in patients without EAD (9.8 vs 5.9, P < .001). In the multivariate analysis, both the LPR (per 1.0 increase) and EAD were independent risk factors for 3-month graft failure (hazard ratio [HR] =1.03, P = .03; and HR = 9.14, P = .001). The comparison of the AUCs between the LPR and EAD showed no significant difference (0.79 vs 0.78, P = .84), whereas the combination of EAD and LPR had a better predictive capacity than EAD alone (0.86 vs 0.78, P < .001). The LPR showed an inverse relationship for predicting 3-month graft survival. CONCLUSIONS: The LPR is a continuous parameter that enables prediction of initial graft function and estimation of the 3-month graft failure rate with the advantages of early availability and simple calculations.

Surgery

Taylor M, Freeman K, Mehaffey JH, Wallen T, and **Okereke IC**. Applicant perception of virtual interviews in cardiothoracic surgery: A Thoracic Education Cooperative Group Study. *J Thorac Cardiovasc Surg* 2021; Epub ahead of print. PMID: 34955283. Full Text

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OBJECTIVES: Cardiothoracic programs used virtual interviews exclusively this year. As programs consider using virtual interviews permanently, our goal was to evaluate the experience of applicants with virtual interviews. METHODS: All 2020-2021 traditional cardiothoracic fellowship applicants received an anonymous electronic survey after the Match process ended. The survey assessed the number of interviews, strengths, and inadequacies of virtual interviews and factors that affected rank decision. RESULTS: Forty-three percent of applicants responded (60/139). The average number of interviews was 16.0. Eighty percent (48/60) of respondents successfully matched. Eighty-seven percent (52/60) of respondents had a favorable experience with virtual interviews, and 97% (58/60) found them to be convenient. However, only 50% (30/60) were able to evaluate a program fully. Respondents who matched were more likely to have a favorable experience (P = .02), but not more likely to be able to evaluate a program fully (P = .35). The most valued aspect was the informal meet and greet session with fellows (4.2 of 5). The least valued aspect was the program's social media site (2.0 of 5). The factors most frequently used to decide ranking were case numbers by 92% (55/60) and culture/personality by 82% (49/60). CONCLUSIONS: Virtual interviews were perceived more favorably compared with last year, but half of applicants were still unable to evaluate a program fully. Fellow interactions were the most popular aspect of virtual interviews. As programs consider using virtual interviews permanently, more exposure to current trainees and a more robust social media/online presence will improve favorability.

Surgery

Yan Y, John S, Shaik T, Patel B, Lam MT, **Kabbani L**, and Mehrmohammadi M. Photoacoustic-guided endovenous laser ablation: Characterization and in vivo canine study. *Photoacoustics* 2021; 24:100298. PMID: 34504765. Full Text

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Endovenous laser ablation (EVLA) is a minimally invasive surgical procedure, often guided by ultrasound (US) imaging, for treating venous insufficiencies. US imaging limitations in accurately visualizing the catheter and the lack of a temperature monitoring system can lead to sub-optimal outcomes. An integrated photoacoustic (PA)-guided EVLA system has been previously developed and reported to overcome the shortcomings of US-guided procedure. In this study, we further characterized the system and tested the in vivo utility. In addition, PA thermometry was further explored by compensating the variation of PA signal with temperature with respect to the temperature-dependent absorption of blood and water. In vivo imaging results indicated that the PA-guided EVLA system can provide high contrast

and accurate images of the ablation catheter tip overlaid on US images of the background tissue. Additionally, absorption-compensated PA signal amplitudes over a relevant range of temperature were measured and demonstrated.

Urology

Abdullatif VA, **Davis J**, **Cavayero C**, **Toenniessen A**, and **Nelson RJ**. Single-Port Robotic Inguinal Lymph Node Dissection for Penile Cancer. *Urology* 2021; Epub ahead of print. PMID: 34936901. Full Text

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INTRODUCTION: Inguinal lymph node dissection is an essential component in the diagnosis, management, and treatment of penile cancer. Recent advances in minimally invasive surgery may play an important role in decreasing the adverse effects and complications of lymph node dissections. We present our technique utilizing a Single-Port robotic assisted laparoscopic bilateral inguinal lymph node dissection (ILND) in a patient with pT3N2Mx penile cancer s/p partial penectomy and sentinel lymph node biopsy. METHODS: We present a case of a 64-year-old man who underwent a radical penectomy for previously diagnosed penile cancer. Pathology report showed invasive squamous cell carcinoma of the penis. In accordance with NCCN guidelines, we performed a bilateral inguinal and pelvic lymph node dissection using robotic assisted single-port (SP) laparoscopy with the DaVinci Single-Site platform. Our methods are detailed in this technical report. RESULTS: Total operative time was 3 hours and 38 minutes in duration with minimal blood loss (<20 mL). A 3 cm inguinal lymph node was excised and positive for malignancy without involvement of other nodes. The patient was discharged 90 minutes after recovery in PACU without narcotics and returned to normal bowel function within 6 hours. CONCLUSIONS: We present a successful surgical outcome of a Single-Port robotic inguinal lymph node dissection in a treatment of a patient with T3N2M0 penile cancer. At the time of publication, the patient is cancer-free with no palpable lymphadenopathy on exam. Utilization of the SP DaVinci system may soon become the standard of care in select cases as it is currently the least invasive approach and is associated with lower morbidity and mortality.

Urology

Agochukwu-Mmonu N, Qi J, Dunn RL, Montie J, Wittmann D, Miller D, Martin R, Kim T, Johnston WK, 3rd, and **Peabody J**. Patient- and Surgeon-Level Variation in Patient-Reported Sexual Function Outcomes Following Radical Prostatectomy Over 2 Years: Results From a Statewide Surgical Improvement Collaborativep. *JAMA Surg* 2021; Epub ahead of print. PMID: 34851369. Full Text

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IMPORTANCE: Of patient-reported outcomes for individuals undergoing radical prostatectomy, sexual function outcomes are among the most reported and the most detrimental to quality of life. Understanding variations at the patient and surgeon level may inform collaborative quality improvement. OBJECTIVE: To describe patient- and surgeon-level sexual function outcomes for patients undergoing radical prostatectomy in the Michigan Urological Surgery Improvement Collaborative (MUSIC) and to examine the correlation between surgeon case volume and sexual function outcomes. DESIGN, SETTING, AND

PARTICIPANTS: This is a prospective cohort study using the MUSIC registry and patient-reported sexual function outcome data. Patient- and surgeon-level variation in sexual function outcomes were examined among patients undergoing radical prostatectomy from May 2014 to August 2019. Sexual function outcome data were collected using validated questionnaires, which were completed before surgery and at 3, 6, 12, and 24 months' follow-up following surgery. All participants were male. Race and ethnicity data were self-reported and were included to examine potential variation in outcomes by race and/or ethnicity. Data were analyzed from January 2021 to March 2021. MAIN OUTCOMES AND MEASURES: There were 4 outcomes in this study, including the 26-item Expanded Prostate Cancer Index Composite (EPIC-26) sexual function scores at 3, 6, 12, and 24 months' follow-up; patient-level sexual function recovery at 12- and 24-month follow-up; surgeon-level variation in sexual function outcomes at 12- and 24-month follow-up; and correlation between surgeon case volume and sexual function outcomes. RESULTS: A total of 1426 male patients met inclusion criteria for this study. The median (IQR) age was 64 (58-68) years. A total of 115 participants (8%) were Black, 1197 (84%) were White, 25 (2%) were of another race or ethnicity (consolidated owing to low numbers), and 89 (6%) were of unknown race or ethnicity. Among patients undergoing bilateral nerve-sparing radical prostatectomy, mean (SD) EPIC-26 sexual function scores at 12- and 24-month follow-up (12 months, 39 [28]; 24 months, 63 [29]) did not return to baseline levels. There was wide variation in EPIC-26 sexual function scores at both 12-month follow-up (range, 23-69; $P < .001$) and 24-month follow-up (range, 27-64; $P < .001$). Similar variations were found in EPIC-26 sexual function scores and recovery of sexual function by surgeon. Recovery rates ranged from 0% to 40% of patients at 12-month follow-up (18 surgeons; $P < .001$) and 3% to 44% of patients at 24-month follow-up (12 surgeons; $P < .001$). Surgeon case volume and sexual function outcomes were not significantly correlated. On multivariable analysis, the following variables were associated with better recovery at 24-month follow-up: younger age ($P < .001$), lower baseline EPIC-26 sexual function score ($P < .001$), lower Gleason score ($P = .05$), and nonobesity ($P = .03$). CONCLUSIONS AND RELEVANCE: In this study, there was significant patient- and surgeon-level variation in sexual function recovery over 2 years following radical prostatectomy. Variation in surgeon-level sexual function outcomes presents an opportunity and model for surgical collaborative quality improvement.

Urology

Butaney M, and **Rambhatla A**. The impact of COVID-19 on urology office visits and adoption of telemedicine services. *Curr Opin Urol* 2021; Epub ahead of print. PMID: 34930885. Full Text

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PURPOSE OF REVIEW: The purpose of this review article is to discuss the impact of Coronavirus Disease 2019 (COVID-19) on the evolution of telemedicine use for urology office visits. RECENT FINDINGS: The COVID-19 pandemic has caused a dramatic change in the delivery of healthcare. Fraught with numerous barriers previously, the need for healthcare delivery during a time of social distancing and increased healthcare requirements drove the adoption of telemedicine forward. This 'trial period' over the last year has allowed us to appreciate the potential utility of telehealth-associated services in practice and consider its role even after the pandemic. Multiple studies equating its utility to in-person visits whereas simultaneously providing added convenience and cost-related savings have been published in the urologic literature. Permanent regulatory changes will need to be implemented to allow us the flexibility to use telehealth in the future. SUMMARY: It is clear that telemedicine is an effective strategy for delivery of healthcare under the right circumstances. Although it initially started to fill a need out of necessity, it can help us effectively deliver healthcare as long as the regulations surrounding telemedicine allow us to continue to use it. This period has been challenging for healthcare delivery and led to policy changes that served as a catalyst to help us better understand this previously underutilized resource.

Urology

Dalela D, and **Suson K**. Re: Luke Harper, T. Blanc, M. Peycelon, et al. Circumcision and Risk of Febrile Urinary Tract Infection in Boys with Posterior Urethral Valves: Result of the CIRCUP Randomized Trial. Eur Urol. In press. https://doi.org/10.1016/j.eururo.2021.08.024. *Eur Urol* 2021; Epub ahead of print. PMID: 34933755. Full Text

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Urology
Gopalakrishnan D, Elsayed AS, Hussein AA, Jing Z, Li Q, Wagner AA, Aboumohamed A, Roupret M, Balbay D, Wijburg C, Stockle M, Dasgupta P, Khan MS, Wiklund P, Hosseini A, **Peabody J**, Shigemura K, Trump D, Guru KA, and Chatta G. Impact of neoadjuvant chemotherapy on survival and recurrence patterns after robot-assisted radical cystectomy for muscle-invasive bladder cancer: Results from the International Robotic Cystectomy Consortium. *Int J Urol* 2021; Epub ahead of print. PMID: 34923677. Full Text

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Guy's Hospital, London, UK.
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OBJECTIVES: To analyze the impact of neoadjuvant chemotherapy on survival and recurrence patterns in muscle-invasive bladder cancer after robot-assisted radical cystectomy. MATERIALS AND METHODS: The International Robotic Cystectomy Consortium database was reviewed to identify patients who underwent robot-assisted radical cystectomy for muscle-invasive bladder cancer between 2002 and 2019. Survival outcomes, response rates, and recurrence patterns were compared between patients who received neoadjuvant chemotherapy and those who did not. Survival distributions were estimated using Kaplan-Meier analyses and compared using the log-rank test. RESULTS: A total of 1370 patients with muscle-invasive bladder cancer were identified, of whom 353 (26%) received neoadjuvant chemotherapy. After a median follow-up of 27 months, neoadjuvant chemotherapy recipients had higher 3-year overall survival (74% vs 57%; log-rank $P < 0.01$), 3-year cancer-specific survival (83% vs 73%; log-rank $P = 0.03$), and 3-year relapse-free survival (64% vs 48%; log-rank $P < 0.01$). Neoadjuvant chemotherapy was a predictor of higher overall survival, cancer-specific survival, and relapse-free survival in univariate but not multivariate analysis. Pathological downstaging (46% vs 23%; $P < 0.01$), complete responses (24% vs 8%; $P < 0.01$), and margin negativity (95% vs 91%; $P < 0.01$) at robot-assisted radical cystectomy were more common in the neoadjuvant chemotherapy group. Neoadjuvant chemotherapy recipients had lower distant (15% vs 22%; $P < 0.01$) but similar locoregional (12% vs 13%; $P = 0.93$) recurrence rates. CONCLUSIONS: In this analysis from a large international database, patients with muscle-invasive bladder cancer who received neoadjuvant chemotherapy before robot-assisted radical cystectomy had higher rates of survival, pathological downstaging, and margin-negative resections. They also experienced fewer distant recurrences.

Urology
Jamil M, **Etta P**, and **Abdollah F**. AUTHOR REPLY. *Urology* 2021; 158:115-116. PMID: 34895624. Full Text

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Urology

Monga J, **Adrianto I**, **Rogers C**, **Gadgeel S**, **Chitale D**, Alumkal JJ, Beltran H, Zoubeidi A, and **Ghosh J**. Tribbles 2 pseudokinase confers enzalutamide resistance in prostate cancer by promoting lineage plasticity. *J Biol Chem* 2021; 101556. Epub ahead of print. PMID: 34973338. Full Text

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Enzalutamide (Xtandi), a second-generation anti-androgen, is commonly prescribed for therapy of advanced prostate cancer, but enzalutamide-resistant, lethal or incurable disease invariably develops. To understand the molecular mechanism(s) behind enzalutamide resistance, here we comprehensively analyzed a range of prostate tumors and clinically relevant models by gene expression array, immunohistochemistry, and Western blot, which revealed that enzalutamide resistant prostate cancer cells and tumors overexpress the pseudokinase, Tribbles 2 (TRIB2). Inhibition of TRIB2 decreases the viability of enzalutamide-resistant prostate cancer cells, suggesting a critical role of TRIB2 in these cells. Moreover, overexpression of TRIB2 confers resistance in prostate cancer cells to clinically relevant doses of enzalutamide, and this resistance is lost upon inhibition of TRIB2. Interestingly, we found that TRIB2 downregulates the luminal markers AR (androgen receptor) and CK8 (cytokeratin 8) in prostate cancer cells but upregulates the neuronal transcription factor BRN2 (Brain-2) and the stemness factor SOX2 (SRY-box 2) to induce neuroendocrine characteristics. Finally, we show that inhibition of either TRIB2 or its downstream targets, BRN2 or SOX2, re-sensitizes resistant prostate cancer cells to enzalutamide. Thus, TRIB2 emerges as a potential new regulator of trans-differentiation that confers enzalutamide-resistance in prostate cancer cells via a mechanism involving increased cellular plasticity and lineage switching.

Urology

Rogers CG. Editorial comment on END-2021-0854-PC and END-2021-0882-PC Laparoscopic vs. Robotic Nephrectomy: A debate over preferences. *J Endourol* 2021; Epub ahead of print. PMID: 34913727. Full Text

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Urology

Sood A, **Jeong W**, **Palma-Zamora I**, **Abdollah F**, **Butaney M**, **Corsi N**, **Wurst H**, **Arora S**, **Kachroo N**, **Hassan O**, **Gupta N**, Gorin MA, and **Menon M**. Description of Surgical Technique and Oncologic and Functional Outcomes of the Precision Prostatectomy Procedure (IDEAL Stage 1-2b Study). *Eur Urol* 2021; Epub ahead of print. PMID: 34872786. Full Text

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BACKGROUND: The existing treatment options for men with intermediate- or high-volume low-risk prostate cancer (PCa) are associated with a substantial risk of over- or undertreatment. The development of risk-adjusted therapies is an unmet need for these patients. OBJECTIVE: To describe our novel technique of precision prostatectomy, a form of surgical focal therapy that allows radical excision of the index PCa lesion along with >90% prostatic tissue extirpation while preserving the prostatic capsule and seminal vesicle/vas deferens complex on the side contralateral to the dominant cancer lesion, and to report on medium-term functional and oncologic outcomes in the first 88 consecutive men who underwent this procedure between December 2016 and January 2020. DESIGN, SETTING, AND PARTICIPANTS: Men with (1) prostate-specific antigen (PSA) ≤20 ng/ml, (2) clinical T stage ≤cT2, (3) a dominant unilateral lesion with Gleason ≤ 4 + 3 disease with any number or percentage of cores involved ipsilaterally on prostate biopsy, (4) no primary Gleason ≥4 lesion contralaterally, and (5) a preoperative Sexual Health Inventory of Men (SHIM) score of ≥17 (out of 25) with/without phosphodiesterase type-5 inhibitor use who consented to undergo precision prostatectomy were included in this single-arm, single-center, IDEAL stage 2b prospective development study. INTERVENTION: Robotic precision prostatectomy. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: The safety and urinary, sexual, and oncologic outcomes of the precision prostatectomy technique were studied. Descriptive statistics and Kaplan-Meier analyses were used to assess 12-mo urinary continence (0-1 pad), 12-mo sexual potency (SHIM score ≥17), 36-mo freedom from clinically significant PCa (grade group ≥2), secondary treatments, metastatic disease, and mortality. RESULTS AND LIMITATIONS: At study entry, the median age, PSA, and SHIM score were 60.0 yr (interquartile range [IQR] 54.2-65.9), 5.7 ng/ml (IQR 4.2-7.1), and 22 points (IQR 19-24), respectively. The median follow-up was 25 mo (IQR 14-38). At 12 mo, all patients were continent (0-1 pads), with 90.9% of patients using 0 pads. The median time to urinary continence was 1 mo (IQR 1-4). At 12 mo, 85% of all-comers and 90.2% of the preoperatively potent men were potent. The median time to sexual potency was 4 mo (IQR 4-12). From an oncologic standpoint, at 36 mo an estimated 93.4% of the patients were free from clinically significant residual PCa and 91.7% had not undergone any additional treatment. All patients were alive and free of metastatic disease at 36 mo. CONCLUSIONS: Precision prostatectomy is technically safe and reproducible and offers excellent postoperative functional results. At 36-mo follow-up, the oncologic outcomes and secondary treatment rates appear to be superior to existing ablative focal therapy results. Pending long-term data, a risk-stratified surgical approach to PCa may avoid whole-gland therapy and preserve functional quality of life in men with localized PCa. PATIENT SUMMARY: Precision prostatectomy is a new form of focal therapy for intermediate-risk prostate cancer in which a 5-10-mm rim of prostate capsule is left on the opposite side of the gland to where the dominant cancer is located. The technique appears to be safe and efficacious and adds to the growing armamentarium of risk-adapted therapies for treatment of localized prostate cancer that avoid the adverse effects on urinary and erectile function of whole-gland treatments.

Conference Abstracts

Cardiology/Cardiovascular Research

Lee Y, Jehangir Q, **Li P**, **Lin CH**, Sule AA, Krishnamoorthy G, Goodman JR, Halabi A, Patel K, Wang DD, **Poisson L**, and Nair GB. Risk Stratification for Acute Arterial and Venous Thromboembolism using CHA 2DS 2-VASc Score in Hospitalized COVID-19 Patients: A Multicenter Study. *Blood* 2021; 138:2120.

Introduction: Arterial and venous thromboembolism are common complications in COVID-19. Micro-macro thrombosis-related organ dysfunction can confer an increased risk for mortality. The optimal dosage of anticoagulation (AC) in COVID-19 patients remains unclear. Interim data from adaptive randomized control trials (ATTACC, REMAP-CAP, and ACTIV-4a) showed divergent results of therapeutic AC (TAC) versus usual care AC for the primary outcome of organ support free days in hospitalized COVID-19 patients. Components of CHA 2DS 2-VASc, a model originally built for predicting ischemic stroke in atrial fibrillation, are consistent with independent risk factors for COVID-19 severity and mortality. Herein, we analyzed the performance of the CHA 2DS 2-VASc model in hospitalized COVID-19 patients for predicting arterial and venous thromboembolic events, which could potentially aid in risk stratification of hospitalized patients and guide AC dosing. Methods: This is a large, retrospective, multicenter cohort study that included all adult patients from one tertiary care and five community hospitals with PCR-proven SARS-CoV-2 infection between 3/1/2020 and 12/1/2020. The primary composite outcome was acute arterial thromboembolism (ATE) and venous thromboembolism (VTE). We identified patients with ATE [cerebrovascular accident (CVA), myocardial infarction (MI) including both ST-segment elevation MI and non-ST-segment elevation MI], and VTE [deep vein thrombosis (DVT) and pulmonary embolism (PE)] using ICD -10 codes. Mean and standard deviation were reported for continuous variables; proportions were reported for categorical variables. To compare the groups, the Chi-square test was used for categorical variables, and the t-test was used for continuous variables. CHA 2DS 2-VASc scores were calculated on admission and were used as a measure of the predictive accuracy of the scoring system. Sensitivity and specificity with different cut-offs of CHA 2DS 2-VASc scores were calculated. All statistical tests were 2-sided with an α (significance) level of 0.05. All data were analyzed using R version 4.0.5. Results: Among 3526 patients, a total of 619 patients had thromboembolic events: 383 had ATE and 236 had VTE. Of 383 patients who had ATE, 350 patients were found to have acute MI, 48 had CVA, and 15 had both MI and CVA. In patients with VTE, 134 had DVT, 168 had PE, and 66 had both DVT and PE (Figure 1). We analyzed the primary composite outcome of ATE and VTE (group 1) vs no ATE and VTE (group 2). Baseline characteristics are included in Table 1. The in-patient all-cause mortality rate was 28.4% in group 1 vs 12.6% in group 2 ($p<0.001$). The mean hospital length of stay was 12.3 days in group 1 vs 8.8 days in group 2 ($p<0.001$). Group 1 had a mean CHA 2DS 2-VASc score of 3.3 ±1.6. vs 2.7±1.7 in group 2 ($p<0.001$) (Figure 2). At CHA 2DS 2-VASc scores of 3 and 4, the model had a specificity of 46% and 67% and sensitivity of 68% and 42% respectively for predicting ATE/VTE. The CHA 2DS 2-VASc score of 5 had a specificity of 86% and sensitivity of 25%. The score of 7 had 98% specificity but 3% sensitivity (Table 2). Conclusion: Our results suggest that the CHA 2DS 2-VASc model for arterial and venous thromboembolism has a moderate performance. The CHA 2DS 2-VASc score of 5 has a high specificity, though low sensitivity, for predicting thromboembolism. The CHA 2DS 2-VASc score can be used as an adjunct risk stratification tool to initiate TAC. [Formula presented] Disclosures: No relevant conflicts of interest to declare.

Cardiology/Cardiovascular Research

Ya'qoub L, Helmy T, Reeves R, and Bailey S. Valve-in-valve transcatheter aortic valve replacement for a failed bioprosthetic valve in a patient with repaired truncus arteriosus and right-sided aortic arch. *Pediatr Cardiol* 2021; 42(8):1890.

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We are seeing more patients with repaired congenital cardiac diseases. These patients are often complex requiring careful clinical evaluation. In this case report, we present a very interesting case in a patient with repaired truncus arteriosus and right-sided aortic arch, who was hospitalized at our institution for recurrent heart failure exacerbation. He was found to have severe eccentric aortic valve regurgitation due to failed bioprosthetic valve. Given his multiple cardiac surgeries, he was deemed high risk for surgery

and underwent successful valve-in-valve transcatheter aortic valve replacement with immediate improvement in his hemodynamics and symptoms.

Gastroenterology

Nagirimadugu A, **Patel A**, **Nimri F**, **Musleh M**, **Naffouj S**, **Faber A**, **Abu Ghanimeh M**, and **Kaur N**. Impact of PHQ-9 Screen on Early Identification of Depression in IBD Clinic. *Am J Gastroenterol* 2021; 116:S15-S15.

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BACKGROUND: Over the past two decades there has been significant research linking inflammatory bowel disease (IBD) to depression. The chronicity of symptoms coupled with the financial burden of treatment costs, missed days of work/school and interpersonal relationship stress are contributing factors in the diagnosis of depression. The prevalence of depression within the IBD community is 15% and depressive symptoms are noted in 20% of patients. Furthermore, IBD patients with severe uncontrolled disease have higher rates of depression (40.7%) than those in remission (16.5%). The association between IBD and depression is linked to lower quality of life, poor medication compliance, worse disease outcomes, increased hospitalization, and higher suicidal risk. Early diagnosis and treatment of depression in IBD patients is paramount in achieving and maintaining IBD disease remission. While the association between IBD and depression is well-known, identifying depression can be a challenge. Review of recent literature shows that depression is under screened in IBD clinics. We present a prospective quality improvement study at a robust IBD center evaluating the impact of a validated depression screen (PHQ-9) on identifying depression compared to standard of care. METHODS: We compared the prevalence of depression in the IBD clinic in the control group using the history and diagnosis of depression and compared it against the intervention group after HQ-9 screening. Control group patient data was collected from June 2020 to July 2020 via virtual and in person visits. Intervention group PHQ-9 data was collected in person visits from January - March 2020 and post-intervention data collection was placed on hold until November 2020 due to the COVID pandemic. One randomly selected patient from each clinic session was asked to participate in the study at the time of visit. The primary end point was to compare the rates of depression and identify any barriers in providing early treatment for depression. The secondary endpoint was to identify high risk patients that are prone to depression. Categorical variables were analyzed by chi square analysis or fischer exact tests. Numerical data were analyzed using T-test. RESULTS: A total of 111 patients were screened. 60 patients were randomized to the control group (i.e. EMR based review for depression) and 51 patients were screened via survey during in person clinic visit. The identified depression rate from control vs intervention group is 20% vs. 35% ($p = 0.071$). Rates of depression were 15% in non-fistulizing Crohn’s disease vs. 41.4% in fistulizing Crohn’s disease ($p = 0.003$). Multivariate model for predicting depression noted to be significant for extra-intestinal manifestations OR of 3.06 (1.03, 9.12) $p = 0.045$ and age OR of 0.97 (0.94, 1.00) $p = 0.042$. Control vs. intervention identification of depression in patients with extra-intestinal manifestations is notable for OR of 3.31 (1.15, 9.52) $p = 0.026$ in the univariate model and OR of 3.30 (1.07, 10.16) $p = 0.038$ in the multivariate model. CONCLUSION: Key findings including identification of depression is higher in the intervention group compared to the control group. Though the data is not statistically significant, this is likely secondary to the small sample size in the setting of the pandemic. In addition, univariate analysis revealed a statistically significant finding that the older the age of the patient, the less likely they are to have depression. Our data showed that the mean age of depressed patients was 38.3 compared to nondepressed patients whose mean age is 47.1. Further analysis can help elucidate this finding, for example identifying if older patients are being treated for depression or more likely to seek out therapists compared to younger patients. Univariate analysis also revealed that intestinal Crohn's disease was a risk factor for depression. This is possibly secondary to the severity of disease in these individuals, especially if their IBD is causing an impact on their quality of life. Looking into the number of hospitalizations, days off from work or school, and coexisting medical diagnoses can allow us to further understand if depression stems from their disease. Given preliminary findings, we plan to continue this study for a larger sample size and further determine if there is a significant delay in identifying depression with the current standard of care.

Hematology-Oncology

Coutinho F, Gul Z, Berry AB, Thompson MA, **Willner CA**, **Vuyyala S**, McCracken H, Geverd K, Law JW, Wolf FM, Brown TD, and **Kuriakose P**. Molecular Biomarker Testing and Targeted Therapy Patterns in Patients with Acute Myelogenous Leukemia (AML) in Community Health Systems in the United States: A Real-World Data Analysis. *Blood* 2021; 138:4443.

Background and Objective: Molecular testing and treatment patterns for patients (pts) diagnosed with acute myelogenous leukemia (AML) have evolved over recent years. Next-generation sequencing (NGS) technologies allow for detection of somatic gene alterations that have prognostic and/or predictive/therapeutic significance. To describe the real-world testing patterns and clinical management of patients with AML, NGS testing, other molecular testing, mutations detected, and targeted treatment administration were analyzed in 2 large community health systems in the US. Methods: Pts >18 years, diagnosed with AML from January 1, 2015 to December 31, 2020, were identified in the Syapse Learning Health Network, a real-world database with clinical and genomic data from integrated community delivery networks. Study end date was March 31, 2021, allowing for a minimum follow up of 3 months from diagnosis. Pts with less than 2 clinical encounters were excluded. Electronic health records were reviewed retrospectively to analyze molecular biomarker testing patterns, actionable and prognostic biomarkers detected as defined by NCCN guidelines version 3, 2021, and targeted treatments administered. This study received Institutional Review Board (IRB) exemption. Results: The study included 685 pts with median age at AML diagnosis of 70 and median follow up of 5.4 months. 55% were male, 73% were non-Hispanic white, 10% were non-Hispanic black, 31% had ECOG performance status (PS) 0 or 1 and 16% had ECOG PS > 2 at diagnosis, and 69% had de novo AML. Pts with secondary AML consisted of pts evolving from prior myelodysplasia, myeloproliferative disorder, or aplastic anemia, or therapy related AML. 4% had favorable cytogenetic prognosis, 33% intermediate, and 30% adverse, with the remaining 33% unknown. 541 (79%) pts received either NGS or other molecular biomarker tests. 375 (55%) pts received NGS with or without other molecular biomarker tests and 166 (24%) pts received other molecular biomarker tests only [e.g. Sanger Sequencing, RT-PCR (reverse transcription polymerase chain reaction), PCR]. Pts who did not receive molecular biomarker testing (n=144) were older with median age of 78 and median follow-up of 2 months. There was no statistically significant difference in molecular biomarker testing received between non-Hispanic white and non-Hispanic black population (p=0.275) in the study. There was a statistically significant difference in molecular biomarker testing received between de novo (84% tested) and secondary (67% tested) AML (p=<0.001). NGS tested pts had a median time of 0 days from initial diagnosis to specimen drawn and 13 days from specimen drawn to report generation. 80% of pts first received NGS testing in the upfront diagnostic setting, 15% in the relapse or post diagnostic window (>30 days after diagnosis), with 5% missing relevant dates. 294 (78%) pts had NGS performed on bone marrow aspirate. NGS testing rates rose from 9% of pts diagnosed with AML in 2015, to 77% of pts in 2020. Among pts who received molecular testing (n=541), the proportions of pts tested for specific prognostic and actionable biomarkers by year of diagnosis are found in figures 1 and 2. 204 (38%) pts who received molecular testing had an actionable biomarker detected and of those 204 pts, 70 (34%) received at least one targeted therapy. The proportion of pts with one or more actionable mutations (FLT3, IDH1, IDH2) who receive targeted therapy is presented in table 1 below. Conclusions: Real-world data provide insights into molecular testing and targeted therapy patterns in routine clinical practice. In this study, testing uptake has increased over time with most pts diagnosed in 2020 receiving testing for FLT3-TKD, FLT3-ITD, IDH1, IDH2 and NPM1. Testing uptake did not differ by race. Among pts with a documented actionable alteration, one third received a targeted therapy. These findings show progress in testing for pts with targetable biomarkers in AML in the community setting, although further increases in testing and faster results could provid additional clinical benefit. Future directions for this work include analyzing patient outcomes.

Hematology-Oncology

Kim TM, Yoon DH, **Mattour AH**, Chaves JM, Curran E, Jeon YK, Kim BS, and Kim SJ. A Phase 1 Dose Escalation Study of Dual PI3K and DNA PK Inhibitor, BR101801 in Adult Patients with Advanced Hematologic Malignancies. *Blood* 2021; 138:3562.

Background: BR101801 not only blocks the signaling responsible for cell growth caused by PI3K, but also efficiently induces cell cycle arrest and apoptosis through inhibition of DNA-PK activation and stimulates decreasing stability of the oncogenic protein, c-Myc(AACR2020 abstract #655). This phase I study evaluated safety, tolerability, pharmacokinetics and preliminary activity of the BR101801 (PI3Kγ/δ and DNA PK inhibitor) in patients with advanced hematologic malignancies. Method: This is a Phase I, multi-center, open-label, first-in-human study. The Phase Ia (dose escalation) part of the study was designed to determine the maximum tolerated dose (MTD)/recommended dose for expansion (RDE) of BR101801. BR101801 was administered orally once daily in 28-day cycles. The dose escalation part was initiated with a dose titration in the initial cohort, followed by a 3 + 3 design. Results: 11 patients were enrolled and have been treated at 4 dose levels: 50mg, 100mg, 200mg, 325mg and expanded 200mg through fifth cohort escalation. Pathological subtypes include 7 PTCL, 2 DLBCL, 1 MZBL and 1 composite CTCL/MF. 3 females and 8 males have been treated to date. Median age is 58 (range 30-71) and ECOG PS is in the range of 0-1. All patients had taken at least one prior chemotherapy. 10 of total patients have completed at least one cycle except 1 premature drop-out case due to disease progression. First interim analysis after completion of cycle 3 of the last patient of 200mg QD cohort had been conducted, which was to include 5 patients (1 DLBCL and 4 PTCLs). No DLT had been identified in Cohorts 1-3, and 2 patients discontinued the study treatment due to adverse event (G4 thrombocytopenia, not related to IP) and disease progression, respectively. The PK values from multiple dosing range of 50mg to 200mg cohort resulted in an approximate 2.92-fold and 4.97 fold increase in exposure based on Cmax and AUCtau, respectively. BR101801 PK profile showed that the exposure of concentration increased in a dose dependent manner and there was no accumulation observed in the dose range of 50mg to 200mg. 2 DLTs was observed at 325mg QD cohort. The dose was de-escalated to the previous lower dose level (200mg QD) and was expanded to 3 additional patients. The expansion cohort is ongoing at present. 2 of 11 patients had G3 skin reaction and 3 had G3 hepatotoxicites. All adverse effects were manageable and recovered to grade 0-1 upon BR1010801 discontinuation. Total 5 patients have been currently ongoing. For overall tumor response assessment, 4 SDs and 2 PRs have been obsereved. Summary/Conclusion: 200 mg QD of BR101801 was shown to provide target exposure for clinical efficacy with the tolerable and safe profiles. BR101801 was well tolerated and showed preliminary signs of activity in patients with relapsed or refractory hematologic malignancies. The phase Ib/II study of BR101801 is warranted in relapsed/refractory NHL. This study is registered at clinicaltrials.gov identifier NCT04018248.

Hematology-Oncology

Sharma MR, Carvajal RD, Hanna GJ, Kang YK, Lee J, Lee KW, Li BT, Moore KN, Pegram M, Rasco D, Spira A, **Wang D**, Weinberg BA, Alonso M, Fang L, Husain A, Kowanetz M, Perez EA, and Dumbrava EI. Preliminary results from a phase I/II study of BDC-1001, a novel HER2 targeting TLR7/8 immune-stimulating antibody conjugate (ISAC), in patients (pts) with advanced HER2-expressing solid tumors. *Ann Oncol* 2021; 32:S1453-S1454.

Background: BDC-1001 is a novel ISAC consisting of an investigational trastuzumab biosimilar chemically conjugated to a TLR7/8 agonist with a non-cleavable linker. BDC1001 elicits myeloid activation and enhances antigen presentation leading to antibody-mediated effector functions that promote T-cell activation and a durable adaptive immune response. Methods: A 4-part, phase 1/2 dose-escalation/expansion study was initiated to evaluate BDC-1001 PD-1 inhibitor in pts with previously treated advanced/metastatic HER2-expressing (IHC2/3+) or amplified solid tumors (NCT04278144). Pts received BDC-1001 IV in a 3+3 design. Primary objectives are to evaluate safety, tolerability, dose-limiting toxicities (DLTs), and determine a recommended phase 2 dose (RP2D); secondary and exploratory objectives are to assess pharmacokinetics (PK), pharmacodynamics (PD), and preliminary antitumor activity. Results: From the completed monotherapy dose-escalation (Part 1) will be reported including safety, tolerability, PK, and PD biomarker data. The initial subset of pts enrolled include the following cancer types: breast, biliary, cervical, colorectal, lung, gastroesophageal, salivary, urinary tract, and endometrial. Preliminary results of the first 20 pts indicate that BDC-1001 appears well-tolerated. No DLTs have been observed, and the MTD has not been reached. AEs deemed related to BDC-1001 were grade 1-2, including infusion-related reactions and one event of decreased ejection fraction. Early evidence of clinical activity was observed in a pt with a partial response and other pts with stable disease. Increases in plasma biomarkers associated with TLR7/8 and myeloid cell activation (TNFa, CXCL10, MCP-1, MIP-1a) were observed. BDC-1001 treatment led to an increase in myeloid and T-cell infiltration

in a subset of pts. Updated clinical and translational data are anticipated. Conclusions: In this first-in-human study, BDC-1001 appears well-tolerated with early evidence of clinical activity, including pts previously treated with anti-HER2 therapy. Dose escalation is ongoing. Clinical trial identification: NCT04278144.

Hematology-Oncology

Sweidan A, **Vuyyala S**, **Xie P**, **Alhyari M**, **Dabak VS**, and **Otrock ZK**. Hyperhemolysis Syndrome in SCD Patient: Reminder of a Rare but Life-Threatening Complication of Blood Transfusion. *Blood* 2021; 138:4282.

Background: Sickle cell disease (SCD) patients are at risk of developing multiple complications from transfusions, including alloimmunization to red blood cell (RBC) antigens, delayed hemolytic transfusion reactions, and hyperhemolysis syndrome (HS). HS is a serious complication of transfusion characterized by the destruction of both transfused and autologous RBCs with resulting severe anemia and post transfusion hemoglobin lower than pretransfusion levels. We report the case of a middle age female patient with known SCD who developed severe HS following a blood transfusion. We aim to remind physicians of the importance of conservative blood transfusions in SCD patients in order to avoid serious transfusion-related complications. Case report: A 57-year-old African American patient, with known history of SCD who was doing well with a baseline hemoglobin (Hgb) of 6-7 g/dl. Transfusion history included 4 units of Packed Red Blood Cell (PRBC) during the 5 years prior to this presentation, all of which for mild, non-resolving vaso-occlusive pain crisis. Her most recent transfusion was 7 days prior to her presentation, she received 1 unit of PRBC for a Hgb level of 6.3 g/dl, associated with mild musculoskeletal pain and fatigue. She presented to the Emergency Department 4 days later with worsening fatigue, decreased oral intake and dark urine. On presentation, she was normotensive, afebrile and mildly tachycardic. She had increasing oxygen requirements to maintain O2 saturation above 94%. Her blood work showed a Hgb of 2.8 g/dl (12-15 g/dL), hematocrit 8.3 % (36-46 %), RBC count 0.87 M/uL (4.15-5.55 M/uL), Mean Corpuscular Volume 95.5 fl (80-100 fl), elevated White Cell Count at 28.4 K/uL (3.8-10.6 K/uL), and platelet count 125 K/uL (150-450 K/uL). Hemolysis labs showed low haptoglobin of < 30 mg/dl (30-200 mg/dl), elevated Lactate Dehydrogenase at 3420 IU/L (< 250 IU/L), total bilirubin 2.7 mg/dl (< 1.2 mg/dl), direct bilirubin 0.6 mg/dl (0-0.3 mg/dl), and reticulocyte count 3.5% (0.5-1.5 %; reticulocytopenia relative to degree of anemia). A disseminated intravascular coagulation (DIC) panel showed fibrinogen of 263 mg/dL (200-450 mg/dL), D-dimer greater than 20 ug/mL (< 0.50 ug/ml), prothrombin time of 19.8 seconds (s) (11.5-14.5 s), and partial thromboplastin time of 32 s (22-36 s). High sensitivity troponin was elevated at 650 ng/L (< 19 ng/L). Antibody screen and direct antiglobulin test (DAT) were negative. Peripheral blood smear showed severe anemia with marked anisopoikilocytosis including numerous blister cells, occasional sickle cells and numerous nucleated red blood cells. The recent history of blood transfusion and the current laboratory workup were consistent with HS. Patient was admitted to the intensive care unit (ICU) for management; she initially received 1g intravenous iron dextran and intravenous immunoglobulin (IVIG) 0.4 g/kg for 5 days. She was also started on erythropoietin, folic acid, and vitamin B12. Her reticulocyte count improved to 19%. Given no improvement in Hgb levels, systemic steroids were started after ruling out infectious etiologies. She initially received methylprednisolone 125mg daily for 2 days, followed by oral prednisone 60mg daily for 7 days. Patient had increased oxygen requirements during admission, had an elevated lactate to 4 mmol/L, and had a drop in Hgb to 2.1 g/dL. She was still managed conservatively with oxygen supplementation and intravenous crystalloid fluids. The decision was to avoid transfusions unless they were life-saving. Patient remained in the ICU unit for 5 days, then was transferred to the hematology floor where she remained hospitalized for 7 days. Oxygen requirements and patient's symptoms steadily improved, hemolysis labs trended down, and reticulocyte count improved. Hgb levels improved gradually to highest of 5.7 g/dl prior to discharge. Patient was then discharged to follow up with her hematologist in the outpatient setting. Conclusion: This case aims to highlight the importance of early recognition of HS to avoid wrong management with RBC transfusion. ur patient had severe anemia and was managed with transfusion-free approach with good outcome. This case is also meant to remind physicians of the importance of conservative blood transfusions in SCD patients in order to avoid serious and life-threatening transfusion-related complications.

Hospital Medicine

Schaefer JK, Errickson J, Kong X, Alexandris-Souphis T, Ali MA, Edupuganti S, Haymart B, **Kaatz S**, Kline-Rogers E, Kozlowski JH, **Krol GD**, **Shah V**, Sood SL, Froehlich JB, and Barnes GD. Outcomes of Direct Oral Anticoagulants with Aspirin Versus Warfarin with Aspirin for Atrial Fibrillation and/or Venous Thromboembolic Disease. *Blood* 2021; 138:179.

Introduction The direct oral anticoagulants (DOACs) including apixaban, dabigatran, edoxaban, and rivaroxaban are increasingly utilized for the management of venous thromboembolic disease (VTE) and/or non-valvular atrial fibrillation (NVAF). Adding aspirin (ASA) to warfarin or DOAC therapy increases bleeding risk. Patients on combination therapy with ASA and an anticoagulant were not well represented in clinical trials comparing DOACs to warfarin. We sought to compare bleeding and thrombotic outcomes with DOACs and ASA compared to warfarin and ASA in a non-trial setting. Methods We conducted a retrospective registry-based cohort study of adults on DOAC or warfarin therapy for VTE and/or NVAF. Warfarin treated patients were followed by six anticoagulation clinics. Four out of the six clinics contributed data on their patients that were on DOACs in the Michigan Anticoagulation Quality Improvement Initiative (MAQI 2) from January 2009 to June 2021. Patients were excluded if they had a history of heart valve replacement, recent myocardial infarction, or less than 3 months of follow-up. Two propensity matched cohorts (warfarin+ASA vs DOAC+ASA) of patients were analyzed based on ASA use at the time of study enrollment. The primary outcome was any new bleeding event. Secondary outcomes included new episodes of arterial or venous thrombosis, bleeding event type (major, fatal, life threatening, central nervous system, and non-major bleeding), emergency room visits, hospitalizations, transfusions, and death. Random chart audits were done to confirm the accuracy of the abstracted data. Event rates were compared using Poisson regression. Results We identified a total of 1,139 patients on DOACs plus ASA and 4,422 patients on warfarin plus ASA. After propensity matching, we compared two groups of 1,114 matched patients. DOAC treated patients were predominately on apixaban (62.3%) and rivaroxaban (30.4%), most often at therapeutic doses (Table 1). Patients were largely (90.5%) on low dose ASA (≤ 100 mg). Patient demographics, co-morbidities, indication for anticoagulation, history of bleeding or clotting, medications, and duration of follow-up were well-balanced after matching. Patients were followed for a median of 11.7 months (interquartile range 4.4 and 34 months). Patients treated with DOAC+ASA had 2.4 thrombotic events per 100 patient years compared to 2.2 thrombotic events per 100 patient years with warfarin+ASA (P=0.78). There were no significant differences observed between groups by thrombotic subtype (stroke, transient ischemic attack, pulmonary embolism, deep vein thrombosis, table 1). Bleeding was also similar with 30.1 bleeding events per 100 patient years with DOAC+ASA compared to 27.8 bleeds per 100 patient years with warfarin+ASA (P=0.24). There were no significant differences by bleeding subtype (table 1). Hospitalizations for clotting occurred less frequently with DOAC+ASA (0.9 hospitalizations per 100 patient years) compared to warfarin+ASA (1.7 hospitalizations per 100 patient years, P=0.03). Mortality, transfusions, and healthcare utilization were otherwise similar between the two groups. Conclusions For patients on a DOAC versus warfarin with ASA for atrial fibrillation and/or venous thromboembolic disease without a recent myocardial infarction or heart valve replacement, bleeding and thrombotic outcomes were similar.

Hospital Medicine

Zhao W, **Li P**, **Kaatz S**, **Latack K**, **Schultz L**, and **Poisson L**. Extended Thromboprophylaxis in Patients with COVID-19. *Blood* 2021; 138:1065.

Introduction Patients hospitalized with COVID-19 have an increased incidence of venous thromboembolism (VTE) and arterial thromboembolism (ATE) events. These thrombotic events increase readmission and mortality rate in COVID-19 survivors who are recently discharged from hospital. To lower the risk of VTE, a short course of post-discharge anticoagulation at either prophylactic or therapeutic dose has been variably prescribed among different facilities to COVID-19 patients. This practice, however, is challenged by less than 3% incidence of VTE in unselected patients. The net clinical benefit of extended thromboprophylaxis beyond hospitalization remains unclear. Methods We conducted a retrospective multicenter observational study of 5613 hospitalized COVID-19 patients. After applying the inclusion and exclusion criteria, 2838 patients were included in statistical analysis. Patients were excluded if they had negative SARS-CoV-2 PCR, remained hospitalized at the time of analysis, or were discharged to hospice service. The first symptomatic ATE and VTE events up to 90 days after patients' discharge from their

index admission for COVID-19 were identified using ICD-10 codes, and subsequently validated by chart review. The predictors for post-discharge VTE were identified using multivariate logistic regression. The average protective effect of anticoagulation was assessed using inverse propensity score weighting. Results The mean age (SD) of our cohort was 63.4 (16.7) years old and 47.6% were male. Black, white and other races were 38.9%, 50.7% and 10.3%, respectively. Thirty-six (1.3%) patients developed post-discharge VTE events that require hospital visits (18 deep vein thromboses, 16 pulmonary embolisms and 2 portal vein thromboses). Fifteen (0.5%) patients developed post-discharge ATE events (14 acute coronary syndromes and 1 transient ischemic attack). The incidence of VTE decreased with time (p <.001) with the median event time of 16 days (Figure 1). The incidence of ATE was unchanged with time (p =.369) with the median event time of 37 days (Figure 1). Patients who had a history of VTE (OR=3.24, 95% CI 1.34-7.86), peak D-dimer >3 µg/mL (OR=3.76, 95% CI 1.86-7.57), and predischarge C-reactive protein >10 mg/dL (OR=3.02, 95% CI 1.45-6.29) were at a high risk of developing VTE after hospital discharge (Figure 2). A short course of prophylactic or therapeutic anticoagulation after hospital discharge markedly reduced VTE (OR=0, 95% CI 0-0, p<.001, and OR=0.176, 95% CI 0.04-0.75, p=.02, respectively). Conclusions Although extended thromboprophylaxis in unselected COVID-19 patients is not recommended, post-discharge anticoagulation may be considered in high-risk patients who have a history of VTE, peak D-dimer >3 µg/mL and predischarge C-reactive protein >10 mg/dL if their bleeding risk is low. Our study has provided the first evidence to guide the selection of hospitalized COVID-19 patients who may benefit from post-discharge anticoagulation.

Internal Medicine

Lotya J, Dhamane A, Rosenblatt L, Jiang J, Levin D, Gemmen E, Waugh S, Guo JD, Khatib R, **Shah V**, Dorsch M, and Luo X. Discordance between Treatment Guideline Recommendations and Real-World Practice in a Group of Large Integrated Delivery Networks for Venous Thromboembolism (VTE) Patients: A Closer Look at VTE Patients with Cancer. *Blood* 2021; 138:1951.

Background: For patients with VTE, current American Society of Hematology (ASH) guideline panel suggests using direct oral anticoagulants (DOACs) over vitamin K antagonists (VKAs) where VKAs are required to be bridged with a parenteral anticoagulant (PAC). For patients with VTE and cancer, current guidelines recommend DOACs over low molecular weight heparin (LMWH) and LMWH over unfractionated heparin (heparin) for the initial treatment of VTE. Limited evidence is available about the patterns of anticoagulant treatment for VTE in routine clinical practice of large healthcare delivery networks in the United States (US) and whether the VTE treatments are aligned with current guidelines. This study aimed to assess real-world anticoagulant treatment patterns among VTE patients using harmonized electronic health record (EHR) data from four Integrated Delivery Networks (IDNs) in the US. Methods: This was a retrospective, longitudinal, multicenter, cohort study using harmonized EHR data from both inpatient and outpatient settings. The study population included adult patients prescribed DOACs, warfarin, and/or PAC therapy as inpatient or outpatient treatment within ≤30 days of VTE diagnosis, between June 2015 through May 2018. Data from the four IDNs was pooled to describe demographic characteristics and treatment patterns among VTE patients overall and by subgroups. Results: A total of 10,527 patients who were treated with OACs after VTE diagnosis were included for analysis. The mean (SD) age was 61.9 (5.98) years, with 46.1% aged 65 or older. More than half (53.2%) were female, and White patients comprised the majority (74.4%), followed by African American patients (22.8%). Obese and morbidly obese patients comprised 39.1% and 16.1% of patients, respectively. Among all VTE patients, warfarin-only (n=3545; 33.7%) was the most commonly used OAC treatment, followed by warfarin + PAC (n=3128; 29.7%), rivaroxaban-only (n=1357; 12.9%), rivaroxaban + PAC (n=853; 8.1%), apixaban + PAC (n=839; 8.0%), apixaban-only (n=762; 7.2%), and Other OAC (n=357; 3.4%) (Table 1). When stratifying VTE patients by age, gender, race and BMI, some variations in OAC treatment were observed. Among both older (≥65 years) and younger (<65 years) patients, warfarin-only was most commonly used, then warfarin + PAC. Warfarin-only was more commonly used among obese (36.3%) and morbidly obese (40.4%) patients than non-obese (29.8%) patients. OAC treatment patterns were generally comparable among men and women. Among White patients, approximately equal proportions of patients received warfarin + PAC (31.9%) and warfarin-only (31.0%). However, among African-American patients, a higher proportion of patients used warfarin-only (40.9%) vs. warfarin + PAC (24.5%). Patterns of anticoagulant treatments including OACs and/or parental anticoagulants among VTE patients with cancer were further analyzed (Figure 1). Among VTE patients with cancer (n=3657), heparin

had the highest use (26.7%), then enoxaparin (22.7%); approximately the same proportion of cancer patients received warfarin-only (16.0%) and warfarin + PAC (16.9%). Of DOACs, rivaroxaban-only was the most commonly used treatment (4.9%), then apixaban + PAC (3.5%), and lastly, rivaroxaban + PAC (3.4%) among cancer patients. Conclusion: Current VTE treatment guidelines recommend warfarin to be bridged with PAC, however, warfarin-only therapy remained the most used treatment option followed by warfarin + PAC. While rivaroxaban and apixaban are not required to be bridged with PAC, such practices were observed for a large proportion of apixaban- and rivaroxaban-treated VTE patients. VTE treatment among patients with cancer was not completely aligned with current guidelines, as heparin was more commonly used than LMWH (enoxaparin). Our findings suggest greater efforts are needed to improve anticoagulant treatment practices among VTE patients. [Formula presented] Disclosures: Dhamane: Bristol Myers Squibb: Current Employment, Current equity holder in publicly-traded company. Rosenblatt: Bristol Myers Squibb: C rrent Employment, Current equity holder in publicly-traded company. Jiang: Bristol Myers Squibb: Current Employment, Current equity holder in publicly-traded company. Guo: Bristol Myers Squibb: Ended employment in the past 24 months. Dorsch: Agency for Health Research and Quality: Research Funding; National Institutes of Health/National Institute of Aging: Research Funding; American Health Association Health IT Research Network: Research Funding; Janssen Pharmaceuticals: Honoraria; Bristol Myers Squibb/Pfizer: Research Funding; Amgen: Research Funding. Luo: Pfizer Inc: Current Employment, Current equity holder in publicly-traded company.

Internal Medicine

Nagirimadugu A, **Patel A**, **Nimri F**, **Musleh M**, **Naffouj S**, **Faber A**, **Abu Ghanimeh M**, and **Kaur N**. Impact of PHQ-9 Screen on Early Identification of Depression in IBD Clinic. *Am J Gastroenterol* 2021; 116:S15-S15.

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BACKGROUND: Over the past two decades there has been significant research linking inflammatory bowel disease (IBD) to depression. The chronicity of symptoms coupled with the financial burden of treatment costs, missed days of work/school and interpersonal relationship stress are contributing factors in the diagnosis of depression. The prevalence of depression within the IBD community is 15% and depressive symptoms are noted in 20% of patients. Furthermore, IBD patients with severe uncontrolled disease have higher rates of depression (40.7%) than those in remission (16.5%). The association between IBD and depression is linked to lower quality of life, poor medication compliance, worse disease outcomes, increased hospitalization, and higher suicidal risk. Early diagnosis and treatment of depression in IBD patients is paramount in achieving and maintaining IBD disease remission. While the association between IBD and depression is well-known, identifying depression can be a challenge. Review of recent literature shows that depression is under screened in IBD clinics. We present a prospective quality improvement study at a robust IBD center evaluating the impact of a validated depression screen (PHQ-9) on identifying depression compared to standard of care. METHODS: We compared the prevalence of depression in the IBD clinic in the control group using the history and diagnosis of depression and compared it against the intervention group after HQ-9 screening. Control group patient data was collected from June 2020 to July 2020 via virtual and in person visits. Intervention group PHQ-9 data was collected in person visits from January - March 2020 and post-intervention data collection was placed on hold until November 2020 due to the COVID pandemic. One randomly selected patient from each clinic session was asked to participate in the study at the time of visit. The primary end point was to compare the rates of depression and identify any barriers in providing early treatment for depression. The secondary endpoint was to identify high risk patients that are prone to depression. Categorical variables were analyzed by chi square analysis or fischer exact tests. Numerical data were analyzed using T-test. RESULTS: A total of 111 patients were screened. 60 patients were randomized to the control group (i.e. EMR based review for depression) and 51 patients were screened via survey during in person clinic visit. The identified depression rate from control vs intervention group is 20% vs. 35% ($p = 0.071$). Rates of depression were 15% in non-fistulizing Crohn's disease vs. 41.4% in fistulizing Crohn's disease ($p = 0.003$). Multivariate model for predicting depression noted to be significant for extra-intestinal manifestations OR of 3.06 (1.03, 9.12) $p = 0.045$ and age OR of 0.97 (0.94, 1.00) $p = 0.042$. Control vs.

intervention identification of depression in patients with extra-intestinal manifestations is notable for OR of 3.31 (1.15, 9.52) p = 0.026 in the univariate model and OR of 3.30 (1.07, 10.16) p = 0.038 in the multivariate model. CONCLUSION: Key findings including identification of depression is higher in the intervention group compared to the control group. Though the data is not statistically significant, this is likely secondary to the small sample size in the setting of the pandemic. In addition, univariate analysis revealed a statistically significant finding that the older the age of the patient, the less likely they are to have depression. Our data showed that the mean age of depressed patients was 38.3 compared to nondepressed patients whose mean age is 47.1. Further analysis can help elucidate this finding, for example identifying if older patients are being treated for depression or more likely to seek out therapists compared to younger patients. Univariate analysis also revealed that intestinal Crohn's disease was a risk factor for depression. This is possibly secondary to the severity of disease in these individuals, especially if their IBD is causing an impact on their quality of life. Looking into the number of hospitalizations, days off from work or school, and coexisting medical diagnoses can allow us to further understand if depression stems from their disease. Given preliminary findings, we plan to continue this study for a larger sample size and further determine if there is a significant delay in identifying depression with the current standard of care.

Internal Medicine

Schaefer JK, Errickson J, Kong X, Alexandris-Souphis T, Ali MA, Edupuganti S, Haymart B, **Kaatz S**, Kline-Rogers E, Kozlowski JH, **Krol GD**, **Shah V**, Sood SL, Froehlich JB, and Barnes GD. Outcomes of Direct Oral Anticoagulants with Aspirin Versus Warfarin with Aspirin for Atrial Fibrillation and/or Venous Thromboembolic Disease. *Blood* 2021; 138:179.

Introduction The direct oral anticoagulants (DOACs) including apixaban, dabigatran, edoxaban, and rivaroxaban are increasingly utilized for the management of venous thromboembolic disease (VTE) and/or non-valvular atrial fibrillation (NVAF). Adding aspirin (ASA) to warfarin or DOAC therapy increases bleeding risk. Patients on combination therapy with ASA and an anticoagulant were not well represented in clinical trials comparing DOACs to warfarin. We sought to compare bleeding and thrombotic outcomes with DOACs and ASA compared to warfarin and ASA in a non-trial setting. Methods We conducted a retrospective registry-based cohort study of adults on DOAC or warfarin therapy for VTE and/or NVAF. Warfarin treated patients were followed by six anticoagulation clinics. Four out of the six clinics contributed data on their patients that were on DOACs in the Michigan Anticoagulation Quality Improvement Initiative (MAQI 2) from January 2009 to June 2021. Patients were excluded if they had a history of heart valve replacement, recent myocardial infarction, or less than 3 months of follow-up. Two propensity matched cohorts (warfarin+ASA vs DOAC+ASA) of patients were analyzed based on ASA use at the time of study enrollment. The primary outcome was any new bleeding event. Secondary outcomes included new episodes of arterial or venous thrombosis, bleeding event type (major, fatal, life threatening, central nervous system, and non-major bleeding), emergency room visits, hospitalizations, transfusions, and death. Random chart audits were done to confirm the accuracy of the abstracted data. Event rates were compared using Poisson regression. Results We identified a total of 1,139 patients on DOACs plus ASA and 4,422 patients on warfarin plus ASA. After propensity matching, we compared two groups of 1,114 matched patients. DOAC treated patients were predominately on apixaban (62.3%) and rivaroxaban (30.4%), most often at therapeutic doses (Table 1). Patients were largely (90.5%) on low dose ASA (≤ 100 mg). Patient demographics, co-morbidities, indication for anticoagulation, history of bleeding or clotting, medications, and duration of follow-up were well-balanced after matching. Patients were followed for a median of 11.7 months (interquartile range 4.4 and 34 months). Patients treated with DOAC+ASA had 2.4 thrombotic events per 100 patient years compared to 2.2 thrombotic events per 100 patient years with warfarin+ASA (P=0.78). There were no significant differences observed between groups by thrombotic subtype (stroke, transient ischemic attack, pulmonary embolism, deep vein thrombosis, table 1). Bleeding was also similar with 30.1 bleeding events per 100 patient years with DOAC+ASA compared to 27.8 bleeds per 100 patient years with warfarin+ASA (P=0.24). There were no significant differences by bleeding subtype (table 1). Hospitalizations for clotting occurred less frequently with DOAC+ASA (0.9 hospitalizations per 100 patient years) compared to warfarin+ASA (1.7 hospitalizations per 100 patient years, P=0.03). Mortality, transfusions, and healthcare utilization were otherwise similar between the two groups. Conclusions For patients on a DOAC versus warfarin with ASA

for atrial fibrillation and/or venous thromboembolic disease without a recent myocardial infarction or heart valve replacement, bleeding and thrombotic outcomes were similar.

Internal Medicine

Sweidan A, **Vuyyala S**, **Xie P**, **Alhyari M**, **Dabak VS**, and **Otrock ZK**. Hyperhemolysis Syndrome in SCD Patient: Reminder of a Rare but Life-Threatening Complication of Blood Transfusion. *Blood* 2021; 138:4282.

Background: Sickle cell disease (SCD) patients are at risk of developing multiple complications from transfusions, including alloimmunization to red blood cell (RBC) antigens, delayed hemolytic transfusion reactions, and hyperhemolysis syndrome (HS). HS is a serious complication of transfusion characterized by the destruction of both transfused and autologous RBCs with resulting severe anemia and post transfusion hemoglobin lower than pretransfusion levels. We report the case of a middle age female patient with known SCD who developed severe HS following a blood transfusion. We aim to remind physicians of the importance of conservative blood transfusions in SCD patients in order to avoid serious transfusion-related complications. Case report: A 57-year-old African American patient, with known history of SCD who was doing well with a baseline hemoglobin (Hgb) of 6-7 g/dl. Transfusion history included 4 units of Packed Red Blood Cell (PRBC) during the 5 years prior to this presentation, all of which for mild, non-resolving vaso-occlusive pain crisis. Her most recent transfusion was 7 days prior to her presentation, she received 1 unit of PRBC for a Hgb level of 6.3 g/dl, associated with mild musculoskeletal pain and fatigue. She presented to the Emergency Department 4 days later with worsening fatigue, decreased oral intake and dark urine. On presentation, she was normotensive, afebrile and mildly tachycardic. She had increasing oxygen requirements to maintain O2 saturation above 94%. Her blood work showed a Hgb of 2.8 g/dl (12-15 g/dL), hematocrit 8.3 % (36-46 %), RBC count 0.87 M/uL (4.15-5.55 M/uL), Mean Corpuscular Volume 95.5 fl (80-100 fl), elevated White Cell Count at 28.4 K/uL (3.8-10.6 K/uL), and platelet count 125 K/uL (150-450 K/uL). Hemolysis labs showed low haptoglobin of < 30 mg/dl (30-200 mg/dl), elevated Lactate Dehydrogenase at 3420 IU/L (< 250 IU/L), total bilirubin 2.7 mg/dl (< 1.2 mg/dl), direct bilirubin 0.6 mg/dl (0-0.3 mg/dl), and reticulocyte count 3.5% (0.5-1.5 %; reticulocytopenia relative to degree of anemia). A disseminated intravascular coagulation (DIC) panel showed fibrinogen of 263 mg/dL (200-450 mg/dL), D-dimer greater than 20 ug/mL (< 0.50 ug/ml), prothrombin time of 19.8 seconds (s) (11.5-14.5 s), and partial thromboplastin time of 32 s (22-36 s). High sensitivity troponin was elevated at 650 ng/L (< 19 ng/L). Antibody screen and direct antiglobulin test (DAT) were negative. Peripheral blood smear showed severe anemia with marked anisopoikilocytosis including numerous blister cells, occasional sickle cells and numerous nucleated red blood cells. The recent history of blood transfusion and the current laboratory workup were consistent with HS. Patient was admitted to the intensive care unit (ICU) for management; she initially received 1g intravenous iron dextran and intravenous immunoglobulin (IVIG) 0.4 g/kg for 5 days. She was also started on erythropoietin, folic acid, and vitamin B12. Her reticulocyte count improved to 19%. Given no improvement in Hgb levels, systemic steroids were started after ruling out infectious etiologies. She initially received methylprednisolone 125mg daily for 2 days, followed by oral prednisone 60mg daily for 7 days. Patient had increased oxygen requirements during admission, had an elevated lactate to 4 mmol/L, and had a drop in Hgb to 2.1 g/dL. She was still managed conservatively with oxygen supplementation and intravenous crystalloid fluids. The decision was to avoid transfusions unless they were life-saving. Patient remained in the ICU unit for 5 days, then was transferred to the hematology floor where she remained hospitalized for 7 days. Oxygen requirements and patient's symptoms steadily improved, hemolysis labs trended down, and reticulocyte count improved. Hgb levels improved gradually to highest of 5.7 g/dl prior to discharge. Patient was then discharged to follow up with her hematologist in the outpatient setting. Conclusion: This case aims to highlight the importance of early recognition of HS to avoid wrong management with RBC transfusion. ur patient had severe anemia and was managed with transfusion-free approach with good outcome. This case is also meant to remind physicians of the importance of conservative blood transfusions in SCD patients in order to avoid serious and life-threatening transfusion-related complications. Disclosures: No relevant conflicts of interest to declare.

Neurology

Dekker SE, Bambakidis T, Williams AM, Biesterveld B, Bhatti U, Li Y, Pickell Z, **Buller B**, and Alam HB. Early Transfusion with Mesenchymal Stem Cell Derived Extracellular Vesicles: A New Transfusion Strategy for Life-Threatening Hemorrhage and Traumatic Brain Injury. *Blood* 2021; 138:1071.

Background: Life-threatening hemorrhage and traumatic brain injury (TBI) have a significantly increasing global burden and remain leading causes of preventable deaths. Effective interventions may protect the brain against ongoing damage and improve the long-term outcomes. A growing area of interest is transfusion of cell-based therapies, particularly with bone marrow-derived mesenchymal stem cells (MSC). Transfusion using MSC derived extracellular vesicles (EVs) have shown to improve neurologic outcomes in animal models of life-threatening hemorrhage, stroke, and TBI. However, the precise mechanisms remain poorly characterized. In the present study, we aimed to elucidate some of the key cerebral genes, pathways, and networks that were modulated after transfusion of EVs in a porcine model of hemorrhagic shock (HS) and TBI. Methods: Swine were subjected to HS (40% blood volume) and severe TBI (8-mm cortical impact). After 1 hour of shock, animals were randomized (n=4/group) to treatment with either lactated Ringer's (LR) or LR+EV. Both groups received fluid resuscitation after 2 hours of shock, and autologous packed red blood cells 5 hours later. After 7-days, brains were harvested and RNA-sequencing was performed. The transcriptomic data was imported into the iPathway pipeline for bioinformatics analyses. Results: 5,273 genes were differentially expressed in the LR+EV group vs. LR alone (total 9,588 measured genes, Figure 1). Table 1 lists the top 10 genes exhibiting the greatest up- and down-expression based on fold change. Genes with the greatest up-regulation were involved in synaptic transmission and neuronal development and differentiation, while down-regulated genes were involved in inflammation. Gene Ontology terms experiencing the greatest modulation were involved in inflammation, brain development, and cell adhesion. Pathway analysis revealed significant modulation in the glutamatergic and GABAergic systems. Network analysis revealed down-regulation of inflammation (Figure 2), and up-regulation of neurogenesis, and neuron survival and differentiation. Conclusions: In a porcine model of HS+TBI, EV transfusion was associated with an attenuation of cerebral inflammatory networks and a promotion of neurogenesis and neuroplasticity. These transcriptomic changes could explain the observed neuroprotective and neurorestorative properties associated with EV transfusion. EV transfusion reduces the hyper-inflammatory response and may have great promise in improving outcomes in concurrent life-threatening hemorrhage and severe TBI. Further testing of this novel strategy and its implications in transfusion medicine are warranted. [Formula presented] Disclosures: No relevant conflicts of interest to declare.

Pathology and Laboratory Medicine

Sweidan A, **Vuyyala S**, **Xie P**, **Alhyari M**, **Dabak VS**, and **Otrock ZK**. Hyperhemolysis Syndrome in SCD Patient: Reminder of a Rare but Life-Threatening Complication of Blood Transfusion. *Blood* 2021; 138:4282.

Background: Sickle cell disease (SCD) patients are at risk of developing multiple complications from transfusions, including alloimmunization to red blood cell (RBC) antigens, delayed hemolytic transfusion reactions, and hyperhemolysis syndrome (HS). HS is a serious complication of transfusion characterized by the destruction of both transfused and autologous RBCs with resulting severe anemia and post transfusion hemoglobin lower than pretransfusion levels. We report the case of a middle age female patient with known SCD who developed severe HS following a blood transfusion. We aim to remind physicians of the importance of conservative blood transfusions in SCD patients in order to avoid serious transfusion-related complications. Case report: A 57-year-old African American patient, with known history of SCD who was doing well with a baseline hemoglobin (Hgb) of 6-7 g/dl. Transfusion history included 4 units of Packed Red Blood Cell (PRBC) during the 5 years prior to this presentation, all of which for mild, non-resolving vaso-occlusive pain crisis. Her most recent transfusion was 7 days prior to her presentation, she received 1 unit of PRBC for a Hgb level of 6.3 g/dl, associated with mild musculoskeletal pain and fatigue. She presented to the Emergency Department 4 days later with worsening fatigue, decreased oral intake and dark urine. On presentation, she was normotensive, afebrile and mildly tachycardic. She had increasing oxygen requirements to maintain O2 saturation above 94%. Her blood work showed a Hgb of 2.8 g/dl (12-15 g/dL), hematocrit 8.3 % (36-46 %), RBC count 0.87 M/uL (4.15-5.55 M/uL), Mean Corpuscular Volume 95.5 fl (80-100 fl), elevated White Cell Count at 28.4 K/uL

(3.8-10.6 K/uL), and platelet count 125 K/uL (150-450 K/uL). Hemolysis labs showed low haptoglobin of < 30 mg/dl (30-200 mg/dl), elevated Lactate Dehydrogenase at 3420 IU/L (< 250 IU/L), total bilirubin 2.7 mg/dl (< 1.2 mg/dl), direct bilirubin 0.6 mg/dl (0-0.3 mg/dl), and reticulocyte count 3.5% (0.5-1.5 %; reticulocytopenia relative to degree of anemia). A disseminated intravascular coagulation (DIC) panel showed fibrinogen of 263 mg/dL (200-450 mg/dL), D-dimer greater than 20 ug/mL (< 0.50 ug/ml), prothrombin time of 19.8 seconds (s) (11.5-14.5 s), and partial thromboplastin time of 32 s (22-36 s). High sensitivity troponin was elevated at 650 ng/L (< 19 ng/L). Antibody screen and direct antiglobulin test (DAT) were negative. Peripheral blood smear showed severe anemia with marked anisopoikilocytosis including numerous blister cells, occasional sickle cells and numerous nucleated red blood cells. The recent history of blood transfusion and the current laboratory workup were consistent with HS. Patient was admitted to the intensive care unit (ICU) for management; she initially received 1g intravenous iron dextran and intravenous immunoglobulin (IVIG) 0.4 g/kg for 5 days. She was also started on erythropoietin, folic acid, and vitamin B12. Her reticulocyte count improved to 19%. Given no improvement in Hgb levels, systemic steroids were started after ruling out infectious etiologies. She initially received methylprednisolone 125mg daily for 2 days, followed by oral prednisone 60mg daily for 7 days. Patient had increased oxygen requirements during admission, had an elevated lactate to 4 mmol/L, and had a drop in Hgb to 2.1 g/dL. She was still managed conservatively with oxygen supplementation and intravenous crystalloid fluids. The decision was to avoid transfusions unless they were life-saving. Patient remained in the ICU unit for 5 days, then was transferred to the hematology floor where she remained hospitalized for 7 days. Oxygen requirements and patient's symptoms steadily improved, hemolysis labs trended down, and reticulocyte count improved. Hgb levels improved gradually to highest of 5.7 g/dl prior to discharge. Patient was then discharged to follow up with her hematologist in the outpatient setting. Conclusion: This case aims to highlight the importance of early recognition of HS to avoid wrong management with RBC transfusion. ur patient had severe anemia and was managed with transfusion-free approach with good outcome. This case is also meant to remind physicians of the importance of conservative blood transfusions in SCD patients in order to avoid serious and life-threatening transfusion-related complications. Disclosures: No relevant conflicts of interest to declare.

Public Health Sciences

Lee Y, Jehangir Q, **Li P**, **Lin CH**, Sule AA, Krishnamoorthy G, Goodman JR, Halabi A, Patel K, Wang DD, **Poisson L**, and Nair GB. Risk Stratification for Acute Arterial and Venous Thromboembolism using CHA 2DS 2-VASc Score in Hospitalized COVID-19 Patients: A Multicenter Study. *Blood* 2021; 138:2120.

Introduction: Arterial and venous thromboembolism are common complications in COVID-19. Micro-macro thrombosis-related organ dysfunction can confer an increased risk for mortality. The optimal dosage of anticoagulation (AC) in COVID-19 patients remains unclear. Interim data from adaptive randomized control trials (ATTACC, REMAP-CAP, and ACTIV-4a) showed divergent results of therapeutic AC (TAC) versus usual care AC for the primary outcome of organ support free days in hospitalized COVID-19 patients. Components of CHA 2DS 2-VASc, a model originally built for predicting ischemic stroke in atrial fibrillation, are consistent with independent risk factors for COVID-19 severity and mortality. Herein, we analyzed the performance of the CHA 2DS 2-VASc model in hospitalized COVID-19 patients for predicting arterial and venous thromboembolic events, which could potentially aid in risk stratification of hospitalized patients and guide AC dosing. Methods: This is a large, retrospective, multicenter cohort study that included all adult patients from one tertiary care and five community hospitals with PCR-proven SARS-CoV-2 infection between 3/1/2020 and 12/1/2020. The primary composite outcome was acute arterial thromboembolism (ATE) and venous thromboembolism (VTE). We identified patients with ATE [cerebrovascular accident (CVA), myocardial infarction (MI) including both ST-segment elevation MI and non-ST-segment elevation MI], and VTE [deep vein thrombosis (DVT) and pulmonary embolism (PE)] using ICD -10 codes. Mean and standard deviation were reported for continuous variables; proportions were reported for categorical variables. To compare the groups, the Chi-square test was used for categorical variables, and the t-test was used for continuous variables. CHA 2DS 2-VASc scores were calculated on admission and were used as a measure of the predictive accuracy of the scoring system. Sensitivity and specificity with different cut-offs of CHA 2DS 2-VASc scores were calculated. All statistical tests were 2-sided with an α (significance) level of 0.05. All data were analyzed using R version 4.0.5. Results: Among 3526 patients, a total of 619 patients had thromboembolic events: 383 had ATE and 236 had VTE. Of 383 patients who had ATE, 350 patients

were found to have acute MI, 48 had CVA, and 15 had both MI and CVA. In patients with VTE, 134 had DVT, 168 had PE, and 66 had both DVT and PE (Figure 1). We analyzed the primary composite outcome of ATE and VTE (group 1) vs no ATE and VTE (group 2). Baseline characteristics are included in Table 1. The in-patient all-cause mortality rate was 28.4% in group 1 vs 12.6% in group 2 (p<0.001). The mean hospital length of stay was 12.3 days in group 1 vs 8.8 days in group 2 (p<0.001). Group 1 had a mean CHA 2DS 2-VASc score of 3.3 ±1.6. vs 2.7±1.7 in group 2 (p<0.001) (Figure 2). At CHA 2DS 2-VASc scores of 3 and 4, the model had a specificity of 46% and 67% and sensitivity of 68% and 42% respectively for predicting ATE/VTE. The CHA 2DS 2-VASc score of 5 had a specificity of 86% and sensitivity of 25%. The score of 7 had 98% specificity but 3% sensitivity (Table 2). Conclusion: Our results suggest that the CHA 2DS 2-VASc model for arterial and venous thromboembolism has a moderate performance. The CHA 2DS 2-VASc score of 5 has a high specificity, though low sensitivity, for predicting thromboembolism. The CHA 2DS 2-VASc score can be used as an adjunct risk stratification tool to initiate TAC. [Formula presented] Disclosures: No relevant conflicts of interest to declare.

Public Health Sciences

Zhao W, **Li P**, **Kaatz S**, **Latack K**, **Schultz L**, and **Poisson L**. Extended Thromboprophylaxis in Patients with COVID-19. *Blood* 2021; 138:1065.

Introduction Patients hospitalized with COVID-19 have an increased incidence of venous thromboembolism (VTE) and arterial thromboembolism (ATE) events. These thrombotic events increase readmission and mortality rate in COVID-19 survivors who are recently discharged from hospital. To lower the risk of VTE, a short course of post-discharge anticoagulation at either prophylactic or therapeutic dose has been variably prescribed among different facilities to COVID-19 patients. This practice, however, is challenged by less than 3% incidence of VTE in unselected patients. The net clinical benefit of extended thromboprophylaxis beyond hospitalization remains unclear. Methods We conducted a retrospective multicenter observational study of 5613 hospitalized COVID-19 patients. After applying the inclusion and exclusion criteria, 2838 patients were included in statistical analysis. Patients were excluded if they had negative SARS-CoV-2 PCR, remained hospitalized at the time of analysis, or were discharged to hospice service. The first symptomatic ATE and VTE events up to 90 days after patients' discharge from their index admission for COVID-19 were identified using ICD-10 codes, and subsequently validated by chart review. The predictors for post-discharge VTE were identified using multivariate logistic regression. The average protective effect of anticoagulation was assessed using inverse propensity score weighting. Results The mean age (SD) of our cohort was 63.4 (16.7) years old and 47.6% were male. Black, white and other races were 38.9%, 50.7% and 10.3%, respectively. Thirty-six (1.3%) patients developed post-discharge VTE events that require hospital visits (18 deep vein thromboses, 16 pulmonary embolisms and 2 portal vein thromboses). Fifteen (0.5%) patients developed post-discharge ATE events (14 acute coronary syndromes and 1 transient ischemic attack). The incidence of VTE decreased with time (p <.001) with the median event time of 16 days (Figure 1). The incidence of ATE was unchanged with time (p =.369) with the median event time of 37 days (Figure 1). Patients who had a history of VTE (OR=3.24, 95% CI 1.34-7.86), peak D-dimer >3 µg/mL (OR=3.76, 95% CI 1.86-7.57), and predischarge C-reactive protein >10 mg/dL (OR=3.02, 95% CI 1.45-6.29) were at a high risk of developing VTE after hospital discharge (Figure 2). A short course of prophylactic or therapeutic anticoagulation after hospital discharge markedly reduced VTE (OR=0, 95% CI 0-0, p<.001, and OR=0.176, 95% CI 0.04-0.75, p=.02, respectively). Conclusions Although extended thromboprophylaxis in unselected COVID-19 patients is not recommended, post-discharge anticoagulation may be considered in high-risk patients who have a history of VTE, peak D-dimer >3 µg/mL and predischarge C-reactive protein >10 mg/dL if their bleeding risk is low. Our study has provided the first evidence to guide the selection of hospitalized COVID-19 patients who may benefit from post-discharge anticoagulation.

HFHS Publications on COVID-19

Administration
Gifford L, **Johnson CC**, **Haque N**, **Passalacqua KD**, **Swiderek J**, and **Kalkanis S**. COVID-19 in the hotspot of Metropolitan Detroit: A multi-faceted health system experience. *Int J Health Plann Manage* 2021; Epub ahead of print. PMID: 34859491. Full Text

Administration
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Administration
Xiao S, **Sahasrabudhe N**, **Hochstadt S**, **Cabral W**, **Simons S**, **Yang M**, **Lanfear DE**, and **Williams LK**. Predicting death from COVID-19 using pre-existing conditions: implications for vaccination triage. *BMJ Open Respir Res* 2021; 8(1). PMID: 34949575. Full Text

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Fonseca W, Asai N, Yagi K, Malinczak CA, **Savickas G**, **Johnson CC**, **Murray S**, **Zoratti EM**, Lukacs NW, **Li J**, and Schuler Iv CF. COVID-19 Modulates Inflammatory and Renal Markers That May Predict Hospital Outcomes among African American Males. *Viruses* 2021; 13(12). PMID: 34960684. Full Text

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Cardiology/Cardiovascular Research
McKinnon JE, **Wang DD**, **Zervos M**, **Saval M**, **Marshall-Nightengale L**, **Kilgore P**, **Pabla P**, **Szandzik E**, **Maksimowicz-McKinnon K**, and **O'Neill WW**. Safety and Tolerability of Hydroxychloroquine in healthcare workers and first responders for the prevention of COVID-19: WHIP COVID-19 Study. *Int J Infect Dis* 2021; Epub ahead of print. PMID: 34954095. Full Text

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Xiao S, **Sahasrabudhe N**, **Hochstadt S**, **Cabral W**, **Simons S**, **Yang M**, **Lanfear DE**, and **Williams LK**. Predicting death from COVID-19 using pre-existing conditions: implications for vaccination triage. *BMJ Open Respir Res* 2021; 8(1). PMID: 34949575. Full Text

Center for Individualized and Genomic Medicine Research
Xiao S, **Sahasrabudhe N**, **Hochstadt S**, **Cabral W**, **Simons S**, **Yang M**, **Lanfear DE**, and **Williams LK**. Predicting death from COVID-19 using pre-existing conditions: implications for vaccination triage. *BMJ Open Respir Res* 2021; 8(1). PMID: 34949575. Full Text

Dermatology
Arora H, **Boothby-Shoemaker W**, **Braunberger T**, **Lim HW**, and **Veenstra J**. Safety of conventional immunosuppressive therapies for patients with dermatological conditions and coronavirus disease 2019: A review of current evidence. *J Dermatol* 2021; Epub ahead of print. PMID: 34962304. Full Text

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Gifford L, **Johnson CC**, **Haque N**, **Passalacqua KD**, **Swiderek J**, and **Kalkanis S**. COVID-19 in the hotspot of Metropolitan Detroit: A multi-faceted health system experience. *Int J Health Plann Manage* 2021; Epub ahead of print. PMID: 34859491. Full Text

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