

Henry Ford Health System Publication List – August 2020

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 **113 unique citations** listed this month, with **11 articles 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

Xia H, Li S, Li X, Wang W, Bian Y, Wei S, Grove S, Wang W, Vatan L, Liu JR, McLean K, **Rattan R, Munkarah AR**, Guan JL, Kryczek I, and Zou W. Autophagic adaptation to oxidative stress alters peritoneal residential macrophage survival and ovarian cancer metastasis. *JCI Insight* 2020; Epub ahead of print. PMID: 32780724. [Full Text](#)

Department of Surgery, University of Michigan School of Medicine, Ann Arbor, United States of America.

Department of Obstetrics and Gynecology, University of Michigan School of Medicine, Ann Arbor, United States of America.

Department of Women's Health Services, Henry Ford Health System, Detroit, United States of America.

Department of Cancer Biology, University of Cincinnati College of Medicine, Cincinnati, United States of America.

Tumor-associated macrophages (TAMs) affect cancer progression and therapy. Ovarian carcinoma often metastasizes to the peritoneal cavity. Here, we found two peritoneal macrophage subsets in mice bearing ID8 ovarian cancer based on the Tim-4 (T-cell immunoglobulin and mucin domain containing 4) expression. Tim-4+ TAMs were embryonically originated and locally sustained while Tim-4- TAMs were replenished from circulating monocytes. Tim-4+ TAMs, but not Tim-4- TAMs, promoted tumor growth in vivo. Relative to Tim-4- TAMs, Tim-4+ TAMs manifested high oxidative phosphorylation and adapted mitophagy to alleviate oxidative stress. High levels of arginase-1 in Tim-4+ TAMs contributed to potent mitophagy activities via weakened mTORC1 activation due to low arginine resultant from arginase-1-mediated metabolism. Furthermore, genetic deficiency of autophagy element FIP200 resulted in Tim-4+ TAM loss via ROS-mediated apoptosis, and elevated T cell-immunity and ID8 tumor inhibition in vivo. Moreover, human ovarian cancer-associated CR1g (complement receptor of the Immunoglobulin superfamily) positive macrophages were transcriptionally, metabolically, and functionally similar to murine Tim-4+ TAMs. Thus, targeting CR1g+ (Tim-4+) TAMs may potentially treat ovarian cancer patients with peritoneal metastasis.

Anesthesiology

Deer TR, Esposito MF, McRoberts WP, Grider JS, Sayed D, Verrills P, Lamer TJ, Hunter CW, Slavin KV, Shah JM, Hagedorn JM, Simopoulos T, Gonzalez DA, Amirdelfan K, Jain S, Yang A, **Aiyer R**, Antony A, Azeem N, Levy RM, and Mekhail N. A Systematic Literature Review of Peripheral Nerve Stimulation Therapies for the Treatment of Pain. *Pain Med* 2020; 21(8):1590-1603. PMID: 32803220. [Full Text](#)

The Spine and Nerve Center of the Virginias, Charleston, West Virginia.

Florida Pain Institute, Melbourne, Florida.

Anodyne Research, PA, University of Miami, Miami, Florida.

UKHealthCare Pain Services, Department of Anesthesiology, University of Kentucky College of Medicine, Lexington, Kentucky.

University of Kansas Medical Center, Kansas City, Kansas, USA.
Metro Spinal Clinic, Melbourne, Victoria, Australia.
Division of Pain Medicine, Department of Anesthesiology, Mayo Clinic, Rochester, Minnesota.
Ainsworth Institute of Pain Management, New York, New York.
Department of Neurosurgery, University of Illinois at Chicago, Chicago, Illinois.
SamWell Institute for Pain Management, Colonia, New Jersey.
Mayo Clinic, Rochester, Minnesota.
Department of Anesthesiology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA.
Pain Unit, Hospital Universitario Quirón-Salud, Madrid, Spain.
IPM Medical Group, Walnut Creek, California.
Pain Treatment Centers of America, Little Rock, Arkansas.
Mt. Sinai Hospital, New York, New York.
Interventional Pain Management and Pain Psychiatry Faculty, Henry Ford Health System, Detroit, Michigan.
University of Florida College of Medicine, Jacksonville, Florida.
Florida Spine & Pain Specialists, Bradenton, Florida.
Director of Neurosurgical Services, Director of Clinical Research, Anesthesia Pain Care Consultants, Tamarac, Florida.
Evidence-Based Pain Management Research and Education, Cleveland Clinic, Cleveland, Ohio, USA.

OBJECTIVE: To conduct a systematic literature review of peripheral nerve stimulation (PNS) for pain. **DESIGN:** Grade the evidence for PNS. **METHODS:** An international interdisciplinary work group conducted a literature search for PNS. Abstracts were reviewed to select studies for grading. Inclusion/exclusion criteria included prospective randomized controlled trials (RCTs) with meaningful clinical outcomes that were not part of a larger or previously reported group. Excluded studies were retrospective, had less than two months of follow-up, or existed only as abstracts. Full studies were graded by two independent reviewers using the modified Interventional Pain Management Techniques–Quality Appraisal of Reliability and Risk of Bias Assessment, the Cochrane Collaborations Risk of Bias assessment, and the US Preventative Services Task Force level-of-evidence criteria. **RESULTS:** Peripheral nerve stimulation was studied in 14 RCTs for a variety of painful conditions (headache, shoulder, pelvic, back, extremity, and trunk pain). Moderate to strong evidence supported the use of PNS to treat pain. **CONCLUSION:** Peripheral nerve stimulation has moderate/strong evidence. Additional prospective trials could further refine appropriate populations and pain diagnoses.

Anesthesiology

Deer TR, Hunter CW, Mehta P, Sayed D, Grider JS, Lamer TJ, Pope JE, Falowski S, Provenzano DA, Esposito MF, Slavin KV, Baranidharan G, Russo M, Jassal NS, Mogilner AY, Kapural L, Verrills P, Amirdefan K, McRoberts WP, Harned ME, Chapman KB, Liem L, Carlson JD, Yang A, **Aiyer R**, Antony A, Fishman MA, Al-Kaisy AA, Christelis N, Levy RM, and Mekhail N. A Systematic Literature Review of Dorsal Root Ganglion Neurostimulation for the Treatment of Pain. *Pain Med* 2020; 21(8):1581-1589. PMID: 32803221. [Full Text](#)

Spine and Nerve Center of the Virginias, Charleston, West Virginia.
Ainsworth Institute of Pain Management, New York, New York.
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University of Kansas Medical Center, Kansas City, Kansas.
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Pain Management and Neuromodulation Centre at Guy's and St. Thomas' NHS Trust, London, UK.
Pain Specialists Australia, Monash University, Richmond, Victoria, Australia.
Neurosurgical Services and of Clinical Research, Anesthesia Pain Care Consultants, Tamarac, Florida.
Evidence-Based Pain Management Research and Education, Cleveland Clinic, Cleveland, Ohio, USA.

OBJECTIVE: To conduct a systematic literature review of dorsal root ganglion (DRG) stimulation for pain. **DESIGN:** Grade the evidence for DRG stimulation. **METHODS:** An international, interdisciplinary work group conducted a literature search for DRG stimulation. Abstracts were reviewed to select studies for grading. General inclusion criteria were prospective trials (randomized controlled trials and observational studies) that were not part of a larger or previously reported group. Excluded studies were retrospective, too small, or existed only as abstracts. Studies were graded using the modified Interventional Pain Management Techniques-Quality Appraisal of Reliability and Risk of Bias Assessment, the Cochrane Collaborations Risk of Bias assessment, and the US Preventative Services Task Force level-of-evidence criteria. **RESULTS:** DRG stimulation has Level II evidence (moderate) based upon one high-quality pivotal randomized controlled trial and two lower-quality studies. **CONCLUSIONS:** Moderate-level evidence supports DRG stimulation for treating chronic focal neuropathic pain and complex regional pain syndrome.

Behavioral Health Services/Psychiatry

Memon RI, Naveed S, Faquih AE, Fida A, Abbas N, Chaudhary AMD, and Qayyum Z. Effectiveness and Safety of Ketamine for Unipolar Depression: a Systematic Review. *Psychiatr Q* 2020; Epub ahead of print. PMID: 32852658.

[Full Text](#)

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Major Depressive Disorder (MDD) is a common psychiatric disorder with major implications for healthcare system and socioeconomic burden. For chronic and treatment-resistant depression, Ketamine has emerged as a possible treatment option. This systematic review explores the evidence for the effectiveness and tolerability of Ketamine in patients with MDD. This systematic review was conducted following the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) checklist. Eight electronic databases were searched by using search terms: (ketamine) AND (trial OR RCT OR clinical-trial) AND (depressive OR depression OR "depressive-disorder"). After a rigorous screening process against the predetermined eligibility criteria, 35 randomized controlled trials (RCTs) were included. Quality assessment of included studies was done by using the Cochrane risk-of-bias tool for RCTs. Thirty-five RCTs are included in this review article with majority of studies from United States, Iran, and China. Intravenous (IV) Ketamine was effective in 70% (21/30) of the included studies whereas oral and Intranasal (IN) Ketamine were effective in two and three studies, respectively. The majority of studies (6/8) using Ketamine as anesthetic agent during electroconvulsive therapy (ECT) failed to show an improvement compared to the participants receiving ECT and placebo. The most common reported side effects were nausea, vomiting, dizziness, diplopia, drowsiness, dysphoria, hallucinations, and confusion. Ketamine is an effective treatment option for patients with MDD with undesirable effects when administered via oral, IV and IN routes. Ketamine augmentation of ECT requires further exploration in well-designed studies with adequate sample size. The short-lived antidepressant effect of Ketamine is a potential limitation, therefore, further studies administering multiple infusions for acute treatment and maintenance are necessary.

Behavioral Health Services/Psychiatry

Sablabaan IM, and Sivananthan M. Attention-Deficit Hyperactivity Disorder-Associated Impulsive Aggression Treated With Lamotrigine. *Am J Ther* 2020; Epub ahead of print. PMID: 32769396. [Full Text](#)

Behavioral Health Services/Psychiatry

Wong A, and **Mun M**. A Case of Kratom Overdose in a Pediatric Patient. *Case Rep Psychiatry* 2020; 2020:8818095. PMID: 32855833. [Full Text](#)

Kratom is a synthetic opioid that is federally unregulated and thus available for purchase through online retail and smoke shops in most states. Due to its availability, there is concern for misuse in the pediatric population. There is existing literature describing toxicity of kratom in adults; yet, to the best of our knowledge, there are no cases describing kratom toxicity in the pediatric population. Thus, we present the case of kratom overdose in a pediatric patient.

Cardiology/Cardiovascular Research

Afana M, Koenig GC, Seth M, Sukul D, Frazier KM, Fielding S, Jensen A, and Gurm HS. Trends and outcomes of non-primary PCI at sites without cardiac surgery on-site: The early Michigan experience. *PLoS One* 2020; 15(8):e0238048. PMID: 32845908. [Full Text](#)

Division of Cardiovascular Medicine, Henry Ford Health System, Detroit, Michigan, United States of America.
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INTRODUCTION: Non-primary percutaneous coronary intervention (non-PPCI) recently received certificate of need approval in the state of Michigan at sites without cardiac surgery on-site (cSoS). This requires quality oversight through participation in the BMC2 registry. While previous studies have indicated the safety of this practice, real-world comprehensive outcomes, case volume changes, economic impacts, and readmission rates at diverse healthcare centers with and without cSoS remain poorly understood. **METHODS:** Consecutive patients undergoing non-PPCI at 47 hospitals (33 cSoS and 14 non-cSoS) in Michigan from April 2016 to March 2018 were included. Using propensity-matching, patients were analyzed to assess outcomes and trends in non-PPCI performance at sites with and without cSoS. **RESULTS:** Of 61,864 PCI's performed, 50,817 were non-PPCI, with 46,096 (90.7%) performed at sites with cSoS and 4,721 (9.3%) at sites without cSoS. From this cohort, 4,643 propensity-matched patients were analyzed. Rates of major adverse cardiac events (2.6% vs. 2.8%; $p = 0.443$), in-hospital mortality (0.6% vs. 0.5%; $p = 0.465$), and several secondary clinical and quality outcomes showed no clinically significant differences. Among a small subset with available post-discharge data, there were no differences in 90-day readmission rates, standardized episode costs, or post-discharge mortality. Overall PCI volume remained stable, with a near three-fold rise in non-PPCI at sites without cSoS. **CONCLUSIONS:** Non-PPCI at centers without cardiac SoS was associated with similar comprehensive outcomes, quality of care, 90-day episode costs, and post-discharge mortality compared with surgical sites. Mandatory quality oversight serves to maintain appropriate equivalent outcomes and may be considered for other programs, including the performance of non-PPCI at ambulatory surgical centers in the near future.

Cardiology/Cardiovascular Research

Bajwa F, **Jafri SM**, and **Ananthasubramaniam K**. A Review of Selected Adult Congenital Heart Diseases Encountered in Daily Practice. *Curr Cardiol Rev* 2020; Epub ahead of print. PMID: 32778034. [Request Article](#)

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The advancement in corrective surgical procedures and anaesthesia technology has resulted in the increase survival of patients with Congenital Heart Diseases (CHD). Most of the surviving CHD patients have successfully reached adulthood and those surviving adults now outnumber the infants born with the CHD. Unfortunately, the surviving adults with CHD do not get proper care due to either inconsistent follow up or not getting care from a specialist in the field of CHD. It is imperative for general practicing clinicians to be aware of the congenital diseases as well as the current clinical recommendations. This manuscript reviews some of the common congenital diseases seen in adults such as cardiac shunts, left heart obstructive lesions and aortopathies.

Cardiology/Cardiovascular Research

Basir MB, Lemor A, and **O'Neill W**. Reply: Cardiogenic Shock Management Will Never Be All or None. *JACC Cardiovasc Interv* 2020; 13(15):1837-1838. PMID: 32763081. [Full Text](#)

Cardiology/Cardiovascular Research

Chamogeorgakis T, Cowger J, Apostolou D, Tanaka D, and **Nemeh H**. Right Ventricular Device HeartWare Implant to the Right Atrium with Fixation to the Chest Wall in Patient with Biventricular Support. *Asaio j* 2020; 66(8):e102-e104. PMID: 32740361. [Full Text](#)

Cardiology/Cardiovascular Research

Kormos RL, Antonides CFJ, Goldstein DJ, **Cowger JA**, Starling RC, Kirklin JK, Rame JE, Rosenthal D, Mooney ML, Caliskan K, Messe SR, Teuteberg JJ, Mohacsi P, Slaughter MS, Potapov EV, Rao V, Schima H, Stehlik J, Joseph S, Koenig SC, and Pagani FD. Updated definitions of adverse events for trials and registries of mechanical circulatory support: A consensus statement of the mechanical circulatory support academic research consortium. *J Heart Lung Transplant* 2020; 39(8):735-750. PMID: 32386998. [Full Text](#)

Cardiology/Cardiovascular Research

Lanfear DE, Neaton KR, Lu C, Liu Y, and Dent-Acosta RE. A Phase 4, Open-Label, Single-Arm Study Assessing the Efficacy and Safety of Ivabradine in African American Patients with Heart Failure and Reduced Ejection Fraction. *Cardiol Ther* 2020; Epub ahead of print. PMID: 32808163. [Full Text](#)

INTRODUCTION: There are limited data on ivabradine therapy in black patients and none in African Americans. We performed an open-label, prospective study at two centers in the United States. African American patients with heart failure (HF) (N = 30), left ventricular ejection fraction $\leq 35\%$, and in sinus rhythm with resting heart rate (HR) ≥ 70 bpm received ivabradine 2.5-7.5 mg twice daily for 57 days. **METHODS:** The primary endpoint was change in HR from baseline to day 57, compared with the -5 bpm change observed in the absence of ivabradine in the placebo group of the SHIFT study. The safety endpoint was treatment-emergent adverse events (TEAEs). Exploratory endpoints were change from baseline to day 57 in 6-minute walk test (6MWT) distance, HR difference during a 6MWT (i.e. HR at minute 6 - resting HR), and physical activity counts. **RESULTS:** At day 57, the estimated least squares mean change from baseline in HR was -9.5 bpm (95% CI -13.0, -6.0). The estimated mean treatment difference with ivabradine versus a presumed -5 bpm change from baseline HR, as seen in the placebo group of the SHIFT study, was -4.5 bpm (95% CI -8.0, -1.0; $p = 0.013$). The mean (SE) changes in 6MWT distance and HR difference during the 6MWT were 16.3 (10.8) meters and 2.3 (3.7) bpm, respectively. Ivabradine therapy did not result in greater physical activity. TEAEs were reported in 11 (36.7%) patients. **CONCLUSION:** These data support ivabradine use in African American patients with HF with reduced ejection fraction who meet typical treatment criteria. **TRIAL REGISTRATION:** ClinicalTrials.gov identifier, NCT03456856.

Cardiology/Cardiovascular Research

Maskoun W, Raad M, Khan A, Mando R, and Homsy M. Biventricular implantable cardioverter-defibrillator device placement in patients with hostile tricuspid valve anatomy: two case reports and review of the literature. *Europace* 2020; Epub ahead of print. PMID: 32830224. [Full Text](#)

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AIMS: Right ventricular (RV) lead placement can be contraindicated in patients after tricuspid valve (TV) surgery. Placement of the implantable cardiac-defibrillator (ICD) lead in the middle cardiac vein (MCV) can be a viable option in these patients who have an indication for biventricular (BiV) ICD. We aim to describe the case of two patients with MCV lead placement and provide a comprehensive review of patients with complex TV pathology and indications for RV lead placement. **METHODS AND RESULTS:** We describe the cases of two patients with TV pathology unsuitable for the standard transvenous or surgical RV lead placement and undergoing BiV ICD implantation. Their characteristics, procedure, and outcomes are summarized. The BiV ICD was successfully placed with the RV lead positioned in the MCV in both patients. The procedures had no complications and were well-tolerated. On follow-up, both patients had appropriate tachytherapy with no readmissions for heart failure or worsening of cardiac function. **CONCLUSION:** Right ventricular lead placement of BiV ICD in the MCV can be an excellent alternative in patients with significant TV pathology and poor surgical candidacy.

Cardiology/Cardiovascular Research

McCullough PA, Kelly RJ, Ruocco G, Lerma E, Tumlin J, Wheelan K, Katz N, Lepor NE, Vijay K, Carter H, Singh B, McCullough SP, Bhambi BK, Palazzuoli A, De Ferrari GM, Milligan G, Safder T, Tecson KM, **Wang DD, McKinnon JE, O'Neill WW, Zervos M**, and Risch HA. Pathophysiological Basis and Rationale for Early Outpatient Treatment of SARS-CoV-2 (COVID-19) Infection. *Am J Med* 2020; Epub ahead of print. PMID: 32771461. [Full Text](#)

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Cardiology Division, Regina Montis Regalis Hospital, Mondovi, Cuneo, Italy.

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Johns Hopkins School of Medicine, Baltimore, MD.
Cedars Sinai Medical Center, Los Angeles, CA.
Abrazo Arizona Heart Hospital, Abrazo Health System, Phoenix, AZ.
Carter Eye Center, Dallas, TX.
Cardiorenal Society of America, Phoenix, AZ.
University of Texas McGovern Medical School, Houston, TX.
Bakersfield Heart Hospital, Bakersfield, CA.
University of Siena, Le Scotte Hospital Viale Bracci Siena Italy.
University of Torino, Torino, Italy.
Baylor Heart and Vascular Institute.
Henry Ford Hospital, Detroit MI.
Yale University School of Public Health, New Haven, CT.

Approximately 9 months of the SARS-CoV-2 virus spreading across the globe has led to widespread COVID-19 acute hospitalizations and death. The rapidity and highly communicable nature of the SARS-CoV-2 outbreak has hampered the design and execution of definitive randomized, controlled trials of therapy outside of the clinic or hospital. In the absence of clinical trial results, physicians must use what has been learned about the pathophysiology of SARS-CoV-2 infection in determining early outpatient treatment of the illness with the aim of preventing hospitalization or death. This paper outlines key pathophysiological principles that relate to the patient with early infection treated at home. Therapeutic approaches based on these principles include: 1) reduction of reinoculation, 2) combination antiviral therapy, 3) immunomodulation, 4) antiplatelet/antithrombotic therapy 5) administration of oxygen, monitoring, and telemedicine. Future randomized trials testing the principles and agents discussed in this paper will undoubtedly refine and clarify their individual roles, however we emphasize the immediate need for management guidance in the setting of widespread hospital resource consumption, morbidity, and mortality.

Cardiology/Cardiovascular Research

O'Neill WW, and Burkhoff D. Letter by O'Neill and Burkhoff Regarding Article, "The Evolving Landscape of Impella Use in the United States Among Patients Undergoing Percutaneous Coronary Intervention With Mechanical Circulatory Support". *Circulation* 2020; 142(6):e78-e79. PMID: 32776844. [Full Text](#)

Henry Ford Hospital, Detroit, Michigan (W.W.O.).
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Cardiology/Cardiovascular Research

Raad M, Dabbagh M, Gorgis S, Yan J, Chehab O, Dagher C, Jamoor K, Hussein IH, Cook B, Van Harn M, Singh G, McCord J, and Parikh S. Cardiac Injury Patterns and Inpatient Outcomes Among Patients Admitted With COVID-19. *Am J Cardiol* 2020; Epub ahead of print. PMID: 32829913. [Full Text](#)

Division of Cardiology, Department of Medicine, Henry Ford Hospital, Detroit, Michigan.
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Although certain risk factors have been associated with increased morbidity and mortality in patients admitted with Coronavirus Disease 2019 (COVID-19), the impact of cardiac injury and high-sensitivity troponin-I (hs-cTnI) concentrations are not well described. In this large retrospective longitudinal cohort study, we analyzed the cases of 1,044 consecutively admitted patients with COVID-19 from March 9 until April 15. Cardiac injury was defined by hs-cTnI concentration >99th percentile. Patient characteristics, laboratory data, and outcomes were described in patients with cardiac injury and different hs-cTnI cut-offs. The primary outcome was mortality, and the secondary outcomes were length of stay, need for intensive care unit care or mechanical ventilation, and their different composites. The final analyzed cohort included 1,020 patients. The median age was 63 years, 511 (50% patients were female, and 403 (40% were white. 390 (38%) patients had cardiac injury on presentation. These patients were older (median age

70 years), had a higher cardiovascular disease burden, in addition to higher serum concentrations of inflammatory markers. They also exhibited an increased risk for our primary and secondary outcomes, with the risk increasing with higher hs-cTnI concentrations. Peak hs-cTnI concentrations continued to be significantly associated with mortality after a multivariate regression controlling for comorbid conditions, inflammatory markers, acute kidney injury, and acute respiratory distress syndrome. Within the same multivariate regression model, presenting hs-cTnI concentrations were not significantly associated with outcomes, and undetectable hs-cTnI concentrations on presentation did not completely rule out the risk for mechanical ventilation or death. In conclusion, cardiac injury was common in patients admitted with COVID-19. The extent of cardiac injury and peak hs-cTnI concentrations were associated with worse outcomes.

Cardiology/Cardiovascular Research

Sabbah HN, Zhang K, Gupta RC, Jiang X, and Singh-Gupta V. Effects of Angiotensin-Neprilysin Inhibition in Canines with Experimentally-Induced Cardiorenal Syndrome. *J Card Fail* 2020; Epub ahead of print. PMID: 32841710. [Full Text](#)

BACKGROUND: Sacubitril/Valsartan (Sac/Val), a combined angiotensin-II receptor blocker (Val) and neprilysin inhibitor (Sac) in a 1:1 molar ratio, was shown to reduce the risk of cardiovascular death or heart failure (HF) hospitalization in patients with HF and reduced LV ejection fraction (EF). This study examined the effects of Sac/Val on LV structure, function and bioenergetics and on biomarkers of kidney injury and kidney function in dogs with experimental cardiorenal syndrome (CRS). **METHODS AND RESULTS:** 14 dogs with CRS (coronary microembolization-induced HF and renal dysfunction) were randomized to 3 months Sac/Val therapy (100 mg once daily, n=7) or no therapy (control, n=7). LV EF and troponin-I (TnI) as well as biomarkers of kidney injury/function including serum creatinine (sCr) and urinary kidney injury molecule-1 (KIM-1) were measured before and at end of therapy and the change (treatment effect Δ) calculated. Mitochondrial function measures including maximum rate of ATP synthesis (ATPsyn) were measured in isolated cardiomyocytes at end of therapy. In Sac/Val dogs, Δ EF increased compared to controls (6.9 ± 1.4 vs. 0.7 ± 0.6 %, $p<0.002$) while Δ TnI decreased (-0.16 ± 0.03 vs. -0.03 ± 0.02 ng/ml, $p<0.001$). Urinary Δ KIM-1 decreased in Sac/Val treated dogs compared to controls (-17.2 ± 7.9 vs. 7.7 ± 3.0 mg/ml, $p<0.007$) whereas Δ sCr was not significantly different. Treatment with Sac/Val increased ATPsyn compared to control ($3,240\pm 121$ vs. 986 ± 84 RLU/ μ g protein, $p<0.05$). **CONCLUSIONS:** In dogs with CRS, Sac/Val improves LV systolic function, improves mitochondrial function and decreases biomarkers of heart and kidney injury. The results offer mechanistic insights into the benefits of Sac/Val in HF with compromised renal function.

Cardiology/Cardiovascular Research

Swain L, Reyelt L, Bhav S, Qiao X, Thomas CJ, Zweck E, Crowley P, Boggins C, Esposito M, Chin M, Karas RH, **O'Neill W**, and Kapur NK. Transvalvular Ventricular Unloading Before Reperfusion in Acute Myocardial Infarction. *J Am Coll Cardiol* 2020; 76(6):684-699. PMID: 32762903. [Full Text](#)

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BACKGROUND: Myocardial damage due to acute ST-segment elevation myocardial infarction (STEMI) remains a significant global health problem. New approaches to limit myocardial infarct size and reduce progression to heart failure after STEMI are needed. Mechanically reducing left ventricular (LV) workload (LV unloading) before coronary reperfusion is emerging as a potential approach to reduce infarct size. **OBJECTIVES:** Given the central importance of mitochondria in reperfusion injury, we hypothesized that compared with immediate reperfusion (IR), LV unloading before reperfusion improves myocardial energy substrate use and preserves mitochondrial structure and function. **METHODS:** To explore the effect of LV unloading duration on infarct size, we analyzed data from the STEMI-Door to Unload (STEMI-DTU) trial and then tested the effect of LV unloading on ischemia and reperfusion injury, cardiac metabolism, and mitochondrial function in swine models of acute myocardial infarction. **RESULTS:** The duration of LV unloading before reperfusion was inversely associated with infarct size in patients with large anterior STEMI. In preclinical models, LV unloading reduced the expression of hypoxia-sensitive proteins and myocardial damage due to ischemia alone. LV unloading with a transvalvular pump (TV-P) but not with venoarterial extracorporeal membrane oxygenation (ECMO) reduced infarct size. Using unbiased and blinded metabolic profiling, TV-P improved myocardial energy substrate use and preserved mitochondrial structure including cardiolipin content after reperfusion compared with IR or ECMO. Functional testing in mitochondria isolated from the infarct zone showed an intact mitochondrial structure including cardiolipin content, preserved activity of the electron transport chain including mitochondrial complex I, and reduced oxidative stress with TV-P-supported reperfusion but not with IR or ECMO. **CONCLUSIONS:**

These novel findings identify that transvalvular unloading limits ischemic injury before reperfusion, improves myocardial energy substrate use, and preserves mitochondrial structure and function after reperfusion.

Cardiology/Cardiovascular Research

Zein R, Seth M, Othman H, Rosman HS, Lalonde T, **Alaswad K**, Menees D, Daher E, Mehta RH, and Gurm HS. Association of Operator and Hospital Experience With Procedural Success Rates and Outcomes in Patients Undergoing Percutaneous Coronary Interventions for Chronic Total Occlusions: Insights From the Blue Cross Blue Shield of Michigan Cardiovascular Consortium. *Circ Cardiovasc Interv* 2020; 13(8):e008863. PMID: 32791954. [Full Text](#)

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BACKGROUND: An inverse relationship has been described between procedural success and outcomes of all major cardiovascular procedures. However, this relationship has not been studied for percutaneous coronary intervention (PCI) of chronic total occlusion (CTO). **METHODS:** We analyzed the data on patients enrolled in Blue Cross Blue Shield of Michigan Cardiovascular Consortium registry in Michigan (January 1, 2010 to March 31, 2018) to evaluate the association of operator and hospital experience with procedural success and outcomes of patients undergoing CTO-PCI. CTO-PCI was defined as intervention of a 100% occluded coronary artery presumed to be ≥ 3 months old. **RESULTS:** Among 210 172 patients enrolled in the registry, 7389 (3.5%) CTO-PCIs were attempted with a success rate of 53%. CTO-PCI success increased with operator experience (45% and 65% in the lowest and highest experience tertiles) and was the highest for highly experienced operators at higher experience centers and the lowest for inexperienced operators at low experience hospitals. Multivariable logistic regression models (with spline transformed prior operator and institutional experience) demonstrated a positive relationship between prior operator and site experience and procedural success rates (likelihood ratio test=141.12, df=15, $P<0.001$) but no relationship between operator and site experience and major adverse cardiac event (likelihood ratio test=19.12, df=15, $P=0.208$). **CONCLUSIONS:** Operator and hospital CTO-PCI experiences were directly related to procedural success but were not related to major adverse cardiac event among patients undergoing CTO-PCIs. Inexperienced operators at high experience centers had significantly higher success but not major adverse cardiac event rates compared with inexperienced operators at low experience centers. These data suggested that CTO-PCI safety and success could potentially be improved by selective referral of these procedures to experienced operators working at highly experienced centers.

Center for Health Policy and Health Services Research

Mak J, **Shires DA**, Zhang Q, Prieto LR, **Ahmedani BK**, Kattari L, Becerra-Culqui TA, Bradlyn A, Flanders WD, Getahun D, Giannatelli SV, Hunkeler EM, Lash TL, Nash R, Quinn VP, Robinson B, Roblin D, Silverberg MJ, Slovis J, Tangpricha V, Vupputuri S, and Goodman M. Suicide Attempts Among a Cohort of Transgender and Gender Diverse People. *Am J Prev Med* 2020; Epub ahead of print. PMID: 32798005. [Full Text](#)

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INTRODUCTION: Transgender and gender diverse people often face discrimination and may experience disproportionate emotional distress that leads to suicide attempts. Therefore, it is essential to estimate the frequency and potential determinants of suicide attempts among transgender and gender diverse individuals. **METHODS:** Longitudinal data on 6,327 transgender and gender diverse individuals enrolled in 3 integrated healthcare systems were analyzed to assess suicide attempt rates. Incidence was compared between transmasculine and transfeminine people by age and race/ethnicity and according to mental health status at baseline. Cox proportional hazards models

examined rates and predictors of suicide attempts during follow-up. Data were collected in 2016, and analyses were conducted in 2019. RESULTS: During follow-up, 4.8% of transmasculine and 3.0% of transfeminine patients had at least 1 suicide attempt. Suicide attempt rates were more than 7 times higher among patients aged <18 years than among those aged >45 years, more than 3 times higher among patients with previous history of suicide ideation or suicide attempts than among those with no such history, and 2-5 times higher among those with 1-2 mental health diagnoses and more than 2 mental health diagnoses at baseline than among those with none. CONCLUSIONS: Among transgender and gender diverse individuals, younger people, people with previous suicidal ideation or attempts, and people with multiple mental health diagnoses are at a higher risk for suicide attempts. Future research should examine the impact of gender-affirming healthcare use on the risk of suicide attempts and identify targets for suicide prevention interventions among transgender and gender diverse people in clinical settings.

Dermatology

Braunberger TL, Adelman M, **Shwayder TA**, Clarke LE, and **Friedman BJ**. Proliferative nodule resembling angiomatoid Spitz tumor with degenerative atypia arising within a giant congenital nevus. *J Cutan Pathol* 2020; Epub ahead of print. PMID: 32776331. [Full Text](#)

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Proliferative nodules arising within congenital melanocytic nevi (CMN) often present a diagnostic challenge given a close resemblance to melanoma. Several morphologic variants have been characterized. In difficult cases, ancillary molecular tests can be used to better exclude the possibility of malignant degeneration. Herein, we report a case of an unusual proliferative nodule with overlapping features of angiomatoid Spitz tumor and ancient melanocytic nevus, which demonstrated normal findings on both chromosomal microarray and a gene expression profiling assay This article is protected by copyright. All rights reserved.

Dermatology

Horton L, **Torres AE**, **Narla S**, **Lyons AB**, **Kohli I**, Gelfand JM, **Ozog DM**, **Hamzavi IH**, and **Lim HW**. Spectrum of virucidal activity from ultraviolet to infrared radiation. *Photochem Photobiol Sci* 2020; Epub ahead of print. PMID: 32812619. [Request Article](#)

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The COVID-19 pandemic has sparked a demand for safe and highly effective decontamination techniques for both personal protective equipment (PPE) and hospital and operating rooms. The gradual lifting of lockdown restrictions warrants the expansion of these measures into the outpatient arena. Ultraviolet C (UVC) radiation has well-known germicidal properties and is among the most frequently reported decontamination techniques used today. However, there is evidence that wavelengths beyond the traditional 254 nm UVC - namely far UVC (222 nm), ultraviolet B, ultraviolet A, visible light, and infrared radiation - have germicidal properties as well. This review will cover current literature regarding the germicidal effects of wavelengths ranging from UVC through the infrared waveband with an emphasis on their activity against viruses, and their potential applicability in the healthcare setting for general decontamination during an infectious outbreak.

Dermatology

Kohli I, **Lyons AB**, Golding B, **Narla S**, **Torres AE**, **Parks-Miller A**, **Ozog D**, **Lim HW**, and **Hamzavi IH**. UVC Germicidal Units: Determination of Dose Received and Parameters to be Considered for N95 Respirator Decontamination and Reuse. *Photochem Photobiol* 2020; Epub ahead of print. PMID: 32767758. [Full Text](#)

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The COVID-19 pandemic has resulted in an international shortage of personal protective equipment including N95 filtering facepiece respirators (FFRs), resulting in many institutions using ultraviolet germicidal irradiation (UVGI)

technology for N95 FFR decontamination. To ensure proper decontamination, it is crucial to determine the dose received by various parts of the FFR in this process. Recently, our group customized a UVGI unit for N95 decontamination. With experimental and theoretical approach, this manuscript discusses the minimum dose received by various parts of the N95 respirator after one complete decontamination cycle with this UVGI unit. The results demonstrate that all parts of the N95 FFR received at least 1 J/cm² after one complete decontamination cycle with this unit. As there are a variety of UVGI devices and different types of FFRs, this study provides a model by which UVC dose received by different areas of the FFRs can be accurately assessed to ensure proper decontamination for the safety of healthcare providers.

Dermatology

Ma Z, Li L, Livingston MJ, Zhang D, **Mi Q**, Zhang M, Ding HF, Huo Y, Mei C, and Dong Z. p53/microRNA-214/ULK1 axis impairs renal tubular autophagy in diabetic kidney disease. *J Clin Invest* 2020; Epub ahead of print. PMID: 32804155. [Full Text](#)

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Dysregulation of autophagy in diabetic kidney disease (DKD) has been reported, but the underlying mechanism and its pathogenic role remain elusive. We show that autophagy was inhibited in DKD models and in human diabetic kidneys. Ablation of autophagy-related gene 7 (Atg7) from kidney proximal tubules led to autophagy deficiency and worse renal hypertrophy, tubular damage, inflammation, fibrosis, and albuminuria in diabetic mice, indicating a protective role of autophagy in DKD. Autophagy impairment in DKD was associated with the downregulation of unc-51-like autophagy-activating kinase 1 (ULK1), which was mediated by the upregulation of microRNA-214 (miR-214) in diabetic kidney cells and tissues. Ablation of miR-214 from kidney proximal tubules prevented a decrease in ULK1 expression and autophagy impairment in diabetic kidneys, resulting in less renal hypertrophy and albuminuria. Furthermore, blockade of p53 attenuated miR-214 induction in DKD, leading to higher levels of ULK1 and autophagy, accompanied by an amelioration of DKD. Compared with nondiabetic samples, renal biopsies from patients with diabetes showed induction of p53 and miR-214, associated with downregulation of ULK1 and autophagy. We found a positive correlation between p53/miR-214 and renal fibrosis, but a negative correlation between ULK1/LC3 and renal fibrosis in patients with diabetes. Together, these results identify the p53/miR-214/ULK1 axis in autophagy impairment in diabetic kidneys, pinpointing possible therapeutic targets for DKD.

Dermatology

Xu Y, Dimitrion P, Cvetkovski S, Zhou L, and Mi QS. Epidermal resident $\gamma\delta$ T cell development and function in skin. *Cell Mol Life Sci* 2020; Epub ahead of print. PMID: 32803399. [Full Text](#)

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Epidermal resident $\gamma\delta$ T cells, or dendritic epidermal T cells (DETCs) in mice, are a unique and conserved population of $\gamma\delta$ T cells enriched in the epidermis, where they serve as the regulators of immune responses and sense skin injury. Despite the great advances in the understanding of the development, homeostasis, and function of DETCs in the past decades, the origin and the underlying molecular mechanisms remain elusive. Here, we reviewed the recent research progress on DETCs, including their origin and homeostasis in the skin, especially at transcriptional and epigenetic levels, and discuss the involvement of DETCs in skin diseases.

Diagnostic Radiology

Leschied JR, and **Soliman SB**. Pediatric Musculoskeletal Trauma: Special Considerations. *Seminars in Roentgenology* 2020; Epub ahead of print. PMID: Not assigned. [Full Text](#)

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Diagnostic Radiology

Rozenshtein A, **Griffith BD**, Slanetz PJ, DeBenedictis CM, Gould JE, Kohr JR, Mohammed TL, Paladin AM, Rochon PJ, Sheth M, Wiggins Iii EF, and Swanson JO. "What Program Directors Think" V: Results of the 2019 Spring Survey of the Association of Program Directors in Radiology (APDR). *Acad Radiol* 2020; Epub ahead of print. PMID: 32778482. [Full Text](#)

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RATIONALE AND OBJECTIVES: The Association of Program Directors in Radiology (APDR) surveys its membership annually on hot topics and new developments in radiology residency training. Here we report the results of that annual survey. **MATERIALS AND METHODS:** A web-based survey was posed to the APDR membership in the Fall of 2018. Members were asked 43 questions on program staffing, resident education resources/funding, impact of the integrated-Interventional Radiology residency program on Diagnostic Radiology program resources, resident interest in imaging informatics, Accreditation Council for Graduate Medical Education requirements on resident practice habits data reporting, institutional reliance on residents for clinical coverage, teaching format in the post-oral board era, resident conference attendance, confidentiality of the Match rank list, Early Specialization in Interventional Radiology pathway recruitment and selection, Diagnostic Radiology and Interventional Radiology program relationships, independent resident call, pediatric radiology training, diversity and unconscious bias training, and social media in radiology education. **RESULTS:** Responses were collected electronically, results were tallied using Qualtrics software, and qualitative responses were tabulated or summarized as comments. There were 86 respondents with a response rate of 31.3%. **CONCLUSION:** Survey result highlights include perceived resident interest in imaging informatics with the vast majority of residency programs offering an informatics curriculum; the provision of resident practice habits data by nearly all residency programs despite lack of clarity surrounding this Accreditation Council for Graduate Medical Education requirement; continued use of case-taking in the post-oral boards era; frequent disclosure of the Match rank list to departmental and hospital administration; low penetration of unconscious bias training in academic radiology; and finally, the successful integration of interventional and diagnostic radiology training programs.

Diagnostic Radiology

Touma R, Palla M, **Alam K**, Mastromatteo JF, and Abidov A. Giant Calcified Left Circumflex Coronary Artery Aneurysm With Complex Coronary-to-Left Ventricular Communication. *JACC: Case Reports* 2020; Epub ahead of print. PMID: Not assigned. [Full Text](#)

A 64-year-old asymptomatic man had an incidental finding of a giant left circumflex artery (LCX) aneurysm, with the distal LCX draining into a confluence receiving terminal portions of all coronary arteries and communicating with the

left ventricle through a transmural fistulous tract. We believe that this is the first case reported with such a complex LCX abnormality. (Level of Difficulty: Beginner.)

Emergency Medicine

Horiuchi Y, Wettersten N, Patel MP, Mueller C, Neath SX, Christenson RH, Morgenthaler NG, **McCord J, Nowak RM**, Vilke GM, Daniels LB, Hollander JE, Apple FS, Cannon CM, Nagurney JT, Schreiber D, deFilippi C, Hogan C, Diercks DB, Headden G, Limkakeng AT, Anand I, Wu AHB, Ebmeyer S, Jaffe AS, Peacock WF, and Maisel AS. Biomarkers Enhance Discrimination and Prognosis of Type 2 Myocardial Infarction. *Circulation* 2020; Epub ahead of print. PMID: 32820656. [Full Text](#)

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Background: The observed incidence of type 2 myocardial infarction (T2MI) is expected to increase with the implementation of increasingly sensitive cardiac troponin (cTn) assays. However, it remains to be determined how to diagnose, risk stratify and treat patients with T2MI. We aimed to discriminate and risk-stratify T2MI using biomarkers. **Methods:** Patients presenting to the Emergency Department with chest pain, enrolled in the CHOPIN study, were retrospectively analyzed. Two cardiologists adjudicated type 1 MI (T1MI) and T2MI. The prognostic ability of several biomarkers alone or in combination to discriminate T2MI from T1MI was investigated using receiver operating characteristic (ROC) curve analysis. The biomarkers analyzed were cTnI, copeptin, mid-regional pro-atrial natriuretic peptide (MRproANP), C-terminal pro-endothelin-1 (CT-proET1), mid-regional pro-adrenomedullin (MRproADM) and procalcitonin. Prognostic utility of these biomarkers for all-cause mortality and major adverse cardiovascular event (MACE: a composite of acute MI, unstable angina pectoris, reinfarction, heart failure, and stroke) at 180-day follow-up was also investigated. **Results:** Among the 2071 patients, T1MI and T2MI were adjudicated in 94 and 176 patients, respectively. Patients with T1MI had higher levels of baseline cTnI, while those with T2MI had higher baseline levels of MR-proANP, CT-proET1, MR-proADM, and procalcitonin. The area under the ROC curve (AUC) for the diagnosis of T2MI was higher for CT-proET1, MRproADM and MR-proANP (0.765, 0.750, and 0.733, respectively) than for cTnI (0.631). Combining all biomarkers resulted in a similar accuracy to a model using clinical variables and cTnI (0.854 versus 0.884, $p = 0.294$). Addition of biomarkers to the clinical model yielded the highest AUC (0.917). Other biomarkers, but not cTnI, were associated with mortality and MACE at 180-day among all patients, with no interaction between the diagnosis of T1MI or T2MI. **Conclusions:** Assessment of biomarkers reflecting pathophysiologic processes occurring with T2MI might help differentiate it from T1MI. Additionally, all biomarkers measured, except cTnI, were significant predictors of prognosis, regardless of type of MI.

Emergency Medicine

Miller J, Bruen C, Schnaus M, Zhang J, Ali S, Lind A, Stoecker Z, Stauderman K, and Hebbar S. Auxora versus standard of care for the treatment of severe or critical COVID-19 pneumonia: results from a randomized controlled trial. *Crit Care* 2020; 24(1):502. PMID: 32795330. [Full Text](#)

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BACKGROUND: Calcium release-activated calcium (CRAC) channel inhibitors stabilize the pulmonary endothelium and block proinflammatory cytokine release, potentially mitigating respiratory complications observed in patients with COVID-19. This study aimed to investigate the safety and efficacy of Auxora, a novel, intravenously administered CRAC channel inhibitor, in adults with severe or critical COVID-19 pneumonia. **METHODS:** A randomized, controlled, open-label study of Auxora was conducted in adults with severe or critical COVID-19 pneumonia. Patients were randomized 2:1 to receive three doses of once-daily Auxora versus standard of care (SOC) alone. The primary objective was to assess the safety and tolerability of Auxora. Following FDA guidance, study enrollment was halted early to allow for transition to a randomized, blinded, placebo-controlled study. **RESULTS:** In total, 17 patients with severe and three with critical COVID-19 pneumonia were randomized to Auxora and nine with severe and one with critical COVID-19 pneumonia to SOC. Similar proportions of patients receiving Auxora and SOC experienced ≥ 1 adverse event (75% versus 80%, respectively). Fewer patients receiving Auxora experienced serious adverse events versus SOC (30% versus 50%, respectively). Two patients (10%) receiving Auxora and two (20%) receiving SOC died during the 30 days after randomization. Among patients with severe COVID-19 pneumonia, the median time to recovery with Auxora was 5 days versus 12 days with SOC; the recovery rate ratio was 1.87 (95% CI, 0.72, 4.89). Invasive mechanical ventilation was needed in 18% of patients with severe COVID-19 pneumonia receiving Auxora versus 50% receiving SOC (absolute risk reduction = 32%; 95% CI, -0.07, 0.71). Outcomes measured by an 8-point ordinal scale were significantly improved for patients receiving Auxora, especially for patients with a baseline PaO₂/FiO₂ = 101-200. **CONCLUSIONS:** Auxora demonstrated a favorable safety profile in patients with severe or critical COVID-19 pneumonia and improved outcomes in patients with severe COVID-19 pneumonia. These results, however, are limited by the open-label study design and small patient population resulting from the early cessation of enrollment in response to regulatory guidance. The impact of Auxora on respiratory complications in patients with severe COVID-19 pneumonia will be further assessed in a planned randomized, blinded, placebo-controlled study. **TRIAL REGISTRATION:** ClinicalTrials.gov, NCT04345614.

Endocrinology & Metabolism

Qiu S, Divine G, Warner E, and Rao SD. Reference Intervals for Bone Histomorphometric Measurements Based on Data from Healthy Premenopausal Women. *Calcif Tissue Int* 2020; Epub ahead of print. PMID: 32814991. [Full Text](#)

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This study has established the normal reference intervals for bone histomorphometric measurements derived from healthy premenopausal women, which is rarely available. We presented the static and dynamic bone histomorphometric data from trans-iliac bone biopsies in 62 healthy premenopausal women (19 blacks and 43 whites, ages 20-53 years). There were no significant differences in age and BMI between black and white women. Since there was no significant difference in bone remodeling between the two ethnic groups, we pooled data of all 62 premenopausal women to establish normal reference intervals for bone histomorphometry. The results provide normal reference intervals for both static and dynamic histomorphometric variables in cancellous and cortical bone of the ilium. None of the bone remodeling-related variables correlated with age or BMI. This study provides reference intervals for bone histomorphometric measurements in both cancellous and cortical bone of the ilium, which would be helpful in the evaluation of bone health in women.

Gastroenterology

Caines A, Selim R, and Salgia R. The Changing Global Epidemiology of Hepatocellular Carcinoma. *Clinics in Liver Disease* 2020; Epub ahead of print. PMID: Not assigned. [Full Text](#)

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Hepatocellular carcinoma is among the leading causes of morbidity and mortality. Owing to the current epidemic of metabolic syndrome, the population affected by nonalcoholic fatty liver disease/nonalcoholic steatohepatitis continues to increase and now comprises a significant portion with those with hepatocellular carcinoma. The World Health Organization goal of obtaining universal hepatitis B virus vaccination has led to a global effort to improve vaccination, prevent mother-to-child transmission, and implement linkage to care to avoid the development of hepatocellular carcinoma. In contrast with the decreased burden of chronic hepatitis C virus, there has been an increase in new-onset acute hepatitis C virus.

Gastroenterology

Iqbal U, Siddique O, Khara HS, Khan MA, **Haq KF, Siddiqui MA**, Solanki S, Zuchelli TE, Shellenberger MJ, and Birk JW. Post-endoscopic retrograde cholangiopancreatography pancreatitis prevention using topical epinephrine: systematic review and meta-analysis. *Endosc Int Open* 2020; 8(8):e1061-e1067. PMID: 32743060. [Full Text](#)

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Background and study aims Post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP) is a common complication of endoscopic retrograde cholangiopancreatography (ERCP). Multiple drugs and techniques have been studied for the prevention of PEP. Topical epinephrine has shown mixed results and is still not widely accepted as an alternative for prevention of PEP. We performed a systematic review and meta-analysis to evaluate the efficacy of topical epinephrine in preventing PEP. **Methods** A comprehensive literature review was conducted by searching Cochrane library database, Embase and PubMed up to August 2019, to identify all studies that evaluated use of topical epinephrine alone or in conjunction with other agents for prevention of PEP. Outcomes included prevention of PEP with use of topical epinephrine and evaluation of whether adding epinephrine provides any additional benefit in preventing PEP. All analysis was conducted using Revman 5.3. **Results** Eight studies, including six randomized controlled trials and two observational studies with 4123 patients, were included in the meta-analysis. Overall, there was no difference in incidence of PEP in patients who underwent ERCP and were treated with epinephrine spray versus those who were not, RR=0.63 (CI 0.32-1.24) with heterogeneity (I²=72%). However, on a subgroup analysis, topical epinephrine significantly decreases the risk of PEP when compared to placebo alone (means no intervention was done including no rectal indomethacin), RR=0.32 (0.18-0.57). In another subgroup analysis, there was no statistically significant difference in using topical epinephrine along with rectal indomethacin in preventing PEP compared to rectal indomethacin alone RR=0.87 (0.46-1.64). **Conclusion** Topical epinephrine does not provide any additional benefit in preventing PEP when used in conjunction with rectal indomethacin. In subgroup analysis, topical epinephrine appeared to decrease risk of PEP in the absence of rectal indomethacin, and could be considered when rectal indomethacin is unavailable or if there is a contraindication to its use.

Gastroenterology

Ivanics T, Rizzari M, Moonka D, Al-Kurd A, Delvecchio K, Kitajima T, Elsabbagh A, Collins K, Yoshida A, Abouljoud M, and Nagai S. Re-transplantation outcomes for hepatitis C in the United States before and after DAA-introduction. *Am J Transplant* 2020; Epub ahead of print. PMID: 32794649. [Full Text](#)

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The success of direct-acting antiviral (DAA) therapy has led to near-universal cure for patients chronically infected with hepatitis C virus (HCV) and improved post-liver transplant(LT) outcomes. We investigated the trends and outcomes of re-transplantation in HCV and non-HCV patients before and after the introduction of DAA. Adult patients who underwent re-LT were identified in the OPTN/UNOS database. Multi-organ transplants and patients with more than two total LTs were excluded. Two eras were defined, pre-DAA(2009-2012), and post-DAA(2014-2017). A total of 2,112 re-LT patients were eligible(HCV: n=499 pre-DAA and n=322 post-DAA; non-HCV: n=547 pre-DAA and n=744 post-DAA). HCV patients had both improved graft and patient survival after re-LT in the post-DAA era. One-year graft survival was 69.8% pre-DAA and 83.8% post-DAA(p<0.001). One-year patient survival was 73.1% pre-DAA and 86.2% post-DAA(p<0.001). Graft and patient survival was similar between eras for non-HCV patients. When adjusted, the post-DAA era represented an independent positive predictive factor for graft and patient survival(HR:0.67;p=0.005, and HR:0.65;p=0.004) only in HCV patients. The positive post-DAA era effect was observed only in HCV patients with first graft loss due to disease recurrence(HR:0.31;p=0.002, HR 0.32;p=0.003, respectively). Among HCV patients, receiving a re-LT in the post-DAA era was associated with improved patient and graft survival.

Gastroenterology

Noureddin N, Alkhouri N, **Brown KA**, and Noureddin M. Driving NASH forward using the FAST score but obey the traffic lights. *Hepatology* 2020; Epub ahead of print. PMID: 32757393. [Full Text](#)

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Accurate tests to identify high-risk individuals in a population that could progress to severe forms of the disease are crucial strategies when tackling the nonalcoholic fatty liver disease (NAFLD) epidemic. NAFLD is projected to increase from affecting 83.1 million people in 2015 to 100.9 million in 2030, and its more severe form, nonalcoholic steatohepatitis (NASH) is estimated to increase from 16.52 million to 27.00 million in the US alone (1). These staggering numbers emphasize the need to precisely identify patients with NASH who could potentially develop life-threatening cirrhosis and hepatocellular carcinoma (2). By doing so, patients can be correctly selected to enter clinical trials designed to treat NASH with new drugs targeting different stages of the disease.

Gastroenterology

Wong RJ, Kachru N, Martinez DJ, Moynihan M, Ozbay AB, and **Gordon SC**. Real-world Comorbidity Burden, Health Care Utilization, and Costs of Nonalcoholic Steatohepatitis Patients With Advanced Liver Diseases. *J Clin Gastroenterol* 2020; Epub ahead of print. PMID: 32815873. [Full Text](#)

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GOALS: This study evaluates the real-world comorbidity burden, health care resource utilization (HRU), and costs among nonalcoholic fatty liver disease/nonalcoholic steatohepatitis (NAFLD/NASH) patients with advanced liver diseases [compensated cirrhosis (CC), decompensated cirrhosis (DCC), liver transplantation (LT), hepatocellular carcinoma (HCC)]. **BACKGROUND:** NAFLD/NASH is a leading cause of liver diseases. **MATERIALS AND METHODS:** Adult NAFLD/NASH patients were identified retrospectively from MarketScan Commercial claims (2006-2016). Following initial NAFLD/NASH diagnosis, advanced liver diseases were identified using the first diagnosis as their index date. Mean annual all-cause HRU and costs (2016 USD) were reported. Adjusted costs were estimated through generalized linear models. Cumulative costs were illustrated for patient subsets with variable follow-up for each stage. **RESULTS:** Within the database, 485,774 NAFLD/NASH patients met eligibility criteria. Of these, 93.4% (453,564) were NAFLD/NASH patients without advanced liver diseases, 1.6% (7665) with CC, 3.3% (15,833) with DCC, 0.1% (696) with LT, and 0.1% (428) with HCC. Comorbidity burden was high and increased as patients progressed through liver disease severity stages. Compared with NAFLD/NASH without advanced liver diseases (adjusted costs: \$23,860), the annual cost of CC, DCC, LT, and HCC were 1.22, 5.64, 8.27, and 4.09 times higher [adjusted costs: \$29,078, \$134,448, \$197,392, and \$97,563 ($P < 0.0001$)]. Inpatient admissions significantly drove increasing HRU. **CONCLUSION:** Study findings suggest the need for early identification and effective management of NAFLD/NASH patients to minimize comorbidity burden, HRU, and costs in the privately insured US population.

Hematology-Oncology

Domchek SM, Postel-Vinay S, Im SA, Park YH, Delord JP, Italiano A, Alexandre J, You B, Bastian S, Krebs MG, **Wang D**, Waqar SN, Lanasa M, Rhee J, Gao H, Rocher-Ros V, Jones EV, Gulati S, Coenen-Stass A, Kozarewa I, Lai Z, Angell HK, Opincar L, Herbolzheimer P, and Kaufman B. Olaparib and durvalumab in patients with germline BRCA-mutated metastatic breast cancer (MEDIOLA): an open-label, multicentre, phase 1/2, basket study. *Lancet Oncol* 2020; Epub ahead of print. PMID: 32771088. [Full Text](#)

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BACKGROUND: Poly (ADP-ribose) polymerase inhibitors combined with immunotherapy have shown antitumour activity in preclinical studies. We aimed to assess the safety and activity of olaparib in combination with the PD-L1-inhibitor, durvalumab, in patients with germline BRCA1-mutated or BRCA2-mutated metastatic breast cancer. **METHODS:** The MEDIOLA trial is a multicentre, open-label, phase 1/2, basket trial of durvalumab and olaparib in solid tumours. Patients were enrolled into four initial cohorts: germline BRCA-mutated, metastatic breast cancer; germline BRCA-mutated, metastatic ovarian cancer; metastatic gastric cancer; and relapsed small-cell lung cancer. Here, we report on the cohort of patients with breast cancer. Patients who were aged 18 years or older (or aged 19 years or older in South Korea) with germline BRCA1-mutated or BRCA2-mutated or both and histologically confirmed, progressive, HER2-negative, metastatic breast cancer were enrolled from 14 health centres in the UK, the USA, Israel, France, Switzerland, and South Korea. Patients should not have received more than two previous lines of chemotherapy for metastatic breast cancer. Patients received 300 mg olaparib in tablet form orally twice daily for 4 weeks and thereafter a combination of olaparib 300 mg twice daily and durvalumab 1.5 g via intravenous infusion every 4 weeks until disease progression. Primary endpoints were safety and tolerability, and 12-week disease control rate. Safety was analysed in patients who received at least one dose of study treatment, and activity analyses were done in the full-analysis set (patients who received at least one dose of study treatment and were not excluded from the study). Recruitment has completed and the study is ongoing. This trial is registered with ClinicalTrials.gov, NCT02734004. **FINDINGS:** Between June 14, 2016, and May 2, 2017, 34 patients were enrolled and received both study drugs and were included in the safety analysis. 11 (32%) patients experienced grade 3 or worse adverse events, of which the most common were anaemia (four [12%]), neutropenia (three [9%]), and pancreatitis (two [6%]). Three (9%) patients discontinued due to adverse events and four (12%) patients experienced a total of six serious adverse events. There were no treatment-related deaths. 24 (80%; 90% CI 64.3-90.9) of 30 patients eligible for activity analysis had disease control at 12 weeks. **INTERPRETATION:** Combination of olaparib and durvalumab showed promising antitumour activity and safety similar to that previously observed in olaparib and durvalumab monotherapy studies. Further research in a randomised setting is needed to determine predictors of therapeutic benefit and whether addition of durvalumab improves long-term clinical outcomes compared with olaparib monotherapy. **FUNDING:** AstraZeneca.

Hematology-Oncology

Mosalem O, **Abu Rous F**, Elshafie A, and Isaac D. Bilateral breast masses as a presentation for T-cell acute lymphoblastic leukaemia. *BMJ Case Rep* 2020; 13(8). PMID: 32847887. [Full Text](#)

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Here we describe a 27-year-old woman, 5 months post partum, who presented to the emergency department with bilateral breast masses. She was initially treated as lactational mastitis with no improvement. Breast ultrasound showed bilateral breast and axillary lymphadenopathy suggestive of metastatic/neoplastic process, and chest X-ray showed a large anterior mediastinal mass. Further work-up led to the diagnosis of T-cell acute lymphoblastic leukaemia. The patient was started on a paediatric regimen using the children's oncology group AALL0434 protocol. The patient achieved a complete remission following induction chemotherapy with resolution of her presenting symptoms.

Hematology-Oncology

Mosalem O, Hernandez Garcilazo N, Saleh Y, and **Abu Rous F**. Pulmonary embolism as the primary presentation of IgA vasculitis. *BMJ Case Rep* 2020; 13(8). PMID: 32859624. [Full Text](#)

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A 47-year-old man presented to the emergency department with acute onset of dyspnoea and a week history of painful erythematous rash on both of his legs. CT angiogram of the chest showed saddle pulmonary embolism resulting in right ventricular strain and obstructive shock. Due to the atypical nature of his skin rash, a skin biopsy from one of these lesions was done and came consistent with the diagnosis of IgA vasculitis.

Hematology-Oncology

Paul T, Yadav DK, Alhamar M, and Dabak V. Primary Pleural Extranodal Marginal Zone Lymphoma Presenting as Bilateral Chylothorax. *Case Reports in Oncology* 2020; 929-934. Epub ahead of print. PMID: Not assigned. [Full Text](#)

Here we describe a case of pleural extranodal marginal zone lymphoma presenting as bilateral chylothorax which has not been reported in the literature prior to this. Primary pleural lymphomas are a rare entity most commonly associated with chronic infections, autoimmune conditions or long-standing pyothorax which were not seen in this case. Chylous pleural effusions in this patient were successfully managed with chemotherapy for the underlying lymphoma.

Hematology-Oncology

Singh SRK, Thanikachalam K, Jabbour-Aida H, Poisson LM, and Khan G. COVID-19 and Cancer: Lessons Learnt from a Michigan Hotspot. *Cancers (Basel)* 2020; 12(9). PMID: 32842584. [Full Text](#)

Background: Outcomes with coronavirus disease 2019 (COVID-19) have been worse in those with comorbidities and amongst minorities. In our study, we describe outcomes amongst cancer patients in Detroit, a major COVID-19 hotspot with a predominant inner-city population. Methods: We retrospectively analyzed 85 patients with active invasive cancers who were infected with COVID-19. The primary outcome was death or transition to hospice. Results: The majority were males (55.3%, n = 47), ≤70 years old (58.5%, n = 50), and African Americans (65.5%, n = 55). The most common primary site was prostate (18.8%, n = 16). Inpatient admission was documented in 85.5% (n = 73), ICU admission in 35.3% (n = 30), and primary outcome in 43.8% (n = 32) of hospitalized patients. On a multivariate analysis, factors associated with increased odds of a primary outcome included an age of >70 years versus ≤70 years (OR 4.7, p = 0.012) and of male gender (OR 4.8, p = 0.008). Recent cancer-directed therapy was administered in 66.7% (n = 20) of ICU admissions versus 39.5% (n = 17) of general floor admissions (Chi-square p-value of 0.023). Conclusions: High rates of mortality/transition to hospice and ICU utilization were noted amongst our patients with active invasive cancer, following a COVID-19 infection. Men and those of >70 years of age had a greater than four-fold increase in odds of death or transition to hospice.

Hospital Medicine

Warkentin TE, and **Kaatz S.** COVID-19 versus HIT hypercoagulability. *Thromb Res* 2020; 196:38-51. PMID: 32841919. [Full Text](#)

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A striking feature of COVID-19 is the high frequency of thrombosis, particularly in patients who require admission to intensive care unit because of respiratory complications (pneumonia/adult respiratory distress syndrome). The spectrum of thrombotic events is wide, including in situ pulmonary thrombosis, deep-vein thrombosis and associated pulmonary embolism, as well as arterial thrombotic events (stroke, myocardial infarction, limb artery thrombosis). Unusual thrombotic events have also been reported, e.g., cerebral venous sinus thrombosis, mesenteric artery and vein thrombosis. Several hematology abnormalities have been observed in COVID-19 patients, including lymphopenia, neutrophilia, thrombocytopenia (usually mild), thrombocytosis, elevated prothrombin time and partial thromboplastin times (the latter abnormality often indicating lupus anticoagulant phenomenon), hyperfibrinogenemia, elevated von Willebrand factor levels, and elevated fibrin d-dimer. Many of these abnormal hematologic parameters—even as early as the time of initial hospital admission—indicate adverse prognosis, including greater frequency of progression to severe respiratory illness and death. Progression to overt disseminated intravascular coagulation in fatal COVID-19 has been reported in some studies, but not observed in others. We compare and contrast COVID-19 hypercoagulability, and associated increased risk of venous and arterial thrombosis, from the perspective of heparin-induced thrombocytopenia (HIT), including the dilemma of providing thromboprophylaxis and treatment recommendations when available data are limited to observational studies. The frequent use of heparin—both low-molecular-weight and unfractionated—in preventing and treating COVID-19 thrombosis, means that vigilance for HIT occurrence is required in this patient population.

Hypertension and Vascular Research

Pavlov TS, Palygin O, Isaeva E, Levchenko V, Khedr S, Blass G, Ilatovskaya DV, Cowley AW, Jr., and Staruschenko A. NOX4-dependent regulation of ENaC in hypertension and diabetic kidney disease. *Faseb j* 2020; Epub ahead of print. PMID: 32799394. [Full Text](#)

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NADPH oxidase 4 (NOX4) is the most abundant NOX isoform in the kidney; however, its importance for renal function has only recently emerged. The NOX4-dependent pathway regulates many factors essential for proper sodium handling in the distal nephron. However, the functional significance of this pathway in the control of sodium reabsorption during the initiation of chronic kidney disease is not established. The goal of this study was to test Nox4-dependent ENaC regulation in two models: SS hypertension and STZ-induced type 1 diabetes. First, we showed that genetic ablation of Nox4 in Dahl salt-sensitive (SS) rat attenuated a high-salt (HS)-induced increase in epithelial Na⁽⁺⁾ channel (ENaC) activity in the cortical collecting duct. We also found that H₂O₂ upregulated ENaC activity, and H₂O₂ production was reduced in both the renal cortex and medulla in SS(Nox4^{-/-}) rats fed an HS diet. Second, in the streptozotocin model of hyperglycemia-induced renal injury ENaC activity in hyperglycemic animals was elevated in SS but not SS(Nox4^{-/-}) rats. NaCl cotransporter (NCC) expression was increased compared to healthy controls, while expression values between SS and SS(Nox4^{-/-}) groups were similar. These data emphasize a critical contribution of the NOX4-mediated pathway in maladaptive upregulation of ENaC-mediated sodium reabsorption in the distal nephron in the conditions of HS- and hyperglycemia-induced kidney injury.

Infectious Diseases

Bhagwat SS, Hariharan P, Joshi PR, Palwe SR, Shrivastava R, Patel MV, Devanga Ragupathi NK, Bakthavatchalam YD, **Ramesh MS**, Soman R, and Veeraraghavan B. Activity of cefepime/zidebactam against MDR Escherichia coli isolates harbouring a novel mechanism of resistance based on four-amino-acid inserts in PBP3. *J Antimicrob Chemother* 2020; Epub ahead of print. PMID: 32772098. [Full Text](#)

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BACKGROUND: Recent reports reveal the emergence of Escherichia coli isolates harbouring a novel resistance mechanism based on four-amino-acid inserts in PBP3. These organisms concomitantly expressed ESBLs or/and serine-/metallo-carbapenemases and were phenotypically detected by elevated aztreonam/avibactam MICs. **OBJECTIVES:** The in vitro activities of the investigational antibiotic cefepime/zidebactam and approved antibiotics (ceftazidime/avibactam, ceftolozane/tazobactam, imipenem/relebactam and others) were determined against E. coli isolates harbouring four-amino-acid inserts in PBP3. **METHODS:** Whole-genome sequenced E. coli isolates (n = 89) collected from a large tertiary care hospital in Southern India (n = 64) and from 12 tertiary care hospitals located across India (n = 25) during 2016-18, showing aztreonam/avibactam MICs ≥1 mg/L (≥4 times the aztreonam epidemiological cut-off) were included in this study. The MICs of antibiotics were determined using the reference broth microdilution method. **RESULTS:** Four-amino-acid inserts [YRIK (n = 30) and YRIN (n = 53)] were found in 83/89 isolates. Among 83 isolates, 65 carried carbapenemase genes [bla_{NDM} (n = 39), bla_{OXA-48-like} (n = 11) and bla_{NDM} + bla_{OXA-48-like} (n = 15)] and 18 isolates produced ESBLs/class C β-lactamases only. At least 16 unique STs were noted. Cefepime/zidebactam demonstrated potent activity, with all isolates inhibited at ≤1 mg/L. Comparator antibiotics including ceftazidime/avibactam and imipenem/relebactam showed limited activities. **CONCLUSIONS:** E. coli isolates concurrently harbouring four-amino-acid inserts in PBP3 and NDM are an emerging therapeutic challenge. Assisted by the PBP2-binding action of zidebactam, the cefepime/zidebactam combination overcomes both target modification (PBP3 insert)- and carbapenemase (NDM)-mediated resistance mechanisms in E. coli.

Infectious Diseases

Kates OS, Haydel BM, Florman SS, Rana MM, **Chaudhry ZS**, **Ramesh MS**, Safa K, Kotton CN, Blumberg EA, Besharatian BD, Tanna SD, Ison MG, Malinis M, Azar MM, Rakita RM, Morillas JA, Majeed A, Sait AS, Spaggiari M, Hemmige V, Mehta SA, Neumann H, Badami A, Goldman JD, Lala A, Hemmersbach-Miller M, McCort ME, Bajrovic V, Ortiz-Bautista C, Friedman-Moraco R, Sehgal S, Lease ED, Fisher CE, and Limaye AP. COVID-19 in solid organ transplant: A multi-center cohort study. *Clin Infect Dis* 2020. PMID: 32766815. [Full Text](#)

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BACKGROUND: The COVID-19 pandemic has led to significant reductions in transplantation, motivated in part by concerns of disproportionately more severe disease among solid organ transplant (SOT) recipients. However, clinical features, outcomes, and predictors of mortality in SOT recipients are not well-described. **METHODS:** We performed a multi-center cohort study of SOT recipients with laboratory-confirmed COVID-19. Data were collected using standardized intake and 28-day follow-up electronic case report forms. Multivariable logistic regression was used to identify risk factors for the primary endpoint, 28-day mortality, among hospitalized patients. **RESULTS:** Four hundred eighty-two SOT recipients from >50 transplant centers were included: 318 (66%) kidney or kidney/pancreas, 73 (15.1%) liver, 57 (11.8%) heart, and 30 (6.2%) lung. Median age was 58 (IQR 46-57), median time post-transplant was 5 years (IQR 2-10), 61% were male, and 92% had ≥ 1 underlying comorbidity. Among those hospitalized (376 [78%]), 117 (31%) required mechanical ventilation, and 77 (20.5%) died by 28 days after diagnosis. Specific underlying comorbidities (age >65 [aOR 3.0, 95%CI 1.7-5.5, $p < 0.001$], congestive heart failure [aOR 3.2, 95%CI 1.4-7.0, $p = 0.004$], chronic lung disease [aOR 2.5, 95%CI 1.2-5.2, $p = 0.018$], obesity [aOR 1.9, 95% CI 1.0-3.4, $p = 0.039$]) and presenting findings (lymphopenia [aOR 1.9, 95%CI 1.1-3.5, $p = 0.033$], abnormal chest imaging [aOR 2.9, 95%CI 1.1-7.5, $p = 0.027$]) were independently associated with mortality. Multiple measures of immunosuppression intensity were not associated with mortality. **CONCLUSIONS:** Mortality among SOT recipients hospitalized for COVID-19 was 20.5%. Age and underlying comorbidities rather than immunosuppression intensity-related measures were major drivers of mortality.

Infectious Diseases

McCullough PA, Kelly RJ, Ruocco G, Lerma E, Tumlin J, Wheelan K, Katz N, Lepor NE, Vijay K, Carter H, Singh B, McCullough SP, Bhambi BK, Palazzuoli A, De Ferrari GM, Milligan G, Safder T, Tecson KM, **Wang DD, McKinnon JE, O'Neill WW, Zervos M**, and Risch HA. Pathophysiological Basis and Rationale for Early Outpatient Treatment of SARS-CoV-2 (COVID-19) Infection. *Am J Med* 2020; Epub ahead of print. PMID: 32771461. [Full Text](#)

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Abrazo Arizona Heart Hospital, Abrazo Health System, Phoenix, AZ.

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University of Texas McGovern Medical School, Houston, TX.
Bakersfield Heart Hospital, Bakersfield, CA.
University of Siena, Le Scotte Hospital Viale Bracci Siena Italy.
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Approximately 9 months of the SARS-CoV-2 virus spreading across the globe has led to widespread COVID-19 acute hospitalizations and death. The rapidity and highly communicable nature of the SARS-CoV-2 outbreak has hampered the design and execution of definitive randomized, controlled trials of therapy outside of the clinic or hospital. In the absence of clinical trial results, physicians must use what has been learned about the pathophysiology of SARS-CoV-2 infection in determining early outpatient treatment of the illness with the aim of preventing hospitalization or death. This paper outlines key pathophysiological principles that relate to the patient with early infection treated at home. Therapeutic approaches based on these principles include: 1) reduction of reinoculation, 2) combination antiviral therapy, 3) immunomodulation, 4) antiplatelet/antithrombotic therapy 5) administration of oxygen, monitoring, and telemedicine. Future randomized trials testing the principles and agents discussed in this paper will undoubtedly refine and clarify their individual roles, however we emphasize the immediate need for management guidance in the setting of widespread hospital resource consumption, morbidity, and mortality.

Internal Medicine

Caines A, Selim R, and Salgia R. The Changing Global Epidemiology of Hepatocellular Carcinoma. *Clinics in Liver Disease* 2020; Epub ahead of print. PMID: Not assigned. [Full Text](#)

Hepatocellular carcinoma is among the leading causes of morbidity and mortality. Owing to the current epidemic of metabolic syndrome, the population affected by nonalcoholic fatty liver disease/nonalcoholic steatohepatitis continues to increase and now comprises a significant portion with those with hepatocellular carcinoma. The World Health Organization goal of obtaining universal hepatitis B virus vaccination has led to a global effort to improve vaccination, prevent mother-to-child transmission, and implement linkage to care to avoid the development of hepatocellular carcinoma. In contrast with the decreased burden of chronic hepatitis C virus, there has been an increase in new-onset acute hepatitis C virus.

Internal Medicine

EI-Khatib L, Alrayes H, Sallam O, and Elbanna A. Quinidine hypersensitivity: a side effect of a forgotten antiarrhythmic. *BMJ Case Rep* 2020; 13(8). PMID: 32843415. [Full Text](#)

Quinidine is one of the oldest antiarrhythmics known. Over the years, its use has decreased along with its side effects. Our case describes a 69-year-old woman with recurrent resistant ventricular tachycardia on Quinidine and Amiodarone who presented with acute liver toxicity. Drug-induced liver toxicity was at the top of our differential diagnosis list. Taking multiple factors into consideration, a decision was made to discontinue Quinidine, the patient's symptoms and lab abnormalities resolved within 1 week, yielding the diagnosis of Quinidine hypersensitivity.

Internal Medicine

EI-Khatib LA, De Feijter-Rupp H, Janoudi A, Fry L, Kehdi M, and Abela GS. Cholesterol induced heart valve inflammation and injury: efficacy of cholesterol lowering treatment. *Open Heart* 2020; 7(2). PMID: 32747455. [Full Text](#)

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BACKGROUND: Heart valves often undergo a degenerative process leading to mechanical dysfunction that requires valve replacement. This process has been compared with atherosclerosis because of shared pathology and risk factors. In this study, we aimed to elucidate the role of inflammation triggered by cholesterol infiltration and cholesterol crystals formation causing mechanical and biochemical injury in heart valves. **METHODS:** Human and atherosclerotic rabbit heart valves were evaluated. New Zealand White male rabbits were fed an enriched cholesterol diet alone or with simvastatin and ezetimibe simultaneous or after 6 months of initiating cholesterol diet. Inflammation was measured using C-reactive protein (CRP) and RAM 11 of tissue macrophage content. Cholesterol crystal

presence and content in valves was evaluated using scanning electron microscopy. RESULTS: Cholesterol diet alone induced cholesterol infiltration of valves with associated increased inflammation. Tissue cholesterol, CRP levels and RAM 11 were significantly lower in simvastatin and ezetimibe rabbit groups compared with cholesterol diet alone. However, the treatment was effective only when initiated with a cholesterol diet but not after lipid infiltration in valves. Aortic valve cholesterol content was significantly greater than all other cardiac valves. Extensive amounts of cholesterol crystals were noted in rabbit valves on cholesterol diet and in diseased human valves. CONCLUSIONS: Prevention of valve infiltration with cholesterol and reduced inflammation by simvastatin and ezetimibe was effective only when given during the initiation of high cholesterol diet but was not effective when given following infiltration of cholesterol into the valve matrix.

Internal Medicine

Harnish P, Nesheiwat Z, **Mahmood S**, Soni R, and Eltahawy E. Echocardiography in Detecting Mechanical Complications in Acute Coronary Syndrome. *CASE* 2020; Epub ahead of print. PMID: Not assigned. [Full Text](#)

Internal Medicine

Horiuchi Y, Wettersten N, Patel MP, Mueller C, Neath SX, Christenson RH, Morgenthaler NG, **McCord J, Nowak RM**, Vilke GM, Daniels LB, Hollander JE, Apple FS, Cannon CM, Nagurney JT, Schreiber D, deFilippi C, Hogan C, Diercks DB, Headden G, Limkakeng AT, Anand I, Wu AHB, Ebmeyer S, Jaffe AS, Peacock WF, and Maisel AS. Biomarkers Enhance Discrimination and Prognosis of Type 2 Myocardial Infarction. *Circulation* 2020; Epub ahead of print. PMID: 32820656. [Full Text](#)

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Background: The observed incidence of type 2 myocardial infarction (T2MI) is expected to increase with the implementation of increasingly sensitive cardiac troponin (cTn) assays. However, it remains to be determined how to diagnose, risk stratify and treat patients with T2MI. We aimed to discriminate and risk-stratify T2MI using biomarkers. Methods: Patients presenting to the Emergency Department with chest pain, enrolled in the CHOPIN study, were retrospectively analyzed. Two cardiologists adjudicated type 1 MI (T1MI) and T2MI. The prognostic ability of several biomarkers alone or in combination to discriminate T2MI from T1MI was investigated using receiver operating characteristic (ROC) curve analysis. The biomarkers analyzed were cTnI, copeptin, mid-regional pro-atrial natriuretic peptide (MRproANP), C-terminal pro-endothelin-1 (CT-proET1), mid-regional pro-adrenomedullin (MRproADM) and procalcitonin. Prognostic utility of these biomarkers for all-cause mortality and major adverse cardiovascular event (MACE: a composite of acute MI, unstable angina pectoris, reinfarction, heart failure, and stroke) at 180-day follow-up was also investigated. Results: Among the 2071 patients, T1MI and T2MI were adjudicated in 94 and 176 patients, respectively. Patients with T1MI had higher levels of baseline cTnI, while those with T2MI had higher baseline levels of MR-proANP, CT-proET1, MR-proADM, and procalcitonin. The area under the ROC curve (AUC) for the diagnosis of T2MI was higher for CT-proET1, MRproADM and MR-proANP (0.765, 0.750, and 0.733, respectively) than for cTnI (0.631). Combining all biomarkers resulted in a similar accuracy to a model using clinical variables and cTnI (0.854 versus 0.884, $p = 0.294$). Addition of biomarkers to the clinical model yielded the highest AUC (0.917). Other biomarkers, but not cTnI, were associated with mortality and MACE at 180-day among all patients, with no interaction between the diagnosis of T1MI or T2MI. Conclusions: Assessment of biomarkers reflecting pathophysiologic processes occurring with T2MI might help differentiate it from T1MI. Additionally, all biomarkers measured, except cTnI, were significant predictors of prognosis, regardless of type of MI.

Internal Medicine

Raad M, Dabbagh M, Gorgis S, Yan J, Chehab O, Dagher C, Jamoor K, Hussein IH, Cook B, Van Harn M, Singh G, McCord J, and Parikh S. Cardiac Injury Patterns and Inpatient Outcomes Among Patients Admitted With COVID-19. *Am J Cardiol* 2020; Epub ahead of print. PMID: 32829913. [Full Text](#)

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Although certain risk factors have been associated with increased morbidity and mortality in patients admitted with Coronavirus Disease 2019 (COVID-19), the impact of cardiac injury and high-sensitivity troponin-I (hs-cTnI) concentrations are not well described. In this large retrospective longitudinal cohort study, we analyzed the cases of 1,044 consecutively admitted patients with COVID-19 from March 9 until April 15. Cardiac injury was defined by hs-cTnI concentration >99th percentile. Patient characteristics, laboratory data, and outcomes were described in patients with cardiac injury and different hs-cTnI cut-offs. The primary outcome was mortality, and the secondary outcomes were length of stay, need for intensive care unit care or mechanical ventilation, and their different composites. The final analyzed cohort included 1,020 patients. The median age was 63 years, 511 (50% patients were female, and 403 (40% were white. 390 (38%) patients had cardiac injury on presentation. These patients were older (median age 70 years), had a higher cardiovascular disease burden, in addition to higher serum concentrations of inflammatory markers. They also exhibited an increased risk for our primary and secondary outcomes, with the risk increasing with higher hs-cTnI concentrations. Peak hs-cTnI concentrations continued to be significantly associated with mortality after a multivariate regression controlling for comorbid conditions, inflammatory markers, acute kidney injury, and acute respiratory distress syndrome. Within the same multivariate regression model, presenting hs-cTnI concentrations were not significantly associated with outcomes, and undetectable hs-cTnI concentrations on presentation did not completely rule out the risk for mechanical ventilation or death. In conclusion, cardiac injury was common in patients admitted with COVID-19. The extent of cardiac injury and peak hs-cTnI concentrations were associated with worse outcomes.

Internal Medicine

Tawfik GM, Giang HTN, Ghozy S, **Altibi AM**, Kandil H, Le HH, Eid PS, Radwan I, Makram OM, Hien TTT, Sherif M, Hossain AS, Thang TLL, Puljak L, Salem H, Numair T, Moji K, and Huy NT. Protocol registration issues of systematic review and meta-analysis studies: a survey of global researchers. *BMC Med Res Methodol* 2020; 20(1):213. PMID: 32842968. [Full Text](#)

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BACKGROUND: Although protocol registration of systematic reviews/meta-analysis (SR/MA) is still not mandatory, it is highly recommended that authors publish their SR/MA protocols prior to submitting their manuscripts for publication

as recommended by the Cochrane guidelines for conducting SR/MAs. our aim was to assess the awareness, obstacles, and opinions of SR/MA authors about the protocol registration process. METHODS: A cross-sectional survey study included the authors who published SR/MAs during the period from 2010 to 2016, and they were contacted for participation in our survey study. They were identified through the literature search of SR/MAs in Scopus database. An online questionnaire was sent to each participant via e-mail after receiving their approval to join the study. We have sent 6650 emails and received 275 responses. RESULTS: A total of 270 authors responses were complete and included in the final analysis. Our results has shown that PROSPERO was the most common database used for protocol registration (71.3%). The registration-to-acceptance time interval in PROSPERO was less than 1 month (99.1%). Almost half of the authors (44.2%) did not register their protocols prior to publishing their SR/MAs and according to their opinion that the other authors lack knowledge of protocol importance and mandance to be registered, was the most commonly reported reason (44.9%). A significant percnatge of respondents (37.4%) believed that people would steal their ideas from protocol databases, while only 5.3% reported that their SR/MA had been stolen. However, the majority (72.9%) of participants have agreed that protocol registries play a role in preventing unnecessary duplication of reviews. Finally, 37.4% of participants agree that SR/MA protocol registration should be mandatory. CONCLUSION: About half of the participants believes that the main reason for not registering protocols, is that the other authors lack knowledge concerning obligation and importance to register the SR/MA protocols in advance. Therefore, tools should be available to mandate protocol registration of any SRs beforehand and increasing awareness about the benefits of protocol registration among researchers.

Obstetrics, Gynecology and Women's Health Services

Vadlamudi G, Hong L, and Keerthy M. Evans Syndrome Associated with Pregnancy and COVID-19 Infection. *Case Rep Obstet Gynecol* 2020; 2020:8862545. PMID: 32850163. [Full Text](#)

BACKGROUND: Evans syndrome (ES) is a chronic autoimmune disease characterized by autoimmune hemolytic anemia along with immune thrombocytopenic purpura. Few case reports of ES in pregnancy have been published, and ES may be difficult to distinguish from other diagnoses more common in pregnancy. Guidelines for treatment of ES are not well-defined. CASE: A 23-year-old multigravid woman in active labor was found to have severe anemia and thrombocytopenia. She was diagnosed with ES and started on immunosuppressive treatments for persistent immune thrombocytopenic purpura. In the postpartum period, she was found to have coronavirus (COVID-19) infection and acute pulmonary embolism. CONCLUSION: Evans syndrome is a challenge to diagnose in pregnancy and poses important considerations for intrapartum and postpartum management.

Obstetrics, Gynecology and Women's Health Services

Wang A, Zawadzki N, Hedlin H, LeBlanc E, **Budrys N**, Van Horn L, Gass M, Westphal L, and Stefanick ML. Reproductive history and osteoarthritis in the Women's Health Initiative. *Scand J Rheumatol* 2020; Epub ahead of print. PMID: 32757806. [Request Article](#)

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OBJECTIVE: To investigate the relationship between self-reported osteoarthritis (OA) and reproductive factors in the Women's Health Initiative (WHI). METHOD: We used multivariable logistic regression to study the association of self-reported OA and reproductive factors in the WHI Observational Study and Clinical Trial cohorts of 145 965 postmenopausal women, in a retrospective cross-sectional format. RESULTS: In our cohort, we observed no clinically significant associations between reproductive factors and OA given small effect sizes. The following factors were associated with statistically significant increased likelihood of developing OA: younger age at menarche ($p < 0.001$), history of hysterectomy [adjusted odds ratio (aOR) 1.013, 95% confidence interval (CI) 1.004-1.022, $p = 0.04$ vs no hysterectomy], history of unilateral oophorectomy (aOR 1.015, 95% CI 1.004-1.026, $p < 0.01$ vs no oophorectomy), parity (aOR 1.017, 95% CI 1.009-1.026, $p < 0.001$), ever use of oral contraceptives (aOR 1.008, 95% CI 1.001-1.016, $p < 0.01$ vs never use), and current use of hormonal therapy (reference current users, aOR 0.951, 95% CI 0.943-0.959 for never users; aOR 0.981, 95% CI 0.972-0.989 for past users; global $p < 0.001$). Age at menopause, first birth, and pregnancy were not associated with OA. Among parous women, no clear pattern was observed with number of pregnancies, births, or duration of breastfeeding in relation to OA. CONCLUSION: Our study showed that reproductive factors did not have significant clinical associations with OA after controlling for confounders. This may be due to complex hormonal effects. Additional investigation is warranted in prospective cohort studies. The Women's Health Initiative is registered under ClinicalTrials.gov. Trial registration ID: NCT00000611.

Obstetrics, Gynecology and Women's Health Services

Xia H, Li S, Li X, Wang W, Bian Y, Wei S, Grove S, Wang W, Vatan L, Liu JR, McLean K, **Rattan R, Munkarah AR**, Guan JL, Kryczek I, and Zou W. Autophagic adaptation to oxidative stress alters peritoneal residential macrophage survival and ovarian cancer metastasis. *JCI Insight* 2020; Epub ahead of print. PMID: 32780724. [Full Text](#)

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Tumor-associated macrophages (TAMs) affect cancer progression and therapy. Ovarian carcinoma often metastasizes to the peritoneal cavity. Here, we found two peritoneal macrophage subsets in mice bearing ID8 ovarian cancer based on the Tim-4 (T-cell immunoglobulin and mucin domain containing 4) expression. Tim-4+ TAMs were embryonically originated and locally sustained while Tim-4- TAMs were replenished from circulating monocytes. Tim-4+ TAMs, but not Tim-4- TAMs, promoted tumor growth in vivo. Relative to Tim-4- TAMs, Tim-4+ TAMs manifested high oxidative phosphorylation and adapted mitophagy to alleviate oxidative stress. High levels of arginase-1 in Tim-4+ TAMs contributed to potent mitophagy activities via weakened mTORC1 activation due to low arginine resultant from arginase-1-mediated metabolism. Furthermore, genetic deficiency of autophagy element FIP200 resulted in Tim-4+ TAM loss via ROS-mediated apoptosis, and elevated T cell-immunity and ID8 tumor inhibition in vivo. Moreover, human ovarian cancer-associated CR1g (complement receptor of the Immunoglobulin superfamily) positive macrophages were transcriptionally, metabolically, and functionally similar to murine Tim-4+ TAMs. Thus, targeting CR1g+ (Tim-4+) TAMs may potentially treat ovarian cancer patients with peritoneal metastasis.

Nephrology

Palsson R, Colona MR, Hoenig MP, Lundquist AL, **Novak JE**, Perazella MA, and Waikar SS. Assessment of Interobserver Reliability of Nephrologist Examination of Urine Sediment. *JAMA Netw Open* 2020; 3(8):e2013959. PMID: 32821922. [Full Text](#)

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IMPORTANCE: Urine sediment microscopy is commonly performed during the evaluation of kidney disease. Interobserver reliability of nephrologists' urine sediment examination has not been well studied. **OBJECTIVE:** Assess interobserver reliability of the urine sediment examination. **DESIGN, SETTING, AND PARTICIPANTS:** In this diagnostic test study, urine samples were prospectively collected from a convenience sample of adult patients from an academic hospital in the United States undergoing kidney biopsy from July 11, 2018, to March 20, 2019. Digital images and videos of urine sediment findings were captured using a bright-field microscope. These images and videos along with urine dipstick results were incorporated in online surveys and sent to expert nephrologists at 15 US teaching hospitals. They were asked to identify individual sediment findings and the most likely underlying disease process. **EXPOSURES:** Urine dipstick results and urine sediment images from patients undergoing native kidney biopsy. **MAIN OUTCOMES AND MEASURES:** Interobserver reliability of urine sediment microscopy findings estimated by overall percent agreement and Fleiss κ coefficients. Secondary outcomes included concordance of diagnoses suspected by nephrologists with corresponding kidney biopsy results. **RESULTS:** In total, 10 surveys from 10 patients containing 76 study questions on individual features were sent to 21 nephrologists, 14 (67%) of whom completed them all. Their combined 1064 responses were analyzed. Overall percent agreement for casts was an estimated 59% (95% CI, 50%-69%), $\kappa = 0.52$ (95% CI, 0.42-0.62). For other sediment findings, overall percent agreement was an estimated 69% (95% CI, 61%-77%), $\kappa = 0.65$ (95% CI, 0.56-0.73). The κ estimates ranged from 0.13 (95% CI, 0.10-0.17) for mixed cellular casts to 0.90 (95% CI, 0.87-0.94) for squamous epithelial cells. **CONCLUSIONS AND RELEVANCE:** In this study, substantial variability occurred in the interpretation of urine sediment findings, even among expert nephrologists. Educational or technological innovations may help improve the urine sediment as a diagnostic tool.

Nephrology

Wheeler DC, Stefansson BV, Batiushin M, Bilchenko O, Cherney DZI, Chertow GM, Douthat W, Dwyer JP, Escudero E, Pecoits-Filho R, Furuland H, Górriz JL, Greene T, Haller H, Hou FF, Kang SW, Isidto R, Khullar D, Mark PB, McMurray JJV, Kashihara N, Nowicki M, Persson F, Correa-Rotter R, Rossing P, Toto RD, **Umanath K**, Van Bui P, Wittmann I, Lindberg M, Sjöström CD, Langkilde AM, and Heerspink HJL. The dapagliflozin and prevention of adverse outcomes in chronic kidney disease (DAPA-CKD) trial: baseline characteristics. *Nephrol Dial Transplant* 2020; Epub ahead of print. PMID: 32862232. [Full Text](#)

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BACKGROUND: The Dapagliflozin and Prevention of Adverse outcomes in Chronic Kidney Disease (DAPA-CKD; NCT03036150) trial was designed to assess the effect of the sodium-glucose co-transporter 2 (SGLT2) inhibitor dapagliflozin on kidney and cardiovascular events in participants with CKD with and without type 2 diabetes (T2D). This analysis reports the baseline characteristics of those recruited, comparing them with those enrolled in other trials. **METHODS:** In DAPA-CKD, 4304 participants with a urinary albumin:creatinine ratio (UACR) ≥ 200 mg/g and estimated glomerular filtration rate (eGFR) between 25 and 75 mL/min/1.73 m² were randomized to dapagliflozin 10 mg once daily or placebo. Mean eGFR was 43.1 mL/min/1.73 m² and median UACR was 949 mg/g (108 mg/mmol). **RESULTS:** Overall, 2906 participants (68%) had a diagnosis of T2D and of these, 396 had CKD ascribed to a cause other than diabetes. The most common causes of CKD after diabetes (n = 2510) were ischaemic/hypertensive nephropathy (n = 687) and chronic glomerulonephritis (n = 695), of which immunoglobulin A nephropathy (n = 270) was the most common. A total of 4174 participants (97%) were receiving an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, 1882 (43.7%) diuretics, 229 (5.3%) mineralocorticoid receptor antagonists and 122 (2.8%) glucagon-like peptide 1 receptor agonists. In contrast to the Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE), the DAPA-CKD trial enrolled participants with CKD due to diabetes and to causes other than diabetes. The mean eGFR of participants in the DAPA-CKD trial was 13.1 mL/min/1.73 m² lower than in CREDENCE, similar to that in the Finerenone in

Reducing Kidney Failure and Disease Progression in DKD (FIDELIO-DKD) trial and the Study Of diabetic Nephropathy with AtRasentan (SONAR). CONCLUSIONS: Participants with a wide range of underlying kidney diseases receiving renin-angiotensin system blocking therapy have been enrolled in the DAPA-CKD trial. The trial will examine the efficacy and safety of dapagliflozin in participants with CKD Stages 2-4 and increased albuminuria, with and without T2D.

Neurology

Affan M, Mahajan A, Rehman T, Kananeh M, **Schultz L**, and **Cerghet M**. The effect of race on clinical presentation and outcomes in neurosarcoidosis. *J Neurol Sci* 2020; 417:117073. PMID: 32771711. [Full Text](#)

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BACKGROUND: Nervous system is affected in 25% of patients with sarcoidosis. Current literature is largely limited to case reports with disproportionate Caucasian population. We aim to evaluate differences in presentation, management and outcomes by race in neurosarcoidosis. **METHODS:** Clinical and demographic data on consecutive patients fulfilling Zajicek criteria for neurosarcoidosis from 1995 to 2016 at Henry Ford Hospital were extracted. Disparities in clinical presentation, laboratory values, radiological features, treatment and outcomes, were compared between two groups: African Americans (AA) and non-AA using chi-squared tests, two sample t-test for age and Wilcoxon two sample tests. **RESULTS:** A total of 118 patients were included, of which 58% were female and 73% were AA. The diagnosis of neurosarcoidosis was noted to be definite (25%), probable (64%) and possible (11%). AA patients had a significantly higher rate of elevated erythrocyte sedimentation rate (62% vs 24%, $P = .005$) and had lower resolution of abnormalities on follow-up imaging (14% vs 41%, $P = .017$). There was no difference in disability on follow-up (25% vs 33%, $P = .43$) or mortality (13% vs 9%, $P = .6$). **CONCLUSIONS:** There were no differences in presentation, management and outcomes by race. Discordance in the clinical and radiological data by race has clinical implications and needs further investigation.

Neurology

Bansal P, **Fory EK**, **Malik S**, and **Memon AB**. Clinical Course of a Patient with Radiographically Described Acute Necrotizing Encephalopathy (ANE). *Radiology* 2020;203132. Epub ahead of print. PMID: 32787703. [Full Text](#)

Neurology

Barohn RJ, Gajewski B, Pasnoor M, Brown A, Herbelin LL, Kimminau KS, Mudarantkham DP, Jawdat O, Dimachkie MM, Iyadurai S, Stino A, Kissel J, Pascuzzi R, Brannagan T, Wicklund M, Ahmed A, Walk D, Smith G, Quan D, Heitzman D, Tobon A, Ladha S, Wolfe G, Pulley M, Hayat G, Li Y, Thaisetthawatkul P, Lewis R, Biliciler S, Sharma K, Salajegheh K, Trivedi J, Mallonee W, Burns T, Jacoby M, Bril V, Vu T, Ramchandren S, Bazant M, Austin S, Karam C, Hussain Y, Kutz C, Tywdell P, Scelsa S, Kushlaf H, Wymer J, Hehir M, Kolb N, Ralph J, Barboi A, Verma N, Ahmed M, **Memon A**, Saperstein D, Lou JS, Swenson A, and Cash T. Patient Assisted Intervention for Neuropathy: Comparison of Treatment in Real Life Situations (PAIN-CONTRoLS): Bayesian Adaptive Comparative Effectiveness Randomized Trial. *JAMA Neurol* 2020; Epub ahead of print. PMID: 32809014. [Full Text](#)

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Saint Louis University, St Louis, Missouri.
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 University of Nebraska Medical Center, Omaha.
 Cedars-Sinai Medical Center, Los Angeles, California.
 University of Texas Health Science Center at Houston.
 University of Miami, Miami, Florida.
 Brigham and Women's Hospital, Boston, Massachusetts.
 UT Southwestern Medical Center, Dallas, Texas.
 Hutchinson Clinic, Hutchinson, Kansas.
 University of Virginia, Charlottesville.
 Mercy Medical Center, Des Moines, Iowa.
 University of Toronto, Toronto, Ontario, Canada.
 University of South Florida-Tampa, Tampa.
 University of Michigan, Ann Arbor.
 Norton Neurology Services, Louisville, Kentucky.
 Seton Brain and Spine, Austin, Texas.
 Oregon Health and Science University, Portland.
 Austin Neuromuscular Center, Austin, Texas.
 Colorado Springs Neurological Associates, Colorado Springs.
 Spectrum Health, Grand Rapids, Michigan.
 Mt Sinai Beth Israel, New York, New York.
 University of Cincinnati, Cincinnati, Ohio.
 University of Florida-Gainesville, Gainesville.
 University of Vermont, Burlington.
 University of California, San Francisco.
 NorthShore University Health System, Evanston, Illinois.
 Neurological Services of Orlando Research, Orlando, Florida.
 Grand Medical Clinic, Katy, Texas.
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 University of Iowa Hospitals and Clinics, Iowa City.
 University of California-Irvine, Irvine.

IMPORTANCE: Cryptogenic sensory polyneuropathy (CSPN) is a common generalized slowly progressive neuropathy, second in prevalence only to diabetic neuropathy. Most patients with CSPN have significant pain. Many medications have been tried for pain reduction in CSPN, including antiepileptics, antidepressants, and sodium channel blockers. There are no comparative studies that identify the most effective medication for pain reduction in CSPN. **OBJECTIVE:** To determine which medication (pregabalin, duloxetine, nortriptyline, or mexiletine) is most effective for reducing neuropathic pain and best tolerated in patients with CSPN. **DESIGN, SETTING, AND PARTICIPANTS:** From December 1, 2014, through October 20, 2017, a bayesian adaptive, open-label randomized clinical comparative effectiveness study of pain in 402 participants with CSPN was conducted at 40 neurology care clinics. The trial included response adaptive randomization. Participants were patients with CSPN who were 30 years or older, with a pain score of 4 or greater on a numerical rating scale (range, 0-10, with higher scores indicating a higher level of pain). Participant allocation to 1 of 4 drug groups used the utility function and treatment's sample size for response adaptation randomization. At each interim analysis, a decision was made to continue enrolling (up to 400 participants) or stop the whole trial for success (80% power). Patient engagement was maintained throughout the trial, which helped guide the study and identify ways to communicate and disseminate information. Analysis was performed from December 11, 2015, to January 19, 2018. **INTERVENTIONS:** Participants were randomized to receive nortriptyline (n = 134), duloxetine (n = 126), pregabalin (n = 73), or mexiletine (n = 69). **MAIN OUTCOMES AND MEASURES:** The primary outcome was a utility function that was a composite of the efficacy (participant reported pain reduction of $\geq 50\%$ from baseline to week 12) and quit (participants who discontinued medication) rates. **RESULTS:** Among the 402 participants (213 men [53.0%]; mean [SD] age, 60.1 [13.4] years; 343 White [85.3%]), the utility function of nortriptyline was 0.81 (95% bayesian credible interval [CrI], 0.69-0.93; 34 of 134 [25.4%] efficacious; and 51 of 134 [38.1%] quit), of duloxetine was 0.80 (95% CrI, 0.68-0.92; 29 of 126 [23.0%] efficacious; and 47 of 126 [37.3%] quit), pregabalin was 0.69 (95% CrI, 0.55-0.84; 11 of 73 [15.1%] efficacious; and 31 of 73 [42.5%] quit), and mexiletine was 0.58 (95% CrI, 0.42-0.75; 14 of 69 [20.3%] efficacious; and 40 of 69 [58.0%] quit). The probability each medication yielded the highest utility was 0.52 for nortriptyline, 0.43 for duloxetine, 0.05 for pregabalin, and 0.00 for mexiletine. **CONCLUSIONS AND RELEVANCE:** This study found that, although there was no clearly superior medication, nortriptyline and duloxetine outperformed pregabalin and mexiletine when pain reduction and undesirable adverse effects are combined to a single end point. **TRIAL REGISTRATION:** ClinicalTrials.gov Identifier: NCT02260388.

Neurology

Carneiro T, Dashkoff J, Leung LY, Nobleza COS, Marulanda-Londono E, Hathidara M, Koch S, Sur N, Boske A, Voetsch B, **Aboul Nour H, Miller DJ**, Daneshmand A, Shulman J, Curiale G, Greer DM, Romero JR, Anand P, and Cervantes-Arslanian AM. Intravenous tPA for Acute Ischemic Stroke in Patients with COVID-19. *Journal of Stroke and Cerebrovascular Diseases* 2020; 29(11). PMID: Not assigned. [Full Text](#)

Background/Purpose: Coronavirus disease 2019 (COVID-19) is associated with increased risk of acute ischemic stroke (AIS), however, there is a paucity of data regarding outcomes after administration of intravenous tissue plasminogen activator (IV tPA) for stroke in patients with COVID-19. Methods: We present a multicenter case series from 9 centers in the United States of patients with acute neurological deficits consistent with AIS and COVID-19 who were treated with IV tPA. Results: We identified 13 patients (mean age 62 (± 9.8) years, 9 (69.2%) male). All received IV tPA and 3 cases also underwent mechanical thrombectomy. All patients had systemic symptoms consistent with COVID-19 at the time of admission: fever (5 patients), cough (7 patients), and dyspnea (8 patients). The median admission NIH stroke scale (NIHSS) score was 14.5 (range 3–26) and most patients (61.5%) improved at follow up (median NIHSS score 7.5, range 0–25). No systemic or symptomatic intracranial hemorrhages were seen. Stroke mechanisms included cardioembolic (3 patients), large artery atherosclerosis (2 patients), small vessel disease (1 patient), embolic stroke of undetermined source (3 patients), and cryptogenic with incomplete investigation (1 patient). Three patients were determined to have transient ischemic attacks or aborted strokes. Two out of 12 (16.6%) patients had elevated fibrinogen levels on admission (mean 262.2 ± 87.5 mg/dl), and 7 out of 11 (63.6%) patients had an elevated D-dimer level (mean 4284.6 ± 3368.9 ng/ml). Conclusions: IV tPA may be safe and efficacious in COVID-19, but larger studies are needed to validate these results.

Neurology

Dickey AS, **Mitsias PD**, Olango WM, Agan MC, Roche WP, Thomas JR, Rodrigues GM, Frankel MR, Ratcliff JJ, Nogueira RG, Haussen DC, and Karakis I. The Prognostic Value of Quantitative EEG in Patients Undergoing Mechanical Thrombectomy for Acute Ischemic Stroke. *J Clin Neurophysiol* 2020; Epub ahead of print. PMID: 32804879. [Full Text](#)

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PURPOSE: Previous work has shown that quantitative EEG measures correlate with the severity of ischemic stroke. This has not been systematically validated in patients with acute ischemic stroke who have undergone mechanical thrombectomy. METHODS: Data were collected from 73 patients who underwent mechanical thrombectomy and had a standard head set EEG performed during their hospital admission. For each patient, the global delta-alpha ratio (DAR) and its difference between the two hemispheres were calculated. Associations between the global and interhemispheric DAR difference with the patients' National Institutes of Health Stroke and Modified Rankin Scale scores at discharge and 3 months after thrombectomy were assessed. RESULTS: The interhemispheric DAR difference correlated with the National Institutes of Health Stroke scores at discharge (Spearman $R = 0.41$, $P = 0.0008$), National Institutes of Health Stroke scores at 3 months (Spearman $R = 0.60$, $P = 0.02$) and Modified Rankin Scale scores at 3 months (Spearman $R = 0.27$, $P = 0.01$). In contrast, the global DAR did not correlate significantly with any of these clinical outcomes when evaluated as continuous variables. In a multivariate logistic regression model, both the interhemispheric DAR difference ($\beta = 0.25$, $P = 0.03$) and the infarct volume ($\beta = 0.02$, $P = 0.03$) were independently predictive of good versus poor functional outcome (Modified Rankin Scale score ≤ 2 vs. > 2) at 3 months. CONCLUSIONS: The quantitative EEG measure of interhemispheric slow relative to fast frequencies power asymmetry correlated with the discharge and 3-month National Institutes of Health Stroke and Modified Rankin Scale scores and provided added value to infarct volume in predicting functional outcome at 3 months. These data support the prognostic value of quantitative EEG in ischemic stroke patients who have undergone mechanical thrombectomy.

Neurology

Li L, Chopp M, Ding G, Davoodi-Bojd E, Zhang L, Li Q, Zhang Y, Xiong Y, and Jiang Q. MRI Detection of Impairment of Glymphatic Function in Rat after Mild Traumatic Brain Injury. *Brain Res* 2020; Epub ahead of print. PMID: 32818526. [Full Text](#)

We investigated the effect of mild traumatic brain injury (mTBI) on the glymphatic pathway using contrast-enhanced magnetic resonance imaging (CE-MRI) and quantified with kinetic parameters obtained from an advanced two-compartment model. mTBI was induced in male Wistar rats using a closed head impact. Animals with and without mTBI ($n = 7$ /group) underwent the identical MRI protocol 10-weeks post-injury, including T2-weighted imaging and 3D T1-weighted imaging with intra-cisterna magna injection of contrast agent (Gd-DTPA). The parameters of infusion rate, clearance rate and clearance time constant, characterizing the kinetic features of glymphatic tracer transport in a

living brain, were quantified in multiple brain tissue regions. In the majority of examined regions, our quantification demonstrated significantly reduced infusion and clearance rates, and significantly increased clearance time constant in the mTBI animals compared to the healthy controls. These data indicate that mTBI induces chronic changes in influx and efflux of contrast agent and glymphatic pathway dysfunction. While the reduced efficiency of glymphatic function after mTBI was apparent in brain, regional evaluation revealed heterogeneous glymphatic effects of the mTBI in different anatomical regions. The suppression of glymphatic function, rather than the presence of focal lesions, indicates a persistent injury of the brain after mTBI. Thus, dynamic CE-MRI in conjunction with advanced kinetic analysis may offer a useful methodology for an objective assessment and confirmatory diagnosis of mTBI.

Neurology

Li W, Chopp M, Zacharek A, Yang W, Chen Z, Landschoot-Ward J, Venkat P, and Chen J. SUMO1 Deficiency Exacerbates Neurological and Cardiac Dysfunction after Intracerebral Hemorrhage in Aged Mice. *Transl Stroke Res* 2020; Epub ahead of print. PMID: 32761461. [Request Article](#)

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Small ubiquitin-like modifier 1 (SUMO1) reduces cardiac hypertrophy and induces neuroprotective effects. Previous studies have found that intracerebral hemorrhage (ICH) provokes cardiac deficit in the absence of primary cardiac diseases in mice. In this study, we tested the hypothesis that SUMO1 deficiency leads to worse brain and heart dysfunction after ICH and SUMO1 plays a key role in regulating brain-heart interaction after ICH in aged mice. Aged (18-20 months) female SUMO1 null (SUMO1^{-/-}) mice and wild-type (WT) C57BL/6 J mice were randomly divided into four groups (n = 8/group): (1) WT-sham group, (2) SUMO1^{-/-}-sham group, (3) WT-ICH group, and (4) SUMO1^{-/-}-ICH group. Cardiac function was measured by echocardiography. Neurological and cognitive functional tests were performed. Mice were sacrificed at 10 days after ICH for histological and immunohistochemically staining. Compared with WT-sham mice, WT-ICH mice exhibited (1) significantly (P < 0.05) decreased SUMO1 expression in heart tissue, (2) evident neurological and cognitive dysfunction as well as brain white matter deficits, (3) significantly increased cardiac dysfunction, and (4) inflammatory factor expression in the heart and brain. Compared with WT-ICH mice, SUMO1^{-/-}-ICH mice exhibited significantly increased: (1) brain hemorrhage volume, worse neurological and cognitive deficits, and increased white matter deficits; (2) cardiac dysfunction and cardiac fibrosis; (3) inflammatory response both in heart and brain tissue. Aged SUMO1-deficient female mice subjected to ICH not only exhibit increased neurological and cognitive functional deficit but also significantly increased cardiac dysfunction and inflammatory cell infiltration into the heart and brain. These data suggest that SUMO1 plays an important role in brain-heart interaction.

Neurology

Maideniuc C, and Memon AB. Acute necrotizing myelitis and acute motor axonal neuropathy in a COVID-19 patient. *J Neurol* 2020; Epub ahead of print. PMID: 32772172. [Full Text](#)

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A 61-year-old woman with COVID 19 infection developed acute necrotizing myelitis (ANM) and acute motor axonal neuropathy (AMAN), a rare variant of Guillain-Barré syndrome (GBS) without systemic signs of infection. MRI of the cervical spine demonstrated longitudinally extensive transverse myelitis, and EMG was consistent with the diagnosis of AMAN. CSF testing was negative for SARS-CoV-2. High dose steroids followed by plasma exchange were administered, and the patient made a clinical recovery. Immunotherapy has some role in fastening the improvement of immune-mediated neurological conditions associated with COVID-19.

Neurology

Manara A, Varelas P, and Smith M. Neurological determination of death in isolated brainstem lesions: A case report to highlight the issues involved. *J Intensive Care Soc* 2020; 21(3):269-273. PMID: 32782467. [Full Text](#)

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The neurological determination of death in patients with isolated brainstem lesions or by disruption of the posterior cerebral circulation is uncommon and many intensivists may never see such a case in their career. It is also the only

major difference between the "whole brain" and "brain stem" formulations for the neurological determination of death. We present a case of a patient with infarction of the structures supplied by the posterior cerebral circulation in whom death was diagnosed using neurological criteria, to illustrate the issues involved. We also suggest that international consensus may be achieved if ancillary tests, such as CT angiography, are made mandatory in this situation to demonstrate loss of blood flow in the anterior cerebral circulation as well the posterior circulation.

Neurology

Mitsias PD. Early Neurological Deterioration After Intravenous Thrombolysis: Still No End in Sight in the Quest for Understanding END. *Stroke* 2020; 51(9):2615-2617. PMID: 32811379. [Full Text](#)

Department of Neurology, School of Medicine, University of Crete, Heraklion, Greece (P.D.M.).
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Neurology

Wang C, Chopp M, Huang R, Li C, Zhang Y, Golembieski W, Lu M, Hazan Z, Zhang ZG, and Zhang L. Delayed (21 Days) Post Stroke Treatment With RPh201, a Botany-Derived Compound, Improves Neurological Functional Recovery in a Rat Model of Embolic Stroke. *Front Neurosci* 2020; 14:813. PMID: 32848574. [Full Text](#)

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BACKGROUND: Despite the recent advances in the acute stroke care, treatment options for long-term disability are limited. RPh201 is a botany-derived bioactive compound that has been shown to exert beneficial effects in various experimental models of neural injury. The present study evaluated the effect of delayed RPh201 treatment on long term functional recovery after stroke. **METHODS:** Adult male Wistar rats subjected to embolic middle cerebral artery occlusion (MCAO) were randomized into the following experimental groups (n = 20/group): (1) RPh201 treatment, and (2) Vehicle (cottonseed oil). RPh201 (20 µl) or Vehicle were subcutaneously administered twice a week for 16 consecutive weeks starting at 21 days after MCAO. An array of behavioral tests was performed up to 120 days after MCAO. **RESULTS:** Ischemic rats treated with RPh201 exhibited significant (p < 0.05) improvement of neurological function measured by adhesive removal test, foot-fault test, and modified neurological severity score at 90 and 120 days after MCAO. Immunohistochemistry analysis showed that RPh201 treatment robustly increased neurofilament heavy chain positive axons and myelin basic protein densities in the peri-infarct area by 61% and 31%, respectively, when compared to the Vehicle treatment, which were further confirmed by Western blot analysis. The RPh201 treatment did not reduce infarct volume. **CONCLUSION:** Our data demonstrated that RPh201 has a therapeutic effect on improvement of functional recovery in male ischemic rats even when the treatment was initiated 21 days post stroke. Enhanced axonal and myelination densities by RPh201 in ischemic brain may contribute to improved stroke recovery.

Neurology

Xin H, Liu Z, Buller B, Li Y, Golembieski W, Gan X, Wang F, Lu M, Ali MM, Zhang ZG, and Chopp M. MiR-17-92 enriched exosomes derived from multipotent mesenchymal stromal cells enhance axon-myelin remodeling and motor electrophysiological recovery after stroke. *J Cereb Blood Flow Metab* 2020; Epub ahead of print. PMID: 32811262.

[Full Text](#)

MiR-17-92 cluster enriched exosomes derived from multipotent mesenchymal stromal cells (MSCs) increase functional recovery after stroke. Here, we investigate the mechanisms underlying this recovery. At 24 h (h) post transient middle cerebral artery occlusion, rats received control liposomes or exosomes derived from MSCs infected with pre-miR-17-92 expression lentivirus (Exo-miR-17-92(+)) or control lentivirus (Exo-Con) intravenously. Compared to the liposomes, exosomes significantly reduced the intracortical microstimulation threshold current of the contralateral cortex for evoking impaired forelimb movements (day 21), increased the neurite and myelin density in the ischemic boundary area, and contralesional axonal sprouting into the caudal forelimb area of ipsilateral side and in the denervated spinal cord (day 28), respectively. The Exo-miR-17-92(+) further enhanced axon-myelin remodeling and electrophysiological recovery compared with the EXO-Con. Ex vivo cultured rat brain slice data showed that myelin and neuronal fiber density were significantly increased by Exo-miR-17-92(+), while significantly inhibited by application of the PI3K/Akt/mTOR pathway inhibitors. Our studies suggest that the miR-17-92 cluster enriched MSC exosomes enhanced neuro-functional recovery of stroke may be attributed to an increase of axonal extension and myelination, and this enhanced axon-myelin remodeling may be mediated in part via the activation of the PI3K/Akt/mTOR pathway induced by the downregulation of PTEN.

Neurosurgery

Azad S, Oravec D, Baumer T, Schildcrout A, White P, Basheer A, Bey MJ, Bartol SW, Chang V, and Yeni YN. Dynamic foraminal dimensions during neck motion 6.5 years after fusion and artificial disc replacement. *PLoS One* 2020; 15(8):e0237350. PMID: 32780779. [Full Text](#)

OBJECTIVE: To compare changes in foraminal motion at two time points post-surgery between artificial disc replacement (ADR) and anterior cervical discectomy and fusion (ACDF). **METHODS:** Eight ACDF and 6 ADR patients (all single-level C5-6) were tested at 2 years (T1) and 6.5 years (T2) post-surgery. The minimum foraminal height (FH.Min) and width (FW.Min) achieved during neck axial rotation and extension, and the range of these dimensions during motion (FH.Rn and FW.Rn, respectively) were measured using a biplane dynamic x-ray system, CT imaging and model-based tracking while patients performed neck axial rotation and extension tasks. Two-way mixed ANOVA was employed for analysis. **RESULTS:** In neck extension, significant interactions were found between year post-surgery and type of surgery for FW.Rn at C5-6 ($p < 0.006$) and C6-7 ($p < 0.005$), and for FH.Rn at C6-7 ($p < 0.01$). Post-hoc analysis indicated decreases over time in FW.Rn for ACDF ($p < 0.01$) and increases in FH.Rn for ADR ($p < 0.03$) at the C6-7 adjacent level. At index level, FW.Rn was comparable between ACDF and ADR at T1, but was smaller for ACDF than for ADR at T2 ($p < 0.002$). In axial rotation, differences were found between T1 and T2 but did not depend on type of surgery ($p > 0.7$). **CONCLUSIONS:** Changes were observed in the range of foraminal geometry at adjacent levels from 2 years to 6.5 years post-surgery that were different between ACDF and ADR for neck extension. These changes are contrary to the notion that motion at adjacent levels continue to increase following ACDF as compared to ADR over the long term.

Neurosurgery

Li L, Chopp M, Ding G, Davoodi-Bojd E, Zhang L, Li Q, Zhang Y, Xiong Y, and Jiang Q. MRI Detection of Impairment of Glymphatic Function in Rat after Mild Traumatic Brain Injury. *Brain Res* 2020; Epub ahead of print. PMID: 32818526. [Full Text](#)

We investigated the effect of mild traumatic brain injury (mTBI) on the glymphatic pathway using contrast-enhanced magnetic resonance imaging (CE-MRI) and quantified with kinetic parameters obtained from an advanced two-compartment model. mTBI was induced in male Wistar rats using a closed head impact. Animals with and without mTBI ($n = 7$ /group) underwent the identical MRI protocol 10-weeks post-injury, including T2-weighted imaging and 3D T1-weighted imaging with intra-cisterna magna injection of contrast agent (Gd-DTPA). The parameters of infusion rate, clearance rate and clearance time constant, characterizing the kinetic features of glymphatic tracer transport in a living brain, were quantified in multiple brain tissue regions. In the majority of examined regions, our quantification demonstrated significantly reduced infusion and clearance rates, and significantly increased clearance time constant in the mTBI animals compared to the healthy controls. These data indicate that mTBI induces chronic changes in influx and efflux of contrast agent and glymphatic pathway dysfunction. While the reduced efficiency of glymphatic function after mTBI was apparent in brain, regional evaluation revealed heterogeneous glymphatic effects of the mTBI in different anatomical regions. The suppression of glymphatic function, rather than the presence of focal lesions, indicates a persistent injury of the brain after mTBI. Thus, dynamic CE-MRI in conjunction with advanced kinetic analysis may offer a useful methodology for an objective assessment and confirmatory diagnosis of mTBI.

Neurosurgery

Li S, Han C, Asmaro K, Quan S, Li M, Ren C, Zhang J, Zhao W, Xu J, Liu Z, Zhang P, Zhu L, Ding Y, Wang K, Ji X, and Duan L. Remote Ischemic Conditioning Improves Attention Network Function and Blood Oxygen Levels in Unacclimatized Adults Exposed to High Altitude. *Aging Dis* 2020; 11(4):820-827. PMID: 32765948. [Full Text](#)

Beijing Key Laboratory of Hypoxic Conditioning Translational Medicine, Xuanwu Hospital, Capital Medical University, Beijing, China.

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Remote ischemic conditioning (RIC) confers protection on major organs from hypoxic/ischemic injuries; however, its impacts on attention network function and blood oxygen levels in unacclimatized adults exposed to high altitudes have yet to be elucidated. In this study, we recruited 120 healthy male volunteers, of which one was exposed to high altitude and the other was exposed to low altitude. The two cohorts were further divided into RIC and sham control groups. The attentional network test (ANT) was performed to evaluate cognitive function before and after RIC treatment. Other outcomes such as heart rate, blood pressure, blood oxygen saturation, cerebral tissue oxygenation

index (CTOI), and cerebrovascular hemodynamic indices were also evaluated. Prior to RIC treatment, there were no significant differences in orienting or executive function between the treatment and control arms of either cohort. Alerting function was significantly lower in the high-altitude cohort than in the low-altitude cohort. There were significant reductions in both blood oxygen and CTOI in the high-altitude cohort relative to the low-altitude cohort, while the pulse index (PI) of the former cohort was significantly increased. After RIC treatment, there was a significant difference in alerting function between the high-altitude RIC group and its associated control. The CTOI of the treatment group increased from 60.39±3.40% to 62.78±4.40%, and blood oxygenation also improved. Furthermore, this group showed a significant reduction in its PI. Exposure to high-altitude environments had a significant impact on alerting function, blood oxygen, CTOI, and PI. RIC ameliorated changes in attentional function, as well as blood oxygen and CTOI, suggesting that it potentially alters cerebrovascular compliance upon exposure to high altitude.

Ophthalmology and Eye Care Services

Bansal P, Fory EK, Malik S, and Memon AB. Clinical Course of a Patient with Radiographically Described Acute Necrotizing Encephalopathy (ANE). *Radiology* 2020; Epub ahead of print. PMID: 32787703. [Full Text](#)

Orthopaedics/Bone and Joint

Azad S, Oravec D, Baumer T, Schildcrout A, White P, Basheer A, Bey MJ, Bartol SW, Chang V, and Yeni YN. Dynamic foraminal dimensions during neck motion 6.5 years after fusion and artificial disc replacement. *PLoS One* 2020; 15(8):e0237350. PMID: 32780779. [Full Text](#)

OBJECTIVE: To compare changes in foraminal motion at two time points post-surgery between artificial disc replacement (ADR) and anterior cervical discectomy and fusion (ACDF). **METHODS:** Eight ACDF and 6 ADR patients (all single-level C5-6) were tested at 2 years (T1) and 6.5 years (T2) post-surgery. The minimum foraminal height (FH.Min) and width (FW.Min) achieved during neck axial rotation and extension, and the range of these dimensions during motion (FH.Rn and FW.Rn, respectively) were measured using a biplane dynamic x-ray system, CT imaging and model-based tracking while patients performed neck axial rotation and extension tasks. Two-way mixed ANOVA was employed for analysis. **RESULTS:** In neck extension, significant interactions were found between year post-surgery and type of surgery for FW.Rn at C5-6 ($p < 0.006$) and C6-7 ($p < 0.005$), and for FH.Rn at C6-7 ($p < 0.01$). Post-hoc analysis indicated decreases over time in FW.Rn for ACDF ($p < 0.01$) and increases in FH.Rn for ADR ($p < 0.03$) at the C6-7 adjacent level. At index level, FW.Rn was comparable between ACDF and ADR at T1, but was smaller for ACDF than for ADR at T2 ($p < 0.002$). In axial rotation, differences were found between T1 and T2 but did not depend on type of surgery ($p > 0.7$). **CONCLUSIONS:** Changes were observed in the range of foraminal geometry at adjacent levels from 2 years to 6.5 years post-surgery that were different between ACDF and ADR for neck extension. These changes are contrary to the notion that motion at adjacent levels continue to increase following ACDF as compared to ADR over the long term.

Orthopaedics/Bone and Joint

Franovic S, Kuhlmann N, Schlosser C, Pietroski A, Buchta AG, and Muh SJ. Role of preoperative PROMIS scores in predicting postoperative outcomes and likelihood of achieving MCID following reverse shoulder arthroplasty. *Seminars in Arthroplasty* 2020; 30(2):154-161. PMID: Not assigned. [Full Text](#)

Background: The patient-reported outcomes measurement information system (PROMIS) has emerged as an efficient and valid outcome measure in various shoulder surgeries. The purpose of this study was to investigate the influence of preoperative PROMIS scores in predicting postoperative PROMIS scores and the likelihood of achieving a minimal clinically important difference (MCID) following primary reverse total shoulder arthroplasty for cuff tear arthropathy. We hypothesize that preoperative PROMIS scores will influence both postoperative PROMIS scores and the probability of achieving MCID. **Methods:** 73 patients undergoing reverse shoulder arthroplasty by a board-certified shoulder and elbow surgeon were given three PROMIS CAT forms: PROMIS Upper Extremity Physical Function CAT v2.0 ("PROMIS-UE"), PROMIS Pain Interference v1.1 ("PROMIS-PI"), and PROMIS Depression v1.0 ("PROMIS-D"). PROMIS CAT domain t scores were assessed for significance between both time points using a Paired Samples t test. Minimal clinically important difference (MCID) was calculated using the distribution method and each PROMIS domain was subsequently assessed for its discriminatory ability in predicting postoperative improvement equal to or greater than the MCID through receiver operating characteristic (ROC) curve analysis. **Results:** Our cohort consisted of 73 patients (49.3% male) and an average age of 69.7 years (standard deviation, 11.9). Mean follow-up time point was 9.6 months (standard deviation, 5.0) after surgery. Preoperative PROMIS-UE, PROMIS-PI, and PROMIS-D were 29.5 ± 6.2 , 63.3 ± 5.4 , and 50.1 ± 9.2 , respectively. Each domain significantly improved at 10-months, on average, to 40.9 ± 7.8 , 51.4 ± 8.5 , 42.6 ± 8.1 , respectively. Following the distribution-based method for MCID calculation, we found the following MCID values for PROMIS-UE, PROMIS-PI, and PROMIS-D: 3.1, 2.7, and 4.6, respectively. ROC analysis revealed strong predictive ability for PROMIS-UE (AUC = 0.717, $p < 0.05$), moderate predictive ability for PROMIS-PI (AUC = 0.634, $p < 0.05$), and excellent predictive ability for PROMIS-D (AUC = 0.864, $p < 0.05$). Specifically, preoperative cutoff values of <26.0 , >70.0 , and >52.5 for PROMIS-UE, PROMIS-PI, and PROMIS-D are especially predictive of achieving MCID. **Conclusions:** Preoperative baseline scores

can serve as strong predictors of success in patients undergoing primary reverse shoulder arthroplasty and can be used to both counsel patients on surgery and to tailor postoperative protocols. Level of evidence: Level II.

Orthopaedics/Bone and Joint

Franovic S, Taylor K, Kuhlmann N, Aboona F, Schlosser C, and Muh SJ. PROMIS CAT forms demonstrate responsiveness in patients following reverse shoulder arthroplasty across numerous health domains: Responsiveness of PROMIS after RSA. *Seminars in Arthroplasty* 2020; 30(1):28-34. PMID: Not assigned. [Full Text](#)

Background: To better optimize the administration and postoperative tracking of patients using PROM, the Patient-Reported Outcomes Measurement Information System (PROMIS) was established by the National Institutes of Health. PROMIS CAT domains have been since validated in multiple orthopedic interventions of the shoulder. However, no one to date has studied the responsiveness of PROMIS CAT domains in a cohort of patients undergoing reverse shoulder arthroplasty. The purpose of this study was to investigate the responsiveness of three PROMIS CAT domains in patients undergoing reverse shoulder arthroplasty. Methods: Patients undergoing reverse shoulder arthroplasty by a board-certified shoulder and elbow surgeon were included in this study. PROMIS CAT Upper Extremity Physical Function ("PROMIS-UE"), Pain Interference ("PROMIS-PI"), and Depression ("PROMIS-D") scores were collected preoperatively and at five postoperative timepoints. Patient-centric demographic factors, range of motion, and clinical characteristics were also reviewed and analyzed for association with PROMIS scores. Results: 104 patients undergoing primary reverse shoulder arthroplasty were included in this study. The patient cohort consisted of 52 males (50%), with an average age of 70.3 years (standard deviation, 11.2), and a BMI of 30.2 (standard deviation, 6.1). All three PROMIS domains showed significant improvement as early as 6 weeks after surgery, with values of 32.4 ± 6.6 , 56.2 ± 7.5 , and 44.6 ± 8.6 , for PROMIS-UE, PROMIS-PI, and PROMIS-D, respectively. Significant improvements were noted for each postoperative timepoint thereafter, with 1-year follow-up values as follows: 42.1 ± 8.7 , 52.5 ± 8.6 , and 43.6 ± 9.5 for PROMIS-UE, PROMIS-PI, and PROMIS-D, respectively. Moderate correlations were identified with postoperative PROMIS-UE and abduction ($r = 0.439$, $p < 0.01$), as well as postoperative PROMIS-PI and PROMIS-D ($r = 0.502$, $p < 0.01$). Conclusions: PROMIS CAT forms demonstrate responsiveness in patients undergoing reverse shoulder arthroplasty. Level of Evidence: Level II; Retrospective Study.

Orthopaedics/Bone and Joint

Kuhlmann NA, Taylor KA, Roche CP, Franovic S, Chen C, Carofino BC, Flurin PH, Wright TW, Schoch BS, Zuckerman JD, and Muh SJ. Acute versus delayed reverse total shoulder arthroplasty for proximal humerus fractures in the elderly: Mid-term outcomes. *Seminars in Arthroplasty* 2020; 30(2):89-95. PMID: Not assigned. [Full Text](#)

Background: Treatment of proximal humerus fractures (PHFs) via reverse total shoulder arthroplasty (RTSA) has shown early promise when compared to historical treatment modalities. Ideal surgical timing remains unclear. The purpose of this study was to compare the outcomes of early versus delayed RTSA for PHF. We hypothesized that acute RTSA would display superior outcomes compared to those receiving delayed surgical intervention. Methods: This multicenter study retrospectively analyzed 142 patients who underwent RTSA for fracture. Patients treated within 4 weeks of injury were placed in the acute group ($n = 102$), and patients treated longer than 4 weeks after injury were placed in the chronic group ($n = 38$). A comprehensive panel of patient reported outcome measures, VAS pain scores, range of motion, and patient satisfaction were evaluated. Results: The acute group had significantly better final follow-up SPADI scores (20.8 ± 23.9 vs. 30.7 ± 31.7) ($p < 0.05$). No further differences were detected in other postoperative range of motion measurements, subjective outcomes, or VAS scores. Conclusions: Our results suggest that patients treated acutely display similar mid-term outcomes to those who receive delayed treatment. With this in mind, surgeons may first give consideration to a period of nonoperative treatment. Level of evidence: Level II.

Orthopaedics/Bone and Joint

Moeller JL. Social Media and the Sports Medicine Physician. *Clin J Sport Med* 2020; Epub ahead of print. PMID: 32852301. [Full Text](#)

Otolaryngology

Law RH, Ko AB, Jones LR, Peterson EL, Craig JR, and Deeb RH. Postoperative pain with or without nasal splints after septoplasty and inferior turbinate reduction. *Am J Otolaryngol* 2020; 41(6):102667. PMID: 32823039. [Full Text](#)

PURPOSE: To determine the effect of intranasal Doyle splints on postoperative pain following septoplasty and inferior turbinate reduction (ITR). Changes in Nasal Obstruction Symptom Evaluation (NOSE) scores were also evaluated. MATERIALS AND METHODS: A prospective cohort study conducted from January 2017 to January 2019. Patients were recruited if they experienced nasal obstruction due to septal deviation and inferior turbinate hypertrophy, and failed a one-month trial of intranasal corticosteroids. All patients underwent septoplasty with ITR, and either had Doyle splints or no splints placed. Patients were prescribed hydrocodone-acetaminophen 5-325 mg and asked to keep a daily log of pain medication use and visual analog scale (VAS) scores. Pain logs and NOSE

scores were compared between patients who had splints versus patients who had no splints placed after septoplasty and ITR over the first postoperative week. NOSE scores were also collected at every postoperative visit (1 week, 1 month, and 6 months). RESULTS: Fifty-seven patients were enrolled (37 splints, 20 no-splints). The median postoperative pain VAS score was 3.0 (interquartile range [IQR] 2.0-5.0) for the splint group and 4.0 (IQR 2.0-5.0) for the no-splint group (P = 0.906). The median postoperative pain medication requirement in morphine equivalents at the first postoperative visit was 5.4 mg/day (IQR 2.0-13.3) for the splint group and 8.4 mg/day (IQR 1.8-15.3) for the no-splint group (P = 0.833). CONCLUSIONS: There were no statistically significant differences in postoperative pain VAS scores or pain medication use between the two groups. All patients experienced significant reductions in NOSE scores postoperatively.

Otolaryngology

Peterson JD, **Goyal V**, Puricelli MD, Thatcher A, and Smith RJ. Neonatal Lateral Epiglottic Defects. *Ann Otol Rhinol Laryngol* 2020; Epub ahead of print. PMID: 32772542. [Full Text](#)

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INTRODUCTION: Multiple congenital abnormalities of the epiglottis have been reported and iatrogenic injuries to the larynx and subglottis are well known. We present a new pattern of defect not previously reported in the literature.

METHODS: Epiglottic abnormalities at two institutions are reviewed. Cases of defects involving the lateral aspect of the epiglottis and aryepiglottic fold are identified. A literature review of known epiglottic defects is performed.

RESULTS: Two children possessing lateral notch injuries at the aryepiglottic attachment to the epiglottis are described. Both children have a history of multiple laryngeal instrumentation attempts and prolonged intubation. Both have swallowing difficulties and are gastrostomy dependent. Congenital epiglottic defects include aplasia and midline bifidity, however, no lateral congenital epiglottic defects have been reported. CONCLUSION: Epiglottic defects, while rare, should be part of the differential for children with aspiration and feeding difficulties. A new pattern of defect is described and iatrogenic etiology proposed.

Otolaryngology

Singer MC, Marchal F, Angelos P, Bernet V, Boucai L, Buchholzer S, Burkey B, Eisele D, Erkul E, Faure F, Freitag SK, Gillespie MB, Harrell RM, Hartl D, Haymart M, Leffert J, Mandel S, Miller BS, Morris J, Pearce EN, Rahmati R, Ryan WR, Schaitkin B, Schlumberger M, Stack BC, Van Nostrand D, Wong KK, and Randolph G. Salivary and lacrimal dysfunction after radioactive iodine for differentiated thyroid cancer: American Head and Neck Society Endocrine Surgery Section and Salivary Gland Section joint multidisciplinary clinical consensus statement of otolaryngology, ophthalmology, nuclear medicine and endocrinology. *Head Neck* 2020; Epub ahead of print. PMID: 32812307. [Full Text](#)

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BACKGROUND: Postoperative radioactive iodine (RAI) administration is widely utilized in patients with differentiated thyroid cancer. While beneficial in select patients, it is critical to recognize the potential negative sequelae of this treatment. The prevention, diagnosis, and management of the salivary and lacrimal complications of RAI exposure are addressed in this consensus statement. **METHODS:** A multidisciplinary panel of experts was convened under the auspices of the American Head and Neck Society Endocrine Surgery and Salivary Gland Sections. Following a comprehensive literature review to assess the current best evidence, this group developed six relevant consensus recommendations. **RESULTS:** Consensus recommendations on RAI were made in the areas of patient assessment, optimal utilization, complication prevention, and complication management. **CONCLUSION:** Salivary and lacrimal complications secondary to RAI exposure are common and need to be weighed when considering its use. The recommendations included in this statement provide direction for approaches to minimize and manage these complications.

Pathology

Chen Y, Sadasivan SM, She R, Datta I, Taneja K, Chitale D, Gupta N, Davis MB, Newman LA, Rogers CG, Paris PL, Li J, Rybicki BA, and Levin AM. Breast and prostate cancers harbor common somatic copy number alterations that consistently differ by race and are associated with survival. *BMC Med Genomics* 2020; 13(1):116. PMID: 32819446. [Full Text](#)

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BACKGROUND: Pan-cancer studies of somatic copy number alterations (SCNAs) have demonstrated common SCNA patterns across cancer types, but despite demonstrable differences in aggressiveness of some cancers by race, pan-cancer SCNA variation by race has not been explored. This study investigated a) racial differences in SCNAs in both breast and prostate cancer, b) the degree to which they are shared across cancers, and c) the impact of these shared, race-differentiated SCNAs on cancer survival. **METHODS:** Utilizing data from The Cancer Genome Atlas (TCGA), SCNAs were identified using GISTIC 2.0, and in each tumor type, differences in SCNA magnitude between African Americans (AA) and European Americans (EA) were tested using linear regression. Unsupervised hierarchical clustering of the copy number of genes residing in race-differentiated SCNAs shared between tumor types was used to identify SCNA-defined patient groups, and Cox proportional hazards regression was used to test for association between those groups and overall/progression-free survival (PFS). **RESULTS:** We identified SCNAs that differed by race in breast (n = 58 SCNAs; permutation p < 10⁻⁴) and prostate tumors (n = 78 SCNAs; permutation p = 0.006). Six race-differentiated SCNAs common to breast and prostate found at chromosomes 5q11.2-q14.1, 5q15-q21.1, 8q21.11-q21.13, 8q21.3-q24.3, 11q22.3, and 13q12.3-q21.3 had consistent differences by race across both tumor types, and all six were of higher magnitude in AAs, with the chromosome 8q regions being the only amplifications. Higher magnitude copy number differences in AAs were also identified at two of these race-differentiated SCNAs in two additional hormonally-driven tumor types: endometrial (8q21.3-q24.3 and 13q12.3-q21.3) and ovarian (13q12.3-q21.3) cancers. Race differentiated SCNA-defined patient groups were significantly associated with survival differences in both cancer types, and these groups also differentiated within triple negative breast cancers based on PFS. While the frequency of the SCNA-defined patient groups differed by race, their effects on survival did not. **CONCLUSIONS:** This study identified race-differentiated SCNAs shared by two related cancers. The association of SCNA-defined patient groups with survival demonstrates the clinical significance of combinations of

these race-differentiated genomic aberrations, and the higher frequency of these alterations in AA relative to EA patients may explain racial disparities in risk of aggressive breast and prostate cancer.

Pathology

Nasr SH, Kudose SS, Said SM, Santoriello D, Fidler ME, **Williamson SR**, Damgard SE, Sethi S, Leung N, D'Agati VD, and Markowitz GS. Immunotactoid glomerulopathy is a rare entity with monoclonal and polyclonal variants. *Kidney Int* 2020; Epub ahead of print. PMID: 32818517. [Full Text](#)

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Immunotactoid glomerulopathy (ITG) is a rare form of glomerulonephritis for which our understanding is limited to case reports and small case series. Herein we describe the clinical, pathologic, and outcome characteristics of 73 patients with ITG who typically presented with proteinuria, hematuria, and renal insufficiency. Hematologic disorders were present in 66% of patients, including lymphoma in 41% (mainly chronic lymphocytic leukemia/small lymphocytic lymphoma), monoclonal gammopathy in 20%, and multiple myeloma in 6%. Light microscopy revealed endocapillary proliferative (35%), membranoproliferative (29%) and membranous (29%) patterns of glomerular involvement. Electron microscopy revealed characteristic microtubular deposits with a diameter of 14-60 nm, hollow cores, frequent parallel alignment, and a predominant distribution outside of the lamina densa of the glomerular basement membrane. Importantly, immunofluorescence revealed IgG-dominant staining which was light chain and IgG subclass restricted in 67% of cases, indicating monoclonal composition. This finding was used to distinguish monoclonal and polyclonal variants of ITG. As compared to polyclonal, monoclonal ITG had a higher incidence of lymphoma (53% vs. 11%), multiple myeloma (8% vs. 0), and monoclonal gammopathy (22% vs. 16%). Monoclonal ITG was more commonly treated with clone-directed therapy, which was associated with more frequent remission and less frequent end stage kidney disease. Thus, a third of ITG cases are polyclonal but a quarter of these cases are associated with hematologic conditions, underscoring the need for hematologic evaluation in all patients with ITG. Hence, based on these distinctions, ITG should be subclassified into monoclonal and polyclonal variants. Prognosis of ITG is good if the underlying hematologic condition is treated.

Pathology

Pagano MB, Trembl A, Stephens LD, Joshi S, Li Y, **Lopez-Plaza I**, Poyyappakkam S, Schwartz J, Tanhehco Y, and Zantek ND. Entrustable professional activities for apheresis medicine education. *Transfusion* 2020; Epub ahead of print. PMID: 32757215. [Full Text](#)

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BACKGROUND: Entrustable professional activities (EPAs) are well-defined, executable, observable, and measurable activities that are performed by a trainee and can be performed independently as training progresses. The purpose of this study is to develop EPAs specific for the practice of apheresis medicine (AM). **METHODS:** Members of the American Society for Apheresis Graduate Medical Education subcommittee developed a list of 28 apheresis medical activities linked to Accreditation Council for Graduate Medical Education milestones and competencies in five areas: (a) consultation, (b) clinical care for therapeutic apheresis, (c) clinical care for donor collections, (d) test optimization, and (e) vascular access. Ten AM experts using a validated tool to measure the quality of the EPAs (QUEPA) evaluated these activities with use of a Likert scale. Per group consensus, an activity was considered acceptable for each domain if it had received an average score greater than 3.7, and it was rated 4 or 5 (agree or strongly agree) by at least 70% of experts. **RESULTS:** Of the 28 activities, 11 did not have acceptable QUEPA scores: 7 activities were rated as unobservable, 4 were rated unfocused, 2 were rated unrealistic and not generalizable, and 2 were rated as

not addressing multiple competencies. Four activities had unacceptable scores in more than one domain. Subcommittee members edited these 11 activities over two review cycles to produce a final list of 26 activities. CONCLUSION: A set of practical, focused, and observable EPAs in AM were systematically developed. These EPAs can be used to assess and support trainee performance in AM.

Pathology

Paul T, Yadav DK, Alhamar M, and Dabak V. Primary Pleural Extranodal Marginal Zone Lymphoma Presenting as Bilateral Chylothorax. *Case Reports in Oncology* 2020; 929-934. Epub ahead of print. PMID: Not assigned. [Full Text](#)

Here we describe a case of pleural extranodal marginal zone lymphoma presenting as bilateral chylothorax which has not been reported in the literature prior to this. Primary pleural lymphomas are a rare entity most commonly associated with chronic infections, autoimmune conditions or long-standing pyothorax which were not seen in this case. Chylous pleural effusions in this patient were successfully managed with chemotherapy for the underlying lymphoma.

Pathology

Raad M, Dabbagh M, Gorgis S, Yan J, Chehab O, Dagher C, Jamoor K, Hussein IH, Cook B, Van Harn M, Singh G, McCord J, and Parikh S. Cardiac Injury Patterns and Inpatient Outcomes Among Patients Admitted With COVID-19. *Am J Cardiol* 2020; Epub ahead of print. PMID: 32829913. [Full Text](#)

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Although certain risk factors have been associated with increased morbidity and mortality in patients admitted with Coronavirus Disease 2019 (COVID-19), the impact of cardiac injury and high-sensitivity troponin-I (hs-cTnI) concentrations are not well described. In this large retrospective longitudinal cohort study, we analyzed the cases of 1,044 consecutively admitted patients with COVID-19 from March 9 until April 15. Cardiac injury was defined by hs-cTnI concentration >99th percentile. Patient characteristics, laboratory data, and outcomes were described in patients with cardiac injury and different hs-cTnI cut-offs. The primary outcome was mortality, and the secondary outcomes were length of stay, need for intensive care unit care or mechanical ventilation, and their different composites. The final analyzed cohort included 1,020 patients. The median age was 63 years, 511 (50% patients were female, and 403 (40% were white. 390 (38%) patients had cardiac injury on presentation. These patients were older (median age 70 years), had a higher cardiovascular disease burden, in addition to higher serum concentrations of inflammatory markers. They also exhibited an increased risk for our primary and secondary outcomes, with the risk increasing with higher hs-cTnI concentrations. Peak hs-cTnI concentrations continued to be significantly associated with mortality after a multivariate regression controlling for comorbid conditions, inflammatory markers, acute kidney injury, and acute respiratory distress syndrome. Within the same multivariate regression model, presenting hs-cTnI concentrations were not significantly associated with outcomes, and undetectable hs-cTnI concentrations on presentation did not completely rule out the risk for mechanical ventilation or death. In conclusion, cardiac injury was common in patients admitted with COVID-19. The extent of cardiac injury and peak hs-cTnI concentrations were associated with worse outcomes.

Pharmacy

Jiang C, Stuart M, Makowski C, Jennings DL, and To L. Safety and Efficacy of a Percutaneously Inserted Ventricular Support Device Purge Solution Heparin 25 U/mL. *Ann Pharmacother* 2020; Epub ahead of print. PMID: 32741200. [Full Text](#)

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Background: The Impella is a percutaneous ventricular assist device (pVAD) that provides temporary hemodynamic support to patients with cardiogenic shock or for protected percutaneous coronary intervention. The manufacturer recommends a 50-U/mL concentration of heparin purge solution (or 25 U/mL as an alternative), with systemic heparin

to maintain therapeutic anticoagulation during device support. Concomitant use of systemic heparin with the purge solution may increase the risk of bleeding. Objectives: The primary objective of this study was to describe the prevalence of thrombosis and bleeding using a less-concentrated heparin purge solution (25 U/mL) in combination with systemic heparin therapy. Methods: This was a retrospective observational cohort study of patients who required at least 12 hours of pVAD support and received 25-U/mL concentration of heparin purge solution between January 1, 2014, and May 31, 2017. The primary end points were the rate of thrombotic and bleeding events. Secondary end points included the percentage of time within the therapeutic activated partial thromboplastin time (aPTT) range. Descriptive statistics were utilized for data analysis. Results: Of the 161 patients screened, 100 met inclusion criteria; 63% of patients experienced a bleeding event, with Bleeding Academic Research Consortium (BARC) type 3a being the most common. Median percentages of subtherapeutic and suprathreshold aPTT values were similar between the bleeding and nonbleeding groups. Two patients experienced thrombotic events. Conclusion and Relevance: Based on our findings, the device thrombosis rate was 2% and the rate of major bleeding (BARC 3a and higher) was 35%. This study provides descriptive outcomes data of a lower-concentration heparin purge solution.

Pharmacy

Summers BB, Yates M, Cleveland KO, Gelfand MS, and Utery J. Fidaxomicin Compared With Oral Vancomycin for the Treatment of Severe Clostridium difficile-Associated Diarrhea: A Retrospective Review. *Hosp Pharm* 2020; 55(4):268-272. PMID: 32742016. [Full Text](#)

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Purpose: The most recent published guidelines on Clostridium difficile-associated diarrhea (CDAD) developed by the Infectious Diseases Society of America (IDSA) were released in 2017 and outline its treatment based on severity of the disease and recurrence; however, a clear first-line agent has not been recommended specifically for severe CDAD. Methods: This retrospective chart review was approved by the institutional review board and consisted of three community hospitals and one academic medical center. To be included, patients need to meet criteria for severe CDAD and receive at least 72 hours of therapy. Patients received either oral vancomycin or fidaxomicin, in addition to other therapies for CDAD, and differences in outcomes such as cost obtained from a common charge center, rates of recurrence, time to recurrence as measured at time of positive to negative polymerase chain reaction (PCR) test, and mortality were assessed. Results: Of the 147 patients, 74 patients received fidaxomicin and 73 patients received oral vancomycin. The average hospitalization cost for patients receiving fidaxomicin was \$129,338.69 and for patients receiving vancomycin was \$153,563.81 (P = .26). Recurrence rates were lower with fidaxomicin compared with vancomycin (6.8% vs 17.6%; P = .047), and time to recurrence was longer with fidaxomicin versus vancomycin, but not statistically significant (96.8 ± 45.9 days vs 63.2 ± 66.9 days; P = .321). Mortality, length of stay in the intensive care unit, and overall length of stay were similar between the two therapies. Conclusions: In the treatment of severe CDAD, recurrence rates were lower and time to recurrence was higher with fidaxomicin compared with oral vancomycin. A clear financial benefit has yet to translate from these known findings.

Public Health Sciences

Affan M, Mahajan A, Rehman T, Kananeh M, **Schultz L**, and **Cerghet M**. The effect of race on clinical presentation and outcomes in neurosarcoidosis. *J Neurol Sci* 2020; 417:117073. PMID: 32771711. [Full Text](#)

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BACKGROUND: Nervous system is affected in 25% of patients with sarcoidosis. Current literature is largely limited to case reports with disproportionate Caucasian population. We aim to evaluate differences in presentation, management and outcomes by race in neurosarcoidosis. METHODS: Clinical and demographic data on consecutive patients fulfilling Zajicek criteria for neurosarcoidosis from 1995 to 2016 at Henry Ford Hospital were extracted. Disparities in clinical presentation, laboratory values, radiological features, treatment and outcomes, were compared between two groups: African Americans (AA) and non-AA using chi-squared tests, two sample t-test for age and Wilcoxon two sample tests. RESULTS: A total of 118 patients were included, of which 58% were female and 73% were AA. The diagnosis of neurosarcoidosis was noted to be definite (25%), probable (64%) and possible (11%). AA

patients had a significantly higher rate of elevated erythrocyte sedimentation rate (62% vs 24%, $P = .005$) and had lower resolution of abnormalities on follow-up imaging (14% vs 41%, $P = .017$). There was no difference in disability on follow-up (25% vs 33%, $P = .43$) or mortality (13% vs 9%, $P = .6$). **CONCLUSIONS:** There were no differences in presentation, management and outcomes by race. Discordance in the clinical and radiological data by race has clinical implications and needs further investigation.

Public Health Sciences

Chen Y, Sadasivan SM, She R, Datta I, Taneja K, Chitale D, Gupta N, Davis MB, Newman LA, Rogers CG, Paris PL, Li J, Rybicki BA, and Levin AM. Breast and prostate cancers harbor common somatic copy number alterations that consistently differ by race and are associated with survival. *BMC Med Genomics* 2020; 13(1):116. PMID: 32819446. [Full Text](#)

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BACKGROUND: Pan-cancer studies of somatic copy number alterations (SCNAs) have demonstrated common SCNA patterns across cancer types, but despite demonstrable differences in aggressiveness of some cancers by race, pan-cancer SCNA variation by race has not been explored. This study investigated a) racial differences in SCNAs in both breast and prostate cancer, b) the degree to which they are shared across cancers, and c) the impact of these shared, race-differentiated SCNAs on cancer survival. **METHODS:** Utilizing data from The Cancer Genome Atlas (TCGA), SCNAs were identified using GISTIC 2.0, and in each tumor type, differences in SCNA magnitude between African Americans (AA) and European Americans (EA) were tested using linear regression. Unsupervised hierarchical clustering of the copy number of genes residing in race-differentiated SCNAs shared between tumor types was used to identify SCNA-defined patient groups, and Cox proportional hazards regression was used to test for association between those groups and overall/progression-free survival (PFS). **RESULTS:** We identified SCNAs that differed by race in breast ($n = 58$ SCNAs; permutation $p < 10^{-4}$) and prostate tumors ($n = 78$ SCNAs; permutation $p = 0.006$). Six race-differentiated SCNAs common to breast and prostate found on chromosomes 5q11.2-q14.1, 5q15-q21.1, 8q21.11-q21.13, 8q21.3-q24.3, 11q22.3, and 13q12.3-q21.3 had consistent differences by race across both tumor types, and all six were of higher magnitude in AAs, with the chromosome 8q regions being the only amplifications. Higher magnitude copy number differences in AAs were also identified at two of these race-differentiated SCNAs in two additional hormonally-driven tumor types: endometrial (8q21.3-q24.3 and 13q12.3-q21.3) and ovarian (13q12.3-q21.3) cancers. Race differentiated SCNA-defined patient groups were significantly associated with survival differences in both cancer types, and these groups also differentiated within triple negative breast cancers based on PFS. While the frequency of the SCNA-defined patient groups differed by race, their effects on survival did not. **CONCLUSIONS:** This study identified race-differentiated SCNAs shared by two related cancers. The association of SCNA-defined patient groups with survival demonstrates the clinical significance of combinations of these race-differentiated genomic aberrations, and the higher frequency of these alterations in AA relative to EA patients may explain racial disparities in risk of aggressive breast and prostate cancer.

Public Health Sciences

Dos Santos JM, Joiakim A, Kaplan DJ, Putt DA, Perez Bakovic G, Servoss SL, **Rybicki BA**, Dombkowski AA, and Kim H. Levels of plasma glycan-binding auto-IgG biomarkers improve the accuracy of prostate cancer diagnosis. *Mol Cell Biochem* 2020; Epub ahead of print. PMID: 32816187. [Full Text](#)

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Strategies to improve the early diagnosis of prostate cancer will provide opportunities for earlier intervention. The blood-based prostate-specific antigen (PSA) assay is widely used for prostate cancer diagnosis but specificity of the assay is not satisfactory. An algorithm based on serum levels of PSA combined with other serum biomarkers may

significantly improve prostate cancer diagnosis. Plasma glycan-binding IgG/IgM studies suggested that glycan patterns differ between normal and tumor cells. We hypothesize that in prostate cancer glycoproteins or glycolipids are secreted from tumor tissues into the blood and induce auto-immunoglobulin (Ig) production. A 24-glycan microarray and a 5-glycan subarray were developed using plasma samples obtained from 35 prostate cancer patients and 54 healthy subjects to identify glycan-binding auto-IgGs. Neu5Ac α 2-8Neu5Ac α 2-8Neu5Ac α (G81)-binding auto-IgG was higher in prostate cancer samples and, when levels of G81-binding auto-IgG and growth differentiation factor-15 (GDF-15 or NAG-1) were combined with levels of PSA, the prediction rate of prostate cancer increased from 78.2% to 86.2% than with PSA levels alone. The G81 glycan-binding auto-IgG fraction was isolated from plasma samples using G81 glycan-affinity chromatography and identified by N-terminal sequencing of the 50 kDa heavy chain variable region of the IgG. G81 glycan-binding 25 kDa fibroblast growth factor-1 (FGF1) fragment was also identified by N-terminal sequencing. Our results demonstrated that a multiplex diagnostic combining G81 glycan-binding auto-IgG, GDF-15/NAG-1 and PSA (≥ 2.1 ng PSA/ml for cancer) increased the specificity of prostate cancer diagnosis by 8%. The multiplex assessment could improve the early diagnosis of prostate cancer thereby allowing the prompt delivery of prostate cancer treatment.

Public Health Sciences

Qiu S, Divine G, Warner E, and Rao SD. Reference Intervals for Bone Histomorphometric Measurements Based on Data from Healthy Premenopausal Women. *Calcif Tissue Int* 2020; Epub ahead of print. PMID: 32814991. [Full Text](#)

This study has established the normal reference intervals for bone histomorphometric measurements derived from healthy premenopausal women, which is rarely available. We presented the static and dynamic bone histomorphometric data from trans-iliac bone biopsies in 62 healthy premenopausal women (19 blacks and 43 whites, ages 20-53 years). There were no significant differences in age and BMI between black and white women. Since there was no significant difference in bone remodeling between the two ethnic groups, we pooled data of all 62 premenopausal women to establish normal reference intervals for bone histomorphometry. The results provide normal reference intervals for both static and dynamic histomorphometric variables in cancellous and cortical bone of the ilium. None of the bone remodeling-related variables correlated with age or BMI. This study provides reference intervals for bone histomorphometric measurements in both cancellous and cortical bone of the ilium, which would be helpful in the evaluation of bone health in women.

Public Health Sciences

Raad M, Dabbagh M, Gorgis S, Yan J, Chehab O, Dagher C, Jamoor K, Hussein IH, Cook B, Van Harn M, Singh G, McCord J, and Parikh S. Cardiac Injury Patterns and Inpatient Outcomes Among Patients Admitted With COVID-19. *Am J Cardiol* 2020; Epub ahead of print. PMID: 32829913. [Full Text](#)

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Although certain risk factors have been associated with increased morbidity and mortality in patients admitted with Coronavirus Disease 2019 (COVID-19), the impact of cardiac injury and high-sensitivity troponin-I (hs-cTnI) concentrations are not well described. In this large retrospective longitudinal cohort study, we analyzed the cases of 1,044 consecutively admitted patients with COVID-19 from March 9 until April 15. Cardiac injury was defined by hs-cTnI concentration >99th percentile. Patient characteristics, laboratory data, and outcomes were described in patients with cardiac injury and different hs-cTnI cut-offs. The primary outcome was mortality, and the secondary outcomes were length of stay, need for intensive care unit care or mechanical ventilation, and their different composites. The final analyzed cohort included 1,020 patients. The median age was 63 years, 511 (50% patients were female, and 403 (40% were white. 390 (38%) patients had cardiac injury on presentation. These patients were older (median age 70 years), had a higher cardiovascular disease burden, in addition to higher serum concentrations of inflammatory markers. They also exhibited an increased risk for our primary and secondary outcomes, with the risk increasing with higher hs-cTnI concentrations. Peak hs-cTnI concentrations continued to be significantly associated with mortality after a multivariate regression controlling for comorbid conditions, inflammatory markers, acute kidney injury, and acute respiratory distress syndrome. Within the same multivariate regression model, presenting hs-cTnI concentrations were not significantly associated with outcomes, and undetectable hs-cTnI concentrations on presentation did not completely rule out the risk for mechanical ventilation or death. In conclusion, cardiac injury was

common in patients admitted with COVID-19. The extent of cardiac injury and peak hs-cTnl concentrations were associated with worse outcomes.

Public Health Sciences

Singh SRK, Thanikachalam K, Jabbour-Aida H, Poisson LM, and Khan G. COVID-19 and Cancer: Lessons Learnt from a Michigan Hotspot. *Cancers (Basel)* 2020; 12(9). PMID: 32842584. [Full Text](#)

Background: Outcomes with coronavirus disease 2019 (COVID-19) have been worse in those with comorbidities and amongst minorities. In our study, we describe outcomes amongst cancer patients in Detroit, a major COVID-19 hotspot with a predominant inner-city population. Methods: We retrospectively analyzed 85 patients with active invasive cancers who were infected with COVID-19. The primary outcome was death or transition to hospice. Results: The majority were males (55.3%, n = 47), ≤70 years old (58.5%, n = 50), and African Americans (65.5%, n = 55). The most common primary site was prostate (18.8%, n = 16). Inpatient admission was documented in 85.5% (n = 73), ICU admission in 35.3% (n = 30), and primary outcome in 43.8% (n = 32) of hospitalized patients. On a multivariate analysis, factors associated with increased odds of a primary outcome included an age of >70 years versus ≤70 years (OR 4.7, p = 0.012) and of male gender (OR 4.8, p = 0.008). Recent cancer-directed therapy was administered in 66.7% (n = 20) of ICU admissions versus 39.5% (n = 17) of general floor admissions (Chi-square p-value of 0.023). Conclusions: High rates of mortality/transition to hospice and ICU utilization were noted amongst our patients with active invasive cancer, following a COVID-19 infection. Men and those of >70 years of age had a greater than four-fold increase in odds of death or transition to hospice.

Public Health Sciences

Stinson LF, Gay MCL, Koleva PT, Eggesbø M, **Johnson CC, Wegienka G**, du Toit E, Shimojo N, Munblit D, Campbell DE, Prescott SL, Geddes DT, and Kozyrskyj AL. Human Milk From Atopic Mothers Has Lower Levels of Short Chain Fatty Acids. *Frontiers in Immunology* 2020; 11. PMID: Not assigned. [Full Text](#)

Short chain fatty acids (SCFAs) are microbial metabolites produced in the gut upon fermentation of dietary fiber. These metabolites interact with the host immune system and can elicit epigenetic effects. There is evidence to suggest that SCFAs may play a role in the developmental programming of immune disorders and obesity, though evidence in humans remains sparse. Here we have quantified human milk (HM) SCFA levels in an international cohort of atopic and non-atopic mothers (n = 109). Our results demonstrate that human milk contains detectable levels of the SCFAs acetate, butyrate, and formate. Samples from atopic mothers had significantly lower concentrations of acetate and butyrate than those of non-atopic mothers. HM SCFA levels in atopic and non-atopic women also varied based on maternal country of residence (Australia, Japan, Norway, South Africa, USA). Reduced exposure to HM SCFA in early life may program atopy or overweight risk in breastfed infants.

Public Health Sciences

Tabriz AA, **Neslund-Dudas C**, Turner K, Rivera MP, Reuland DS, and Lafata JE. How Health Care Organizations Implement Shared Decision Making When It Is Required for Reimbursement: The Case of Lung Cancer Screening. *Chest* 2020; Epub ahead of print. PMID: 32798520. [Full Text](#)

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BACKGROUND: The Centers for Medicare and Medicaid Services stipulated shared decision making (SDM) counseling as a prerequisite to lung cancer screening (LCS) reimbursement, despite well-known challenges implementing SDM in practice. RESEARCH QUESTION: How have health care organizations implemented SDM for LCS? STUDY DESIGN: and Methods: For this qualitative study, we used data from in-depth, semi-structured interviews with key informants directly involved in implementing and/or managing SDM for LCS. We identified respondents using a snowball sampling technique and used template analysis to thematically identify and analyze responses. RESULTS: We interviewed 30 informants representing 23 healthcare organizations located in 12 states and 4 Census regions. Respondents described two types of LCS-SDM programs: centralized models (n=7) in which frontend practitioners (e.g., primary care providers) referred patients to a LCS clinic in which trained staff (e.g. advanced practice nurses) delivered SDM at the time of screening or decentralized models (n=10) in which frontend practitioners delivered SDM prior to referring patients for screening. Some organizations used both models simultaneously (n=6). Respondents discussed tradeoffs between SDM quality and access. They perceived centralized models as enhancing SDM quality but limiting patient access to care, and vice versa. Respondents

reported ongoing challenges with limited resources and budgetary constraints, ambiguity regarding what constitutes SDM, and an absence of benchmarks for evaluating LCS-SDM quality. INTERPRETATION: Those responsible for developing and managing SDM-LCS programs voiced concerns regarding both patient access and SDM quality, regardless of organizational context, or LCS-SDM model implemented. The challenge facing these organizations, and those wanting to help patients and clinicians balance the tradeoffs inherent with LCS, is how to move beyond a "check box" documentation requirement to a process that enables LCS to be offered to all high risk patients, but used only by those who are informed and for whom screening represents a value concordant service.

Public Health Sciences

Wang C, Chopp M, Huang R, Li C, Zhang Y, Golembieski W, Lu M, Hazan Z, Zhang ZG, and Zhang L. Delayed (21 Days) Post Stroke Treatment With RPh201, a Botany-Derived Compound, Improves Neurological Functional Recovery in a Rat Model of Embolic Stroke. *Front Neurosci* 2020; 14:813. PMID: 32848574. [Full Text](#)

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BACKGROUND: Despite the recent advances in the acute stroke care, treatment options for long-term disability are limited. RPh201 is a botany-derived bioactive compound that has been shown to exert beneficial effects in various experimental models of neural injury. The present study evaluated the effect of delayed RPh201 treatment on long term functional recovery after stroke. **METHODS:** Adult male Wistar rats subjected to embolic middle cerebral artery occlusion (MCAO) were randomized into the following experimental groups (n = 20/group): (1) RPh201 treatment, and (2) Vehicle (cottonseed oil). RPh201 (20 µl) or Vehicle were subcutaneously administered twice a week for 16 consecutive weeks starting at 21 days after MCAO. An array of behavioral tests was performed up to 120 days after MCAO. **RESULTS:** Ischemic rats treated with RPh201 exhibited significant (p < 0.05) improvement of neurological function measured by adhesive removal test, foot-fault test, and modified neurological severity score at 90 and 120 days after MCAO. Immunohistochemistry analysis showed that RPh201 treatment robustly increased neurofilament heavy chain positive axons and myelin basic protein densities in the peri-infarct area by 61% and 31%, respectively, when compared to the Vehicle treatment, which were further confirmed by Western blot analysis. The RPh201 treatment did not reduce infarct volume. **CONCLUSION:** Our data demonstrated that RPh201 has a therapeutic effect on improvement of functional recovery in male ischemic rats even when the treatment was initiated 21 days post stroke. Enhanced axonal and myelination densities by RPh201 in ischemic brain may contribute to improved stroke recovery.

Public Health Sciences

Xin H, Liu Z, Buller B, Li Y, Golembieski W, Gan X, Wang F, Lu M, Ali MM, Zhang ZG, and Chopp M. MiR-17-92 enriched exosomes derived from multipotent mesenchymal stromal cells enhance axon-myelin remodeling and motor electrophysiological recovery after stroke. *J Cereb Blood Flow Metab* 2020; Epub ahead of print. PMID: 32811262. [Full Text](#)

MiR-17-92 cluster enriched exosomes derived from multipotent mesenchymal stromal cells (MSCs) increase functional recovery after stroke. Here, we investigate the mechanisms underlying this recovery. At 24 h (h) post transient middle cerebral artery occlusion, rats received control liposomes or exosomes derived from MSCs infected with pre-miR-17-92 expression lentivirus (Exo-miR-17-92(+)) or control lentivirus (Exo-Con) intravenously. Compared to the liposomes, exosomes significantly reduced the intracortical microstimulation threshold current of the contralateral cortex for evoking impaired forelimb movements (day 21), increased the neurite and myelin density in the ischemic boundary area, and contralesional axonal sprouting into the caudal forelimb area of ipsilateral side and in the denervated spinal cord (day 28), respectively. The Exo-miR-17-92(+) further enhanced axon-myelin remodeling and electrophysiological recovery compared with the EXO-Con. Ex vivo cultured rat brain slice data showed that myelin and neuronal fiber density were significantly increased by Exo-miR-17-92(+), while significantly inhibited by application of the PI3K/Akt/mTOR pathway inhibitors. Our studies suggest that the miR-17-92 cluster enriched MSC exosomes enhanced neuro-functional recovery of stroke may be attributed to an increase of axonal extension and myelination, and this enhanced axon-myelin remodeling may be mediated in part via the activation of the PI3K/Akt/mTOR pathway induced by the downregulation of PTEN.

Pulmonary and Critical Care Medicine

Chami HA, Diaz-Mendoza J, Chua A, Duggal A, Jenkins AR, Knight S, Patolia S, Tamae-Kakazu M, Raghu G, and Wilson KC. Transbronchial Biopsy and Cryobiopsy in the Diagnosis of Hypersensitivity Pneumonitis among Patients with Interstitial Lung Disease. *Ann Am Thorac Soc* 2020; Epub ahead of print. PMID: 32810411. [Full Text](#)

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RATIONALE: Hypersensitivity Pneumonitis (HP) is an interstitial lung disease (ILD) whose diagnosis is based on clinical, radiological, and pathological findings. The evidence supporting transbronchial forceps lung biopsy (TBBx) and transbronchial lung cryobiopsy (TBLC) as sampling techniques to diagnose HP in patients with newly detected ILD has not been reviewed systematically. **OBJECTIVE:** A systematic review was performed to assess the diagnostic yield and complication rates of TBBx or TBLC in patients with newly detected ILD whose differential diagnosis includes HP and to inform the development of the American Thoracic Society (ATS), Japanese Respiratory Society (JRS), and Asociación Latinoamericana del Tórax (ALAT) clinical practice guideline on the diagnosis of HP. **METHODS:** Medline, EMBASE and the Cochrane Library were searched through October 2019. Studies that enrolled patients with ILD and reported the diagnostic yield of TBBx or TBLC were selected for inclusion. Data related to diagnostic yield and safety outcomes were extracted and then pooled across studies via meta-analysis. The quality of the evidence was appraised using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach. **RESULTS:** Histopathologic diagnostic yield (number of procedures that yielded a histopathologic diagnosis divided by the total number of procedures performed) of TBBx and TBLC were 37% (95% CI 32-42%) and 82% (95% CI 78-86%) respectively among patients with ILD. Among those diagnosed by TBBx, the proportion with HP could not be determined. However, among those diagnosed by TBLC, 13.4% had HP. TBBx was complicated by moderate to severe bleeding, severe bleeding, and pneumothorax in 4% (95% CI 0-8%), 0% (95% CI 0-1%), and 7% (95% 2-13%) of patients, respectively. TBLC was complicated by any bleeding, severe bleeding, and pneumothorax in 11% (95% CI 7-15%), 0% (95% CI 0-1%), and 11% (95% 9-14%) of patients, respectively. The quality of the evidence was very low due to the uncontrolled study designs, lack of consecutive enrollment, and inconsistent results. **CONCLUSION:** Very low quality evidence indicated that TBLC had a higher diagnostic yield than TBBx among patients with ILD, although complications were more common with TBLC.

Pulmonary and Critical Care Medicine

Chen AC, Pastis NJ, Jr., Mahajan AK, Khandhar SJ, **Simoff MJ**, Machuzak MS, Cicens J, Gildea TR, and Silvestri GA. Robotic Bronchoscopy for Peripheral Pulmonary Lesions: A Multicenter Pilot and Feasibility Study (BENEFIT). *Chest* 2020; Epub ahead of print. PMID: 32822675. [Full Text](#)

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BACKGROUND: The diagnosis of peripheral pulmonary lesions (PPL) continues to present clinical challenges. Despite extensive experience with guided bronchoscopy, the diagnostic yield has not significantly improved. Robotic assisted bronchoscopic platforms have been developed to potentially improve the diagnostic yield for PPL. Presently, limited data exists evaluating the performance of robotic systems in live human subjects. **RESEARCH QUESTION:** What is the safety and feasibility of robotic assisted bronchoscopy in patients with peripheral pulmonary lesions? **STUDY DESIGN AND METHODS:** This was a prospective, multicenter pilot and feasibility study using a robotic bronchoscopic system with a mother-daughter configuration in patients with PPL 1-5cm in size. The primary endpoints were successful lesion localization using radial probe endobronchial ultrasound (R-EBUS) and incidence of procedure related adverse events. Robotic bronchoscopy was performed in patients using direct visualization, electromagnetic navigation and fluoroscopy. Following utilization of R-EBUS, transbronchial needle aspiration (TBNA) was performed. Rapid on-site evaluation (ROSE) was utilized on all cases. TBNA alone was sufficient when ROSE was diagnostic; when ROSE was non-diagnostic, transbronchial biopsy was performed using the robotic platform followed by conventional guided bronchoscopic approaches at the discretion of the investigator. **RESULTS:** Fifty-five patients were enrolled at five centers. One patient withdrew consent, leaving 54 patients for data analysis. Median lesion size was 23mm (IQR 15mm to 29mm). R-EBUS was available in 53/54 cases. Lesion localization was successful in 51/53 (96.2%) patients. Pneumothorax was reported in 2/54 (3.7%) of cases, requiring tube

thoracostomy in 1/54 (1.9 %) case. No additional adverse events occurred. INTERPRETATION: This is the first, prospective, multicenter study of robotic bronchoscopy in patients with peripheral pulmonary lesions. Successful lesion localization was achieved in 96.2% of cases with an adverse event rate comparable to conventional bronchoscopic procedures. Additional large prospective studies are warranted to evaluate procedure characteristics such as diagnostic yield.

Pulmonary and Critical Care Medicine

Jenkins AR, Chua A, Chami H, **Diaz-Mendoza J**, Duggal A, Knight S, Patolia S, Tamae-Kakazu M, Raghu G, and Wilson KC. Questionnaires or Serum IgG Testing in the Diagnosis of Hypersensitivity Pneumonitis among Patients with Interstitial Lung Disease. *Ann Am Thorac Soc* 2020; Epub ahead of print. PMID: 32780584. [Full Text](#)

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RATIONALE: Hypersensitivity Pneumonitis (HP) results from exposure to a variety of stimuli, which are challenging to identify. Questionnaires and serum IgG testing are methods to identify potentially causative exposures. **OBJECTIVE:** To perform a systematic review to determine the usefulness of questionnaires and serum IgG testing in identifying exposures that may have caused HP. **METHODS:** This systematic review informed an international, multi-disciplinary panel that developed a clinical practice guideline on the diagnosis of HP for the American Thoracic Society (ATS), Japanese Respiratory Society (JRS), and Asociación Latinoamericana del Tórax (ALAT). MEDLINE, the Cochrane Library, and EMBASE were searched from January 1946 through October 2019 for studies that utilized a questionnaire or serum IgG testing to identify exposures that may have caused HP. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was used to appraise the quality of the evidence. **RESULTS:** Searches identified 1,141 and 926 potentially relevant articles for questionnaires and serum IgG testing, respectively. The full texts of 32 and 49 articles, respectively, were reviewed. Two observational studies for questionnaires and 17 observational studies for serum IgG testing were selected. Questionnaires were better at detecting potentially relevant exposures compared to clinical history (100% vs. 26%, RR 3.80, 95% CI 1.79-8.06) and serum IgG testing (100% vs. 63%, RR 1.58, 95% CI 1.12-2.23), but were not different compared to serum IgG plus bronchial challenge testing (59% vs. 65%, RR 0.90, 95% CI 0.65-1.24). Longer, detailed questionnaires were more likely to identify potential exposures. Only 70% of potential exposures identified by questionnaires were subsequently confirmed by environmental testing. Serum IgG testing distinguished HP from healthy exposed and unexposed controls with high sensitivity (90% and 92% respectively) and high specificity (91% and 100% respectively) but did not distinguish HP as effectively from interstitial lung diseases (sensitivity 83% and specificity 68%). **CONCLUSION:** Using a questionnaire may help clinicians identify potentially relevant exposures when evaluating a patient with newly identified ILD for HP. Serum IgG testing may also identify potentially relevant exposures, but it is poor at distinguishing HP from other types of ILD.

Pulmonary and Critical Care Medicine

Moskowitz A, Huang DT, Hou PC, Gong J, Doshi PB, Grossestreuer AV, Andersen LW, Ngo L, Sherwin RL, Berg KM, Chase M, Cocchi MN, McCannon JB, Hershey M, Hilewitz A, Korotun M, Becker LB, Otero RM, **Uduman J**, Sen A, and Donnino MW. Effect of Ascorbic Acid, Corticosteroids, and Thiamine on Organ Injury in Septic Shock: The ACTS Randomized Clinical Trial. *Jama* 2020; 324(7):642-650. PMID: 32809003. [Full Text](#)

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IMPORTANCE: The combination of ascorbic acid, corticosteroids, and thiamine has been identified as a potential therapy for septic shock. **OBJECTIVE:** To determine whether the combination of ascorbic acid, corticosteroids, and thiamine attenuates organ injury in patients with septic shock. **DESIGN, SETTING, AND PARTICIPANTS:** Randomized, blinded, multicenter clinical trial of ascorbic acid, corticosteroids, and thiamine vs placebo for adult patients with septic shock. Two hundred five patients were enrolled between February 9, 2018, and October 27, 2019, at 14 centers in the United States. Follow-up continued until November 26, 2019. **INTERVENTIONS:** Patients were randomly assigned to receive parenteral ascorbic acid (1500 mg), hydrocortisone (50 mg), and thiamine (100 mg) every 6 hours for 4 days (n = 103) or placebo in matching volumes at the same time points (n = 102). **MAIN OUTCOMES AND MEASURES:** The primary outcome was change in the Sequential Organ Failure Assessment (SOFA) score (range, 0-24; 0 = best) between enrollment and 72 hours. Key secondary outcomes included kidney failure and 30-day mortality. Patients who received at least 1 dose of study drug were included in analyses.

RESULTS: Among 205 randomized patients (mean age, 68 [SD, 15] years; 90 [44%] women), 200 (98%) received at least 1 dose of study drug, completed the trial, and were included in the analyses (101 with intervention and 99 with placebo group). Overall, there was no statistically significant interaction between time and treatment group with regard to SOFA score over the 72 hours after enrollment (mean SOFA score change from 9.1 to 4.4 [-4.7] points with intervention vs 9.2 to 5.1 [-4.1] points with placebo; adjusted mean difference, -0.8; 95% CI, -1.7 to 0.2; P = .12 for interaction). There was no statistically significant difference in the incidence of kidney failure (31.7% with intervention vs 27.3% with placebo; adjusted risk difference, 0.03; 95% CI, -0.1 to 0.2; P = .58) or in 30-day mortality (34.7% vs 29.3%, respectively; hazard ratio, 1.3; 95% CI, 0.8-2.2; P = .26). The most common serious adverse events were hyperglycemia (12 patients with intervention and 7 patients with placebo), hyponatremia (11 and 7 patients, respectively), and new hospital-acquired infection (13 and 12 patients, respectively). **CONCLUSIONS AND RELEVANCE:** In patients with septic shock, the combination of ascorbic acid, corticosteroids, and thiamine, compared with placebo, did not result in a statistically significant reduction in SOFA score during the first 72 hours after enrollment. These data do not support routine use of this combination therapy for patients with septic shock. **TRIAL REGISTRATION:** ClinicalTrials.gov Identifier: NCT03389555.

Pulmonary and Critical Care Medicine

Patolia S, Tamae Kakazu M, Chami H, Chua A, **Diaz-Mendoza J**, Duggal A, Jenkins AR, Knight SL, Raghu G, and Wilson KC. Bronchoalveolar Lavage Lymphocytes in the Diagnosis of Hypersensitivity Pneumonitis among Patients with Interstitial Lung Disease: A Systematic Review. *Ann Am Thorac Soc* 2020; Epub ahead of print. PMID: 32757946. [Full Text](#)

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RATIONALE: Hypersensitivity Pneumonitis (HP) is an interstitial lung disease (ILD) characterized by inflammation and/or fibrosis in response to an inhalational exposure. **OBJECTIVE:** To determine the value of bronchoalveolar lavage (BAL) fluid lymphocyte cellular analysis in the detection of HP among patients with newly detected ILD. **METHODS:** This systematic review was undertaken in the context of development of an American Thoracic Society (ATS), Japanese Respiratory Society (JRS), and Asociación Latinoamericana del Tórax (ALAT) clinical practice guideline. The clinical question was, "should patients with newly detected ILD undergo BAL fluid lymphocyte analysis to diagnose HP?" Medline, Embase, and grey literature were searched through October 2019. Studies that reported the percentage of BAL fluid lymphocytes for various ILDs were selected for inclusion. Meta-analyses compared the mean percentage of BAL fluid lymphocytes among patients with HP to that among patients with Idiopathic Pulmonary Fibrosis (IPF) or sarcoidosis. The sensitivity and specificity by which various percentages of BAL fluid lymphocytes distinguish HP from IPF and sarcoidosis were also evaluated. **RESULTS:** Eighty-four articles were selected. No randomized trials or observational studies were identified that compared BAL fluid lymphocyte analysis to no BAL fluid lymphocyte analysis in patients with ILD. Included studies were case series describing BAL fluid cell differentials in patients with various ILDs. The percentage of BAL fluid lymphocytes was significantly higher in both fibrotic and nonfibrotic HP compared to IPF. Similarly, the percentage of BAL fluid lymphocytes was significantly higher in both fibrotic and nonfibrotic HP compared to sarcoidosis. A threshold of 20% BAL fluid lymphocytes distinguished fibrotic HP from IPF with a sensitivity and specificity of 69% and 61% respectively, and nonfibrotic HP from IPF with a sensitivity and specificity of 95% and 61% respectively. It distinguished fibrotic HP from sarcoidosis with a sensitivity and specificity of 69% and 26% respectively, and nonfibrotic HP from sarcoidosis with a sensitivity and specificity of 95% and 26% respectively. **CONCLUSION:** The percentage of BAL fluid lymphocytes is higher in HP than IPF or sarcoidosis. However, a threshold that distinguishes HP from IPF or sarcoidosis with both high sensitivity and high specificity was not identified.

Radiation Oncology

Li B, Sarria GR, Hermansen M, Hao J, Martinez D, Garcia B, Liu J, McLeod M, Castaneda S, Oladeru OT, Lee B, Sarria GJ, Gay H, **Chetty IJ**, and Roa D. Impact of a SBRT/SRS longitudinal telehealth training pilot course in Latin America. *Crit Rev Oncol Hematol* 2020; 154:103072. PMID: 32805497. [Full Text](#)

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PURPOSE: To assess the impact of longitudinal telehealth training in stereotactic body radiation therapy (SBRT) and stereotactic radiosurgery (SRS) for clinicians in Latin America. **MATERIALS AND METHODS:** Professionals from two Peruvian centers received an initial SBRT/SRS on-site training course and subsequently received follow-up telehealth training (interventional group) or not (negative control arm). Twelve live video conference sessions were scheduled. Surveys pre- and post-curriculum measured participants' confidence in seven practical domains of SBRT/SRS, based on Likert scales of 1-5, and post-curriculum surveys assessed educators' experiences. **RESULTS:** Sixty-one participants were registered, with an average of 24 attendees per session. Pre- and post- surveys were completed by 22 participants. For interventional and negative-control groups, mean changes in Likert scale were satisfactory for the

former and remained unmodified for the latter. **CONCLUSIONS:** Conducting telehealth educational programs via virtual classroom sessions could be a reliable method to augment training for SBRT and SRS.

Research Administration

Caldwell S, Sagaser K, Nelson Z, **Frey J**, Wardrop J, Boomer T, McCullough R, and Schwartz S. Deletion rescue resulting in segmental homozygosity: A mechanism underlying discordant NIPT results. *Am J Med Genet A* 2020; Epub ahead of print. PMID: 32798301. [Full Text](#)

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With the increasing capabilities of non-invasive prenatal testing (NIPT), detection of sub-chromosomal deletions and duplications are possible. This case series of deletion rescues resulting in segmental homozygosity helps provide a biological explanation for NIPT discrepancies and adds to the dearth of existing literature surrounding segmental UPD cases and their underlying mechanisms. In the three cases presented here, NIPT reported a sub-chromosomal deletion (in isolation or as part of a complex finding). Diagnostic testing, however, revealed segmental homozygosity or UPD for the region reported deleted on NIPT. Postnatal placental testing was pursued in two cases and confirmed the NIPT findings. This discordance between the screening and diagnostic testing is suggestive of a corrective post-zygotic event, such as telomere capture and/or deletion rescue, ultimately resulting in segmental homozygosity and fetoplacental mosaicism. Imprinted chromosomes and autosomal recessive disease genes make homozygosity an important clinical consideration. Amniocentesis with SNP microarray is particularly useful in determining both copy number and UPD issues alike.

Research Administration

Hatton SN, Huynh KH, Bonilha L, Abela E, Alhusaini S, Altmann A, Alvim MKM, Balachandra AR, Bartolini E, Bender B, Bernasconi N, Bernasconi A, Bernhardt B, Bargallo N, Caldaïrou B, Caligiuri ME, Carr SJA, Cavalleri GL, Cendes F, Concha L, **Davoodi-Bojd E**, Desmond PM, Devinsky O, Doherty CP, Domin M, Duncan JS, Focke NK, Foley SF, Gambardella A, Gleichgerrcht E, Guerrini R, Hamandi K, Ishikawa A, Keller SS, Kochunov PV, Kotikalapudi R, Kreilkamp BAK, Kwan P, Labate A, Langner S, Lenge M, Liu M, Lui E, Martin P, Mascacchi M, Moreira JCV, Morita-Sherman ME, O'Brien TJ, Pardoe HR, Pariente JC, Ribeiro LF, Richardson MP, Rocha CS, Rodríguez-Cruces R, Rosenow F, Severino M, Sinclair B, **Soltanian-Zadeh H**, Striano P, Taylor PN, Thomas RH, Tortora D, Velakoulis D, Vezzani A, Vivash L, von Podewils F, Vos SB, Weber B, Winston GP, Yasuda CL, Zhu AH, Thompson PM, Whelan CD, Jahanshad N, Sisodiya SM, and McDonald CR. White matter abnormalities across different epilepsy syndromes in adults: an ENIGMA-Epilepsy study. *Brain* 2020; 143(8):2454-2473. PMID: 32814957. [Full Text](#)

The epilepsies are commonly accompanied by widespread abnormalities in cerebral white matter. ENIGMA-Epilepsy is a large quantitative brain imaging consortium, aggregating data to investigate patterns of neuroimaging abnormalities in common epilepsy syndromes, including temporal lobe epilepsy, extratemporal epilepsy, and genetic generalized epilepsy. Our goal was to rank the most robust white matter microstructural differences across and within syndromes in a multicentre sample of adult epilepsy patients. Diffusion-weighted MRI data were analysed from 1069 healthy controls and 1249 patients: temporal lobe epilepsy with hippocampal sclerosis (n = 599), temporal lobe epilepsy with normal MRI (n = 275), genetic generalized epilepsy (n = 182) and non-lesional extratemporal epilepsy (n = 193). A harmonized protocol using tract-based spatial statistics was used to derive skeletonized maps of fractional anisotropy and mean diffusivity for each participant, and fibre tracts were segmented using a diffusion MRI atlas. Data were harmonized to correct for scanner-specific variations in diffusion measures using a batch-effect correction tool (ComBat). Analyses of covariance, adjusting for age and sex, examined differences between each epilepsy syndrome and controls for each white matter tract (Bonferroni corrected at $P < 0.001$). Across 'all epilepsies' lower fractional anisotropy was observed in most fibre tracts with small to medium effect sizes, especially in the corpus callosum, cingulum and external capsule. There were also less robust increases in mean diffusivity. Syndrome-specific fractional anisotropy and mean diffusivity differences were most pronounced in patients with hippocampal sclerosis in the ipsilateral parahippocampal cingulum and external capsule, with smaller effects across most other tracts. Individuals with temporal lobe epilepsy and normal MRI showed a similar pattern of greater ipsilateral than contralateral abnormalities, but less marked than those in patients with hippocampal sclerosis. Patients with generalized and extratemporal epilepsies had pronounced reductions in fractional anisotropy in the corpus callosum, corona radiata and external capsule, and increased mean diffusivity of the anterior corona radiata. Earlier age of seizure onset and longer disease duration were associated with a greater extent of diffusion abnormalities in patients with hippocampal sclerosis. We demonstrate microstructural abnormalities across major

association, commissural, and projection fibres in a large multicentre study of epilepsy. Overall, patients with epilepsy showed white matter abnormalities in the corpus callosum, cingulum and external capsule, with differing severity across epilepsy syndromes. These data further define the spectrum of white matter abnormalities in common epilepsy syndromes, yielding more detailed insights into pathological substrates that may explain cognitive and psychiatric co-morbidities and be used to guide biomarker studies of treatment outcomes and/or genetic research.

Surgery

Chamogeorgakis T, Cowger J, Apostolou D, Tanaka D, and Neme H. Right Ventricular Device HeartWare Implant to the Right Atrium with Fixation to the Chest Wall in Patient with Biventricular Support. *Asaio j* 2020; 66(8):e102-e104. PMID: 32740361. [Full Text](#)

Surgery

Ivanics T, Rizzari M, Moonka D, Al-Kurd A, Delvecchio K, Kitajima T, Elsabbagh A, Collins K, Yoshida A, Abouljoud M, and Nagai S. Re-transplantation outcomes for hepatitis C in the United States before and after DAA-introduction. *Am J Transplant* 2020; Epub ahead of print. PMID: 32794649. [Full Text](#)

The success of direct-acting antiviral (DAA) therapy has led to near-universal cure for patients chronically infected with hepatitis C virus (HCV) and improved post-liver transplant(LT) outcomes. We investigated the trends and outcomes of re-transplantation in HCV and non-HCV patients before and after the introduction of DAA. Adult patients who underwent re-LT were identified in the OPTN/UNOS database. Multi-organ transplants and patients with more than two total LTs were excluded. Two eras were defined, pre-DAA(2009-2012), and post-DAA(2014-2017). A total of 2,112 re-LT patients were eligible(HCV: n=499 pre-DAA and n=322 post-DAA; non-HCV: n=547 pre-DAA and n=744 post-DAA). HCV patients had both improved graft and patient survival after re-LT in the post-DAA era. One-year graft survival was 69.8% pre-DAA and 83.8% post-DAA(p<0.001). One-year patient survival was 73.1% pre-DAA and 86.2% post-DAA(p<0.001). Graft and patient survival was similar between eras for non-HCV patients. When adjusted, the post-DAA era represented an independent positive predictive factor for graft and patient survival(HR:0.67;p=0.005, and HR:0.65;p=0.004) only in HCV patients. The positive post-DAA era effect was observed only in HCV patients with first graft loss due to disease recurrence(HR:0.31;p=0.002, HR 0.32;p=0.003, respectively). Among HCV patients, receiving a re-LT in the post-DAA era was associated with improved patient and graft survival.

Surgery

Leonard-Murali S, Mohamed A, Woodward A, and Blyden D. Thoracoacromial artery injury after tube thoracostomy for pneumothorax. *BMJ Case Rep* 2020; 13(8). PMID: 32816885. [Full Text](#)

In this case, a patient presented in a delayed fashion after blunt trauma is found to have a large left-sided pneumothorax, and tube thoracostomy is performed. After placement of the apically oriented tube, he developed haemothorax. CT imaging showed an area of questionable extravasation from the left subclavian artery, directly anterior to the thoracostomy tube. His haemothorax was refractory to adequate drainage with a new thoracostomy tube. He ultimately required angiography, coil embolisation and covered stent placement, followed by thoracoscopic evacuation of the haemothorax.

Urology

Chen Y, Sadasivan SM, She R, Datta I, Taneja K, Chitale D, Gupta N, Davis MB, Newman LA, Rogers CG, Paris PL, Li J, Rybicki BA, and Levin AM. Breast and prostate cancers harbor common somatic copy number alterations that consistently differ by race and are associated with survival. *BMC Med Genomics* 2020; 13(1):116. PMID: 32819446. [Full Text](#)

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BACKGROUND: Pan-cancer studies of somatic copy number alterations (SCNAs) have demonstrated common SCNA patterns across cancer types, but despite demonstrable differences in aggressiveness of some cancers by race, pan-cancer SCNA variation by race has not been explored. This study investigated a) racial differences in

SCNAs in both breast and prostate cancer, b) the degree to which they are shared across cancers, and c) the impact of these shared, race-differentiated SCNAs on cancer survival. METHODS: Utilizing data from The Cancer Genome Atlas (TCGA), SCNAs were identified using GISTIC 2.0, and in each tumor type, differences in SCNA magnitude between African Americans (AA) and European Americans (EA) were tested using linear regression. Unsupervised hierarchical clustering of the copy number of genes residing in race-differentiated SCNAs shared between tumor types was used to identify SCNA-defined patient groups, and Cox proportional hazards regression was used to test for association between those groups and overall/progression-free survival (PFS). RESULTS: We identified SCNAs that differed by race in breast (n = 58 SCNAs; permutation p < 10⁻⁴) and prostate tumors (n = 78 SCNAs; permutation p = 0.006). Six race-differentiated SCNAs common to breast and prostate found at chromosomes 5q11.2-q14.1, 5q15-q21.1, 8q21.11-q21.13, 8q21.3-q24.3, 11q22.3, and 13q12.3-q21.3 had consistent differences by race across both tumor types, and all six were of higher magnitude in AAs, with the chromosome 8q regions being the only amplifications. Higher magnitude copy number differences in AAs were also identified at two of these race-differentiated SCNAs in two additional hormonally-driven tumor types: endometrial (8q21.3-q24.3 and 13q12.3-q21.3) and ovarian (13q12.3-q21.3) cancers. Race differentiated SCNA-defined patient groups were significantly associated with survival differences in both cancer types, and these groups also differentiated within triple negative breast cancers based on PFS. While the frequency of the SCNA-defined patient groups differed by race, their effects on survival did not. CONCLUSIONS: This study identified race-differentiated SCNAs shared by two related cancers. The association of SCNA-defined patient groups with survival demonstrates the clinical significance of combinations of these race-differentiated genomic aberrations, and the higher frequency of these alterations in AA relative to EA patients may explain racial disparities in risk of aggressive breast and prostate cancer.

Urology

Martini A, Falagario UG, Villers A, Dell'Oglio P, Mazzone E, Autorino R, Moschovas MC, Buscarini M, Bravi CA, Briganti A, Sawczyn G, Kaouk J, **Menon M**, Secco S, Bocciardi AM, Wang G, Zhou X, Porpiglia F, Mottrie A, Patel V, Tewari AK, Montorsi F, Gaston R, Wiklund NP, and Hemal AK. Contemporary Techniques of Prostate Dissection for Robot-assisted Prostatectomy. *Eur Urol* 2020; Epub ahead of print. PMID: 32747200. [Full Text](#)

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BACKGROUND: Over the years, several techniques for performing robot-assisted prostatectomy have been implemented in an effort to achieve optimal oncological and functional outcomes. OBJECTIVE: To provide an evidence-based description and video-based illustration of currently available dissection techniques for robotic prostatectomy. DESIGN, SETTING, AND PARTICIPANTS: A literature search was performed to retrieve articles describing different surgical approaches and techniques for robot-assisted radical prostatectomy (RARP) and to analyze data supporting their use. Video material was provided by experts in the field to illustrate these approaches and techniques. SURGICAL PROCEDURE: Multiple surgical approaches are available: extraperitoneal, transvesical, transperitoneal posterior, transperitoneal anterior, Retzius sparing, and transperineal. Surgical techniques for prostatic dissection sensu stricto are the following: omission of the endopelvic fascia dissection, bladder neck preservation, incremental nerve sparing by means of an antegrade or retrograde approach, and preservation of the puboprostatic ligaments and dorsal venous complex. Recently, techniques for total or partial prostatectomy have been described. MEASUREMENTS: Different surgical approaches and techniques for robotic prostatectomy have been analyzed. RESULTS AND LIMITATIONS: Two randomized controlled trials evaluating the extraperitoneal versus the transperitoneal approach have demonstrated similar results. Level I evidence on the Retzius-sparing approach demonstrated earlier return to continence than the traditional anterior approach. The question whether

Retzius-sparing RARP is associated with a higher rate of positive surgical margins is still open due to the intrinsic bias in terms of surgical expertise in the available comparative studies. This technique also offers an advantage in patients who have received kidney transplantation. Retrospective evidence suggests that the more the anatomical dissection (eg., more periprostatic tissue is preserved), the better the functional outcome in terms of continence. Yet, two randomized controlled trials evaluating the different techniques of dissection have so far been produced. Partial prostatectomies should not be offered outside clinical trials. CONCLUSIONS: Several techniques and approaches are available for prostate dissection during RARP. While the Retzius-sparing approach seems to provide earlier return to continence than the traditional anterior transperitoneal approach, no technique has been proved to be superior to other(s) in terms of long-term outcomes in randomized studies. PATIENT SUMMARY: We have summarized available approaches for the surgical treatment of prostate cancer. Specifically, we described the different techniques that can be adopted for the surgical removal of the prostate using robotic technology.

Urology

Perkins SQ, Dabaja A, and Atiemo H. Best Approaches to Evaluation and Feedback in Post-Graduate Medical Education. *Curr Urol Rep* 2020; 21(10):36. PMID: 32789759. [Full Text](#)

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PURPOSE OF REVIEW: The objectives of this literature review are to appraise current approaches and assess new technologies that have been utilized for evaluation and feedback of residents, with focus on surgical trainees.

RECENT FINDINGS: In 1999, the Accreditation Council for Graduate Medical Education introduced the Milestone system as a tool for summative evaluation. The organization allows individual program autonomy on how evaluation and feedback are performed. In the past, questionnaire evaluations and informal verbal feedback were employed. However, with the advent of technology, they have taken a different shape in the form of crowdsourcing, mobile platforms, and simulation. Limited data is available on new methods but studies show promise citing low cost and positive impact on resident education. No one "best approach" exists for evaluation and feedback. However, it is apparent that a multimodal approach that is based on the ACGME Milestones can be effective and aid in guiding programs.

Conference Abstracts

Cardiology/Cardiovascular Research

Abdelrahim E, Fuller B, Coriasso N, Alalwan Y, Hughes C, Aljamal A, Wang D, Pantelic M, Song T, Eng M, Frisoli T, Villablanca P, Wyman J, O'Neill W, and Lee J. Utility Of Standardized Pre-CTA Hydration Protocol On Patients Referred For Transcatheter Aortic Valve Replacement. *Journal of Cardiovascular Computed Tomography* 2020; 14(3):S37.

Introduction: ECG-gate computed tomography angiography (CTA) is the standard technique for pre-procedural planning prior to transcatheter aortic valve replacement (TAVR). CTA requires use of potentially nephrotoxic iodinated contrast, limiting use in patients with renal dysfunction. We evaluated the utility of a tiered hydration protocol in patients with renal dysfunction referred for TAVR. Methods: 258 patients (52.7% male, age 79 ± 8 years) who underwent TAVR between 1/1/18 and 12/30/18 were retrospectively evaluated. Pre-procedural CTA was performed per institutional protocols with weight based contrast dosing. Patients requiring hemodialysis prior to CTA were excluded. Patients with GFR <22 ml/min did not receive CTA. Patients with GFR 22 - 40 ml/min underwent hydration protocol guidelines: Outpatients received normal saline (NS) at ≤ 3 mL/kg over one hour pre-procedure/test and 1 to 1.5 mL/kg/hour during and up to six hours post-procedure/test. Inpatients received normal saline for 1 mL/kg/hour for 6 to 12 hours pre-procedure/test, intra-procedure, and up to 12 hours post-procedure. Results: Total baseline creatinine was 1.08 ± 0.41 ng/dL. Hydration protocol patient creatinine levels were 1.67 ± 0.41 ng/dL. Upper quartile of creatinine was 1.91 ng/dL (range 0.79 - 2.65 ng/dL). Average CTA contrast dose was 100 ± 23 mL. 43 (17%) of patients received pre-CTA hydration protocol. Hydration protocol NS total infusion volumes were 490 ± 119 mL (range 40-100ml). Duration between CT and TAVR was 86 ± 155 days. Pre-TAVR creatinine was 1.09 ± 0.39 , creatinine at discharge was 1.06 ± 0.73 . 3 patients (1%) had ≥ 1 increase in CKD grade at discharge. No patients required dialysis prior to discharge or within 1 month of TAVR. No complications from hydration protocol were identified. Conclusions: Utilization of a routine pre-TAVR CT hydration protocol in patients at risk for contrast induced nephropathy is feasible and associated with no new renal dysfunction prior to TAVR, and low rates of new renal dysfunction post TAVR. In TAVR patients hydration carries risks and further study is needed to identify whether a more conservative hydration protocol can be utilized.

Cardiology/Cardiovascular Research

Alalwan Y, Coriasso N, Aljamal A, Hughes CL, Abdelrahim E, Dee Wang D, Pantelic M, Song T, Eng MH, Frisoli T, Villablanca P, Wyman JF, O'Neill WW, and Lee J. Targeted exclusion of proximal obstructive coronary disease on coronary computed tomography angiography for deferral of routine invasive coronary angiography prior to transcatheter aortic valve replacement. *Catheterization and Cardiovascular Interventions* 2020; 95:S115.

Background: Aortic stenosis is associated with coronary artery disease (CAD) and routine invasive coronary angiography (ICA) is performed prior to transcatheter aortic valve replacement (TAVR). Evaluation of CAD on computed tomography angiography (CTA) is limited due to coronary calcification, cardiac motion and absence of sublingual nitroglycerin but may be feasible for the exclusion of only proximal CAD. Methods: 339 patients (52% male, age 79 ± 27) who underwent TAVR between 5/1/18 and 12/20/18 were retrospectively studied. Routine pre-procedure ECG-gated CTA was performed with reconstruction phases in 10% increments. CTA evaluation of proximal CAD performed clinically on request from multidisciplinary heart team. CAD analysis performed on 3D workstations by experienced cardiologists and radiologists. Stenosis grades: 0=normal, 1=1-25%, 2=26-50%, 3=51-70%, 4=71-99%, 5=occluded, 8=absent, 9=uninterpretable. Results: Of 339 patients, 62 (18%) patients had CTA coronary analysis of which 49 (14%) also had ICA before or at time of TAVR. Of these patients, 21 (43%) patients had no stenosis more than 50% on CTA, and of those 21 patients, 19 (91%) also had no stenosis more than 50% on ICA. 28 patients who had both ICA and CTA had ≥50% stenosis in at least one coronary artery on CTA. Of these, 22 (79%) also had ≥50% stenosis on ICA. When excluding those with coronary artery bypass grafts (12 patients), 63% of patients had ≥50% stenosis on both CTA and ICA. 13 patients had CTA without follow up ICA. Overall including all patients with no CAD on ICA and those who were deferred ICA based on CTA results, 32 (52%) patients avoided or could have avoided ICA, leading to a total theoretical cost saving of \$155,000-310,000. No patients had acute coronary syndrome (ACS) at the time of discharge post TAVR. Conclusions: Exclusion of proximal obstructive CAD on routine pre-TAVR CTA is feasible and can decrease utilization of ICA with no increase in ACS at the time discharge post TAVR implantation. This strategy can decrease invasive procedures and potentially reduce cost. Further study is needed on longitudinal outcomes with this strategy.

Cardiology/Cardiovascular Research

Coriasso N, Alalwan Y, Aljamal A, Hughes C, Abdelrahim E, Pantelic M, Song T, Eng M, Frisoli T, Villablanca P, Wyman J, O'Neill W, Wang D, and Lee J. "Transcaval First" Alternative Access Strategy For Transcatheter Aortic Valve Replacement Guided By Computed Tomography Angiography. *Journal of Cardiovascular Computed Tomography* 2020; 14(3):S94.

Introduction: Patients with small caliber or otherwise hostile iliofemoral vasculature are at high risk for vascular injury when undergoing transcatheter aortic valve replacement (TAVR). Computed tomography angiography (CTA) guides alternative access feasibility including techniques such as transcaval access. Methods: 339 patients (51.6% male, 87.0% white, age 79 ± 1 years) who underwent TAVR at an urban tertiary care facility between 1/2/18 and 12/20/18 were retrospectively studied. Pre-procedure CTA of major vasculature was performed per institutional protocol. Femoral arteries with minimal luminal diameter (MLD) ≤5.5 mm triggered alternative access planning for transcaval, transcarotid, transaxillary, and transseptal anterograde routes. Decision for alternative access was made by a multidisciplinary heart team consensus utilizing a "transcaval first" strategy. Results: Of 339 patients, alternative access was used in 72 (21.2%) of patients with outcomes similar to transfemoral. Strategies were transcaval in 58 (17.1%), transcarotid in 10 (2.9%), transaxillary in 3 (0.9%), and transseptal anterograde in 1 (0.3%). Bilateral femoral arteries ≤5.5 mm were present in 25 (7.4%) of patients. Conclusions: CTA planning identifies patients who may benefit from transcaval access as a first line alternative access strategy.

Cardiology/Cardiovascular Research

Hughes CL, Lee J, Coriasso N, Alalwan Y, Aljamal A, Wang DD, Pantelic M, Song T, Eng MH, Frisoli T, Villablanca P, Wyman JF, O'Neill WW, and Abdelrahim E. Utility of ECG-gated computed tomography angiography for the improved diagnosis of bicuspid aortic valve disease prior to transcatheter aortic valve replacement. *Catheterization and Cardiovascular Interventions* 2020; 95:S118-S119.

Background: Diagnosis of a bicuspid aortic valve (BAV) morphology has important prognostic implications due to early valve degeneration and an associated aortopathy. Presence of a BAV also has technical implications for transcatheter aortic valve replacement (TAVR) procedural planning and implantation. BAV is often first identified on transthoracic echocardiography (TTE), but diagnosis may be limited by imaging windows, operator skill, and valve calcification. ECG-gated computed tomography angiography (CTA) may improve identification of BAV. Methods: 335 patients who underwent TAVR between 5/1/18 and 12/20/18 were retrospectively evaluated. Routine pre-procedure planning retrospectively ECG-gated CTA studies were performed with reconstruction phases at 10% increments through the R-R cycle. 50% or greater commissural fusion was categorized as a BAV. Valve morphology from the preprocedural TTE reports was also abstracted. Of 335 patients, 17 patients had prosthetic valves. Of the remaining 318 patients, 267 (52.4% male, age 79 ± 27) had TTE grading of aortic valve morphology. Results: BAV was

identified by TTE in 23 patients (8.6% of cohort, age 75 ± 20 years) whereas CTA identified 26 patients (9.7% of cohort, age 74 ± 21 years) with a bicuspid valve. Direct correlation between CTA and TTE was modest (R-value = 0.38). With CTA as the reference standard, TTE had a sensitivity, specificity, positive predictive value and negative predictive value of 88.5%, 100%, 100% and 98.8% respectively. The age of patients with tricuspid vs BAV was 80 ± 28 years vs 74 ± 21 years, respectively. Aortic size in tricuspid vs BAV patients was 34.2 ± 15 vs 37.9 ± 30 mm ($p=0.001$). In BAV patients, 82% of the patients had no aortic dilation greater than 40mm. Conclusions: In patients referred for TAVR, CTA is valuable tool for diagnosis of BAV and associated aortopathies, particularly when valve morphology cannot be characterized by TTE. In our cohort, BAV patients were older and rarely had significant aortopathy, suggesting an increased prevalence of degenerative valve fusion relative to congenital BAV disease. Further study is required to categorize and distinguish BAV sub-types and their effect on TAVR procedure results.

Cardiology/Cardiovascular Research

Isseh IN, Dagher C, Sharma S, Basir MB, and Parikh S. Escalation of temporary mechanical circulatory support in the setting of deteriorating cardiogenic shock. *Catheterization and Cardiovascular Interventions* 2020; 95:S178.

Background: Cardiogenic shock (CS) is a deadly condition and mechanical circulatory support (MCS) is frequently utilized. We evaluated the characteristics of CS patients who required escalation of MCS due to deteriorating shock. Methods: From 07/2016-07/2018 we identified consecutive CS patients with deteriorating shock requiring escalation of MCS. Deteriorating shock was defined as worsening hypotension, escalating doses of vasopressors or worsening end-organ hypoperfusion. MCS escalation was defined as adding or exchanging a MCS device to existing MCS. All statistical tests were performed with a two-sided P value=.05. Results: 81 CS patients ($61 \pm 14.2y$, 73% men) had deteriorating shock requiring MCS escalation. 23% presented with acute myocardial infarction, 72% with decompensated heart failure (non-ischemic cardiomyopathy 26% and ischemic cardiomyopathy 46%) and 5% undifferentiated. Distribution of CS per SCAI classification was stage C 7%, D 82% and E 11%. Survival to discharge was 32%. Survivors were younger (55 vs $65y$, $P=0.002$) and had lower BMI (29 vs 34 , $P=0.031$). Initial MCS was IABP ($n=32$), Impella 2.5 ($=4$), CP ($=32$), 5.0 ($=2$), TandemHeart ($=3$), ProtekDuo ($=3$), VVECMO ($=2$), VAECMO ($=2$) and ProtekDuo+Impella CP ($=1$). Patients were escalated to Impella 2.5 ($n=1$), CP ($=16$), 5.0 ($=10$), TandemHeart ($=6$), VAECMO ($=8$), VAECMO+(IABP, 2.5 or CP) ($=20$), ProtekDuo+(IABP, CP, 5.0 or TandemHeart) ($=13$), Impella CP+RP ($=2$), TandemHeart+Impella RP ($=1$), central VAECMO ($=3$) and LVAD ($=1$). Lactate levels pre and post escalation were lower in survivors compared to non-survivors (3.3 vs 6.9 , $P=0.02$) and (2 vs 4.4 , $P=0.01$). Non-survivor lactate levels did not significantly improve post escalation (6.9 vs 4.4 , $P=0.06$) and mean arterial pressure decreased (77.1 vs 66.8 , $P=0.002$) despite significant improvement in cardiac index (1.9 vs 3.4 , $P<0.001$) and cardiac power output (0.6 vs 1.1 , $P=0.0001$). Utilization of a PA catheter pre-escalation was associated with improved survival (40% vs 18% , $P=0.04$). Conclusions: CS patients requiring escalation of MCS due to deteriorating shock have low hospital survival (32%). Younger age, lower BMI, lower lactate levels and utilization of PA catheter pre-escalation were associated with increased survival.

Cardiology/Cardiovascular Research

Nikolakopoulos I, **Alaswad K**, Karpaliotis D, Krestyaninov O, Khelinskii D, Khatri J, Doing A, Dattilo P, Sheikh AM, Toma C, Patel T, Jefferson B, Jaffer FA, Chandwaney RH, Samady H, Jaber W, Shah AR, Vemmou E, Xenogiannis I, Rangan BV, Garcia S, Abdullah S, Banerjee S, Burke MN, and Brilakis ES. Follow-up outcomes after chronic total occlusion percutaneous coronary intervention according to target vessel: Insights from the PROGRESS-CTO Registry. *Catheterization and Cardiovascular Interventions* 2020; 95:S53-S54.

Background: Outcomes of Chronic Total Occlusion Percutaneous Coronary Intervention (CTO PCI) according to target vessel have received limited study. Methods: We compared clinical, angiographic, procedural characteristics and outcomes of 1,568 right coronary artery (RCA), left anterior descending artery (LAD) and Left Circumflex (LCX) CTO PCIs with follow-up outcomes available. Results: Mid RCA was the most common target vessel (Figure 1). The J-CTO score was $2 [1,3]$ vs $3 [2,4]$ vs $3 [2,4]$, $p<0.0001$ (LAD vs LCX vs RCA respectively). Technical success was lower in RCA (89% vs 85% vs 84% , $p=0.05$). In-hospital MACE did not differ significantly (2.7% vs 4.8% vs 2.9% , $p=0.3$). LCX CTO had higher incidence of the composite of death, myocardial infarction (MI) and revascularization rates at 1 year (Figure 2) (plog-rank=0.05). Conclusions: LCX lesions are associated with the worst and RCA lesions with the best 1-year outcomes, while LAD CTOs are the least complex. (Figure Presented) .

Cardiology/Cardiovascular Research

Nikolakopoulos I, Krestyaninov O, Khelinskii D, Khatri J, **Alaswad K**, Doing A, Dattilo P, Sheikh AM, Yeh RW, Patel T, Jefferson B, Jaffer FA, Uretsky BF, Love M, Elbarouni B, Koutouzis M, Tsiafoutis I, Choi JW, Vemmou E, Xenogiannis I, Rangan BV, Garcia S, Abdullah S, Banerjee S, Burke MN, and Brilakis ES. In-hospital and follow-up outcomes after chronic total occlusion percutaneous coronary intervention according to left ventricular ejection fraction: Insights from the PROGRESS-CTO Registry. *Catheterization and Cardiovascular Interventions* 2020; 95:S52-S53.

Background: Outcomes of chronic total occlusion percutaneous coronary intervention (CTO PCI) according to baseline left ventricular ejection fraction (LVEF) have received limited study. Methods: We compared clinical, angiographic, procedural characteristics and outcomes of 1,441 CTO PCIs performed in patients with known ejection fraction and available follow-up. We compared patients with LVEF $\geq 50\%$ (N=834), LVEF 35%-49% (N=434) and LVEF $< 35\%$ (N=173). Results: Left anterior descending CTO was significantly more common in the low LVEF group (24% vs 25% vs 42%, $p < 0.001$). The J-CTO score was similar (2.4 ± 1.3 vs 2.5 ± 1.2 vs 2.4 ± 1.2 , $p = 0.5$), as was procedural success (85% vs 83% vs 88%, $p = 0.5$) with the incidence of in-hospital major adverse cardiovascular events being numerically but not statistically higher in the LVEF $< 35\%$ group (2% vs 3.5% vs. 4.6%, $p = 0.12$). The composite endpoint of death, myocardial infarction (MI) and revascularization at 1 year was more common in the LVEF $< 35\%$ group (13% vs 17% vs 25%, $p\text{-log-rank} = 0.001$) (Figure). There was a significant difference in 1-year mortality (12.8% vs 16.8% vs 24.6%, $p < 0.001$), but not in MI (1.9% vs 4.4% vs 5.6%, $p = 0.07$) and revascularization rates (7.4% vs 8.9% vs 10.7%, $p = 0.8$). Conclusions: CTO PCI can be performed with high success rates and acceptable in-hospital complication rates irrespectively of LVEF, but patients with LVEF $< 35\%$ have worse one-year outcomes. (Figure Presented) .

Cardiology/Cardiovascular Research

Nona P, Dhillon D, Mawri S, Cowger J, Alaswad K, Khandelwal AK, O'Neill WW, and Basir MB. Inter-hospital transfers in acute myocardial infarction and cardiogenic shock. *Catheterization and Cardiovascular Interventions* 2020; 95:S180.

Background: Limited data exist on the use of "hub and spoke" models to transfer patients who present in cardiogenic shock. We sought to assess outcomes of patients transferred to our shock center within our network to those who presents from institutions out of our network. Methods: From January 2014 to June 2017, 110 patients transferred to our shock center with an admission diagnosis of acute myocardial infarction and cardiogenic shock (AMICS) based on ICD coding. Demographics, admission, procedural and clinical outcomes were obtained for all patients and compared. Statistical analysis was performed using two-sample t-tests, Wilcoxon rank sum tests, chi-square tests and Fisher exact tests. Results: 35 patients were transferred within our network and 75 patients presented out of our network. The average age of the cohort was 66.4 years. In-network patients were less likely to present with in-hospital cardiac arrest (12.1% vs. 35.7%, $p=0.013$). In-network patients presented with lower cardiac output (CO) (3.2 L/m \pm 0.7 vs 4.5 L/m \pm 1.0; $p=0.019$) but were less likely to be on vasopressors (42.3% vs 72.2%, $p=0.018$) upon transfer. Similarly, in-network patients had a lower cardiac output following initiation of mechanical circulatory support (3.9 L/m \pm 0.9 vs. 5.7 L/m \pm 2.3, $p=0.010$), but higher SBP after initiation of MCS (124.7 mmHg \pm 28.2 vs. 105.5 mmHg \pm 25.2, $p=0.006$). Overall, in-network patients had shorter delays from AMI onset to MCS when compared to out of network patients. In-network patients had improved survival to hospital discharge (62.9% vs 41.3%, $p=0.035$). Conclusions: Patients who presented to our shock center from an in-network hospital had improved survival to hospital discharge when compared to patients who presented from outside our network. Further system based processes are needed to best optimize care of patients transferred with acute myocardial and cardiogenic shock.

Cardiology/Cardiovascular Research

O'Neill WW, Moses JW, and Popma JJ. Outcomes of impella use as prophylactic versus bailout strategy in patients undergoing non-emergent percutaneous coronary intervention. *Catheterization and Cardiovascular Interventions* 2020; 95:S54-S55.

Background: Prophylactic support with Impella in hemodynamically stable patients undergoing non-emergent percutaneous coronary intervention (PCI), also termed Impella protected PCI, is now a well-established indication in a selective patient population at high risk for hemodynamic collapse during PCI. However some physicians may eschew preventive hemodynamic support and prefer a bailout strategy should hemodynamic collapse occur. Methods: We aimed to compare the outcomes of patients entered in the cVAD prospective study who underwent Impella protected PCI (ProPCI group) with those who received bailout Impella support for cardiogenic shock onset during non-emergent PCI (Bailout group). A total of 1,028 patients supported with Impella 2.5 (34.9%) or Impella CP (65.0%) meeting the study inclusion criteria were entered into the cVAD database as of July 2019 (971 in ProPCI group and 40 in Bailout group). An additional 17 were identified in the USpella registry for a total of 57 Bailout patients. In this group the procedural complication leading to hemodynamic collapse was refractory hypotension in 37 (64.9%) patients and coronary perforation/dissection in 20 (35.1%). Results: Females were more prevalent in the Bailout group (50.9% vs. 27.2%, $p = 0.0002$) and the median baseline LVEF was significantly higher (40% vs 30%, $p < 0.0001$). In this group heart failure was less prevalent (42.1% vs 56.9%, $p = 0.04$) as was left main disease (40.0% vs 56.1%, $p = 0.025$). In-hospital mortality was significantly higher in the Bailout group (41.9% vs. 4.3%, $p < 0.0001$) and was similar across patients experiencing hemodynamic collapse secondary to refractory hypotension or coronary perforation/dissection (48.7% vs. 50.0%, $p = 0.99$). Though females were disproportionately more likely to require bailout support, female in-hospital mortality was excessively high but not significantly higher compared to male (55.2% vs 42.9%, $p = 0.43$). Conclusions: Failure to prospectively identify and prophylactically implement hemodynamic support in patients at high risk for hemodynamic collapse during non-emergent PCI leads to excessive

in-hospital mortality. This failure to identify patients who would benefit from prophylactic support appears to be more prevalent in women.

Cardiology/Cardiovascular Research

Qi Z, Wang D, Lee J, Song T, Pantelic M, Keimig T, Nadig J, Reeser N, Zemke D, Seger N, and Bevins N. Prediction Of Contrast Enhancement In Left Atrial Appendage (LAA) CT Through A Numerical Modeling Approach. *Journal of Cardiovascular Computed Tomography* 2020; 14(3):S36-S37.

Introduction: Optimization of contrast protocol is crucial in LAA CT for the diagnosis of LAA thrombus; it ideally requires not only adequate LAA opacification, but also sufficient difference in opacification when a delayed phase is included to aid the diagnosis. Prediction of contrast enhancement with reasonable accuracy prior to the study may allow for patient specific adjustment of contrast protocol for improved outcome. Methods: The proposed approach adopts a previously published model of the cardiovascular system with modifications made to include LAA. In this model, the cardiovascular system consisting of the heart, the vessels and various organs is simplified as a large group of interconnected compartments; the transfer of the iodinated contrast medium among different compartment is governed by a large group of differential equations. A patient's clinical information, including age, gender, height and weight, are used to derive patient specific factors to adjust both the blood volume and the blood flow in the model. The iodine concentration of LAA at any time point is determined by solving the group of differential equations included in the model, and then the resulting HU enhancement is predicted by incorporating the physics of the CT scan process. A total of 20 LAA CT studies performed at our institution are included for evaluation of the proposed approach; the CT protocol included both a peak phase and a delayed phase. For all studies, no evidence of LAA thrombus was found by the interpreting physician teams. The predicted HU enhancements at both phases using the proposed approach are compared against the actual HU enhancements measured from the CT datasets. Results: For the peak phase, the errors of the predicted HU enhancements, compared to the actual enhancements, have a mean value of -32 HU and a standard deviation of 32 HU. For the delayed phase, the errors of the predicted enhancements have a mean value of -31 HU and a standard deviation of 34 HU. In 75% of all comparisons, the deviation of the predicted enhancement from the actual enhancement is under 50 HU in magnitude. Conclusions: A numerical modeling approach is proposed to predict contrast enhancement of LAA CT with the input of both patient specific clinical information and the contrast injection protocol. The proposed approach has potential values in achieving image quality improvement in LAA CT through contrast protocol optimization

Cardiology/Cardiovascular Research

So CY, Kang G, Villablanca P, Lee J, Frisoli T, Wyman JF, Wang DD, O'Neill WW, and Eng MH. Procedural and mid-term outcomes of coronary protection: Insight from a single-center retrospective analysis. *Catheterization and Cardiovascular Interventions* 2020; 95:S222-S223.

Background: Coronary Obstruction is a rare but life-threatening complication of transcatheter aortic valve replacement (TAVR). Previous studies had shown coronary protection with guidewires and an undeployed coronary balloon or stent positioned in the coronary artery is helpful in the prompt diagnosis and treatment of coronary obstruction following TAVR. However, longer term data was limited. Methods: We retrospectively analyzed the institutional TAVR and TVT registry at Henry Ford Hospital from January 2015 to August 2019 and identified patients underwent coronary protection before TAVR. Procedural efficacy (i.e. TAVR without coronary obstruction) and safety endpoints and intermediate-term outcomes including rate of target vessel re-intervention, myocardial infarction or stroke were studied. Results: During the study period, 25 (2.1%) patients underwent TAVR with coronary protection including 10 (40%) valve-in-valve procedures. The mean STS score was 7.2%. A total of 28 coronary arteries were protected, with coronary heights of 9.0+/-1.8mm and virtual valve-to-coronary distance of 4+/-0.9mm. Procedural efficacy endpoint was met in 24/25 (96%) patients. A total of 13/28 (46.4%) coronaries were "chimney"-stented using 9 drug-eluting stents, 3 baremetal stents and 1 biliary stent. Procedure-related complications included 1 stent balloon entrapment requiring subsequent snaring and 1 distal stent edge dissection requiring additional stent implantation. After a mean follow-up period of 16.3 months, there was no target vessel re-intervention, myocardial infarction or stroke. Conclusions: Our study showed promising mid-term coronary patency in low coronary height patients undergone TAVR with coronary protection. However, feasibility of repeat coronary intervention in target vessel remains uncertain.

Cardiology/Cardiovascular Research

Suarez DFH, Kim G, **Villablanca P**, Wiley JM, and Roche-Lima A. Machine learning-based in-hospital mortality prediction for transcatheter mitral valve repair in The United States. *Catheterization and Cardiovascular Interventions* 2020; 95:S68.

Background: Transcatheter mitral valve repair (TMVr) utilization has increased significantly in the United States over the last years. Yet, a risk prediction tool for adverse events has not been developed. We aimed to generate a machine learning-based algorithm to predict in-hospital mortality after TMVr. Methods: Patients who underwent TMVr

between 2012 and 2015 were identified using the national inpatient sample (NIS) database. The study population was randomly divided into a training set (n=636) and a testing set (n=213). Prediction models for in-hospital mortality were obtained using five supervised machine learning classifiers. Results: A total of 849 TMVr were analyzed in our study. The overall in-hospital mortality was 3.1%. A naive Bayes (NB) model had the best discrimination for fifteen variables with an Area Under the Curve of 0.83 (95% CI, 0.80-0.87) compared to 0.77 for logistic regression (95% CI, 0.58-0.95), 0.73 for artificial neural network (95% CI, 0.55-0.91) and 0.67 for both random forest and support vector machine (95% CI, 0.47-0.87). However, both random forest and logistic regression models obtained for ten variables were as good as the best NB model with an AUC=0.82 (95% CI, 0.79-0.86, p=0.34). History of coronary artery disease, renal failure and smoking were the three most significant predictors of in-hospital mortality. Conclusions: We developed a robust machine learning-derived model to predict in-hospital mortality in patients undergoing TMVr. While the best model was obtained by NB, conventional logistic regression generated an alternative model with a comparable performance.

Cardiology/Cardiovascular Research

Vemmou E, **Alaswad K**, Karpaliotis D, Khatri J, Doing A, Dattilo P, Uretsky BF, Elbarouni B, Love M, Sheikh AM, Jaber W, Samady H, Jefferson B, Patel TN, Patel MP, Mahmud E, Yeh RW, Tamez H, Jaffer FA, ElGuindy A, Choi JW, Rafeh NA, Maallouf A, Jaoudeh FA, Xenogiannis I, Nikolakopoulos I, Rangan BV, Omer MA, Megaly MS, Gkargkoulas F, Moses JW, Lembo NJ, Kirtane AJ, Parikh MA, Ali ZA, Toma C, Krestyaninov O, Khelimskii D, Banerjee S, Abdullah S, Garcia S, Burke MN, and Brilakis ES. Radiation dose during CTO-PCI: Insights from the PROGRESS-CTO registry. *Catheterization and Cardiovascular Interventions* 2020; 95:S57-S59.

Background: Chronic total occlusion (CTO) percutaneous coronary intervention (PCI) can be associated with increased risk of excessive radiation. Methods: We examined radiation dose in 5,635 patients undergoing CTO-PCI at 28 US and international centers between 2012 and 2019. We compared the group of patients that had fluoroscopy air kerma (AK) radiation dose above the median (>2.4 Gy) and those who had AK radiation dose below the median (\leq 2.4 Gy). Results: Mean age was 64.5 \pm 10 years and 83% of patients were men. Median AK radiation dose was 2.4 [1.3-4.1] Gy. The proportion of procedures that had AK dose >2.4 Gy decreased over time (Figure, Panel A). Median AK radiation dose was significantly lower in 2019 vs. 2012 (1.9 [1.1, 3.2] vs. 4.4 [2.5, 6.2] Gray, p<0.0001) (Figure, Panel B). Median body mass index was higher in the higher radiation group (31.4 [27.9, 35.8] vs 28.4 [25.5, 32.3], p<0.0001). Patients in the higher radiation dose group were more likely to have previous coronary artery bypass graft surgery compared with patients in the lower radiation group (41% vs. 28%, p<0.0001). Median J-CTO score (3 [2,4] vs. 2 [1, 3], p<0.0001) and median procedure time (167 [119,223] vs. 104 [72,143] min, p<0.0001) were higher in the higher radiation group. Technical and procedural success were lower in the higher radiation group (84% vs. 91%, 82% vs. 90%, respectively, p<0.0001) and the incidence of in-hospital major adverse cardiovascular events was higher (3.3% vs. 1.7%, p=0.0025). There was no reported radiation skin injury. Conclusions: AK radiation dose during CTO-PCI has significantly decreased in recent years among high-volume, experienced centers.

Cardiology/Cardiovascular Research

Vemmou E, **Alaswad K**, Karpaliotis D, Krestyaninov O, Khelimskii D, Choi JW, Khatri J, Jaffer FA, Patel MP, Mahmud E, Doing A, Dattilo P, Koutouzis M, Tsiafoutis I, Uretsky BF, Toma C, Elbarouni B, Love M, Jaber W, Samady H, Jefferson B, Patel TN, Sheikh AM, Yeh RW, Tamez H, ElGuindy A, Rafeh NA, Maallouf A, Jaoudeh FA, Xenogiannis I, Nikolakopoulos I, Rangan BV, Omer MA, Megaly MS, Gkargkoulas F, Moses JW, Lembo NJ, Kirtane AJ, Parikh MA, Ali ZA, Banerjee S, Abdullah S, Garcia S, Burke MN, and Brilakis ES. Contrast utilization patterns during CTO-PCI: Insights from the PROGRESS-CTO registry. *Catheterization and Cardiovascular Interventions* 2020; 95:S56-S57.

Background: Chronic total occlusion (CTO) percutaneous coronary intervention (PCI) may require large contrast volume. Methods: We examined contrast utilization in 5,440 patients undergoing CTO PCI at 30 US and international centers between 2012 and 2019. We compared the group of patients that had contrast volume above vs. below the median (240 mL). Results: Mean age was 64.5 \pm 10 years, 83% of patients were men and 42% had diabetes mellitus. Median pre-procedural creatinine was 1.01 [0.76-1.2] mg/dL and 2% of patients were on dialysis. Median contrast volume was 240 [170,320] mL and decreased over time (Figure). Patients with high contrast volume were more likely to have undergone ad-hoc CTO-PCI (13.2% vs. 8.9%, p<0.0001) and had higher median J-CTO score (3 [2,3] vs. 2 [1, 3], p<0.0001). The higher contrast volume group had higher use of retrograde crossing strategy (43% vs. 27%, p<0.0001), lower procedural and technical success (82% vs. 88% and 84% vs 89%, respectively, p<0.0001), higher incidence of in-hospital major adverse events (3% vs. 1.5%, p=0.0001), and longer procedure time (139 [98,201] vs. 96 [62,148] min, p<0.0001). The use of intravascular ultrasound was associated with lower contrast volume (57% vs 43%, p<0.0001). Conclusions: Contrast volume used during CTO-PCI has been decreasing over the years. Higher lesion complexity, procedural failure, and the occurrence of complications are associated with higher contrast volume.

Cardiology/Cardiovascular Research

Vishwanath R, Iordanou J, Singh V, **Gorgis S, Papukhyan H, Hana A, and Ananthasubramaniam K.** Defining The Incidence And Patient Profile Of Incidental Coronary Artery Calcification On Non-cardiac Computed Tomography: An Opportunity To Identify Subclinical Coronary Atherosclerosis. *Journal of Cardiovascular Computed Tomography* 2020; 14(3):S54.

Introduction: Coronary artery calcification (CAC) is an independent predictor of cardiac events. The increased use of thoracic Computed Tomography (CT) has made coronary calcification a common incidental finding, although the frequency remains unknown. We aimed to identify the incidence of CAC found on routine non-ECG gated CT scans, and risk factors associated with these findings. Methods: A systematic review was conducted through literature search using predetermined search criteria. Applicable studies were screened by 3 investigators for eligibility. Data regarding indication for CT imaging, incidence of CAC, and cardiovascular risk factors was collected. Results: A total of 3,850 study subjects were included for review. CAC was found in 1,231 patients, with an incidence rate of 32%. Indications for CT imaging were; 33% lung cancer screening, 16% for intrapulmonary pathology, 13% for pulmonary thromboembolism, 33% for miscellaneous reasons. In patients with CAC, the average age was 59.4 years old, and 77.9% were male. Hypertension was present in 45.5% of patients, diabetes mellitus was recorded in 25%, and smoking was found in 41.5% of patients. Conclusions: In this systematic review of 6 studies, incidental CAC on non-ECG gated CT scans was found in 32% of patients. The majority of these patients were identified to have major risk factors for coronary artery disease. Incidental CAC should be routinely reported on non-ECG gated CT scans, as it presents opportunity for detecting subclinical atherosclerosis which can impact patient counselling and medical management.

Diagnostic Radiology

Abdelrahim E, Fuller B, Coriasso N, Alalwan Y, Hughes C, Aljamal A, Wang D, Pantelic M, Song T, Eng M, Frisoli T, Villablanca P, Wyman J, O'Neill W, and Lee J. Utility Of Standardized Pre-CTA Hydration Protocol On Patients Referred For Transcatheter Aortic Valve Replacement. *Journal of Cardiovascular Computed Tomography* 2020; 14(3):S37.

Introduction: ECG-gate computed tomography angiography (CTA) is the standard technique for pre-procedural planning prior to transcatheter aortic valve replacement (TAVR). CTA requires use of potentially nephrotoxic iodinated contrast, limiting use in patients with renal dysfunction. We evaluated the utility of a tiered hydration protocol in patients with renal dysfunction referred for TAVR. Methods: 258 patients (52.7% male, age 79 ± 8 years) who underwent TAVR between 1/1/18 and 12/30/18 were retrospectively evaluated. Pre-procedural CTA was performed per institutional protocols with weight based contrast dosing. Patients requiring hemodialysis prior to CTA were excluded. Patients with GFR <22ml/min did not receive CTA. Patients with GFR 22 - 40 ml/min underwent hydration protocol guidelines: Outpatients received normal saline (NS) at ≤3 mL/kg over one hour pre-procedure/test and 1 to 1.5 mL/kg/hour during and up to six hours post-procedure/test. Inpatients received normal saline for 1 mL/kg/hour for 6 to 12 hours pre-procedure/test, intra-procedure, and up to 12 hours post-procedure. Results: Total baseline creatinine was 1.08 ± 0.41 ng/dL. Hydration protocol patient creatinine levels were 1.67 ± 0.41 ng/dL. Upper quartile of creatinine was 1.91 ng/dL (range 0.79 - 2.65 ng/dL). Average CTA contrast dose was 100 ± 23 mL. 43 (17%) of patients received pre-CTA hydration protocol. Hydration protocol NS total infusion volumes were 490 ± 119 mL (range 40-100ml). Duration between CT and TAVR was 86 ± 155 days. Pre-TAVR creatinine was 1.09 ± 0.39, creatinine at discharge was 1.06 ± 0.73. 3 patients (1%) had ≥1 increase in CKD grade at discharge. No patients required dialysis prior to discharge or within 1 month of TAVR. No complications from hydration protocol were identified. Conclusions: Utilization of a routine pre-TAVR CT hydration protocol in patients at risk for contrast induced nephropathy is feasible and associated with no new renal dysfunction prior to TAVR, and low rates of new renal dysfunction post TAVR. In TAVR patients hydration carries risks and further study is needed to identify whether a more conservative hydration protocol can be utilized.

Diagnostic Radiology

Alalwan Y, Coriasso N, Aljamal A, Hughes CL, Abdelrahim E, Dee Wang D, Pantelic M, Song T, Eng MH, Frisoli T, Villablanca P, Wyman JF, O'Neill WW, and Lee J. Targeted exclusion of proximal obstructive coronary disease on coronary computed tomography angiography for deferral of routine invasive coronary angiography prior to transcatheter aortic valve replacement. *Catheterization and Cardiovascular Interventions* 2020; 95:S115.

Background: Aortic stenosis is associated with coronary artery disease (CAD) and routine invasive coronary angiography (ICA) is performed prior to transcatheter aortic valve replacement (TAVR). Evaluation of CAD on computed tomography angiography (CTA) is limited due to coronary calcification, cardiac motion and absence of sublingual nitroglycerin but may be feasible for the exclusion of only proximal CAD. Methods: 339 patients (52% male, age 79 ± 27) who underwent TAVR between 5/1/18 and 12/20/18 were retrospectively studied. Routine pre-procedure ECG-gated CTA was performed with reconstruction phases in 10% increments. CTA evaluation of proximal CAD performed clinically on request from multidisciplinary heart team. CAD analysis performed on 3D

workstations by experienced cardiologists and radiologists. Stenosis grades: 0=normal, 1=1-25%, 2=26-50%, 3=51-70%, 4=71-99%, 5=occluded, 8=absent, 9=uninterpretable. Results: Of 339 patients, 62 (18%) patients had CTA coronary analysis of which 49 (14%) also had ICA before or at time of TAVR. Of these patients, 21 (43%) patients had no stenosis more than 50% on CTA, and of those 21 patients, 19 (91%) also had no stenosis more than 50% on ICA. 28 patients who had both ICA and CTA had $\geq 50\%$ stenosis in at least one coronary artery on CTA. Of these, 22 (79%) also had $\geq 50\%$ stenosis on ICA. When excluding those with coronary artery bypass grafts (12 patients), 63% of patients had $\geq 50\%$ stenosis on both CTA and ICA. 13 patients had CTA without follow up ICA. Overall including all patients with no CAD on ICA and those who were deferred ICA based on CTA results, 32 (52%) patients avoided or could have avoided ICA, leading to a total theoretical cost saving of \$155,000-310,000. No patients had acute coronary syndrome (ACS) at the time of discharge post TAVR. Conclusions: Exclusion of proximal obstructive CAD on routine pre- TAVR CTA is feasible and can decrease utilization of ICA with no increase in ACS at the time discharge post TAVR implantation. This strategy can decrease invasive procedures and potentially reduce cost. Further study is needed on longitudinal outcomes with this strategy.

Diagnostic Radiology

Hughes CL, Lee J, Coriasso N, Alalwan Y, Aljamal A, Wang DD, Pantelic M, Song T, Eng MH, Frisoli T, Villablanca P, Wyman JF, O'Neill WW, and Abdelrahim E. Utility of ECG-gated computed tomography angiography for the improved diagnosis of bicuspid aortic valve disease prior to transcatheter aortic valve replacement. *Catheterization and Cardiovascular Interventions* 2020; 95:S118-S119.

Background: Diagnosis of a bicuspid aortic valve (BAV) morphology has important prognostic implications due to early valve degeneration and an associated aortopathy. Presence of a BAV also has technical implications for transcatheter aortic valve replacement (TAVR) procedural planning and implantation. BAV is often first identified on transthoracic echocardiography (TTE), but diagnosis may be limited by imaging windows, operator skill, and valve calcification. ECG-gated computed tomography angiography (CTA) may improve identification of BAV. Methods: 335 patients who underwent TAVR between 5/1/18 and 12/20/18 were retrospectively evaluated. Routine pre-procedure planning retrospectively ECG-gated CTA studies were performed with reconstruction phases at 10% increments through the R-R cycle. 50% or greater commissural fusion was categorized as a BAV. Valve morphology from the preprocedural TTE reports was also abstracted. Of 335 patients, 17 patients had prosthetic valves. Of the remaining 318 patients, 267 (52.4% male, age 79 ± 27) had TTE grading of aortic valve morphology. Results: BAV was identified by TTE in 23 patients (8.6% of cohort, age 75 ± 20 years) whereas CTA identified 26 patients (9.7% of cohort, age 74 ± 21 years) with a bicuspid valve. Direct correlation between CTA and TTE was modest (R-value = 0.38). With CTA as the reference standard, TTE had a sensitivity, specificity, positive predictive value and negative predictive value of 88.5%, 100%, 100% and 98.8% respectively. The age of patients with tricuspid vs BAV was 80 ± 28 years vs 74 ± 21 years, respectively. Aortic size in tricuspid vs BAV patients was 34.2 ± 15 vs 37.9 ± 30 mm ($p=0.001$). In BAV patients, 82% of the patients had no aortic dilation greater than 40mm. Conclusions: In patients referred for TAVR, CTA is valuable tool for diagnosis of BAV and associated aortopathies, particularly when valve morphology cannot be characterized by TTE. In our cohort, BAV patients were older and rarely had significant aortopathy, suggesting an increased prevalence of degenerative valve fusion relative to congenital BAV disease. Further study is required to categorize and distinguish BAV sub-types and their effect on TAVR procedure results.

Diagnostic Radiology

Qi Z, Wang D, Lee J, Song T, Pantelic M, Keimig T, Nadig J, Reeser N, Zemke D, Seger N, and Bevins N. Prediction Of Contrast Enhancement In Left Atrial Appendage (LAA) CT Through A Numerical Modeling Approach. *Journal of Cardiovascular Computed Tomography* 2020; 14(3):S36-S37.

Introduction: Optimization of contrast protocol is crucial in LAA CT for the diagnosis of LAA thrombus; it ideally requires not only adequate LAA opacification, but also sufficient difference in opacification when a delayed phase is included to aid the diagnosis. Prediction of contrast enhancement with reasonable accuracy prior to the study may allow for patient specific adjustment of contrast protocol for improved outcome. Methods: The proposed approach adopts a previously published model of the cardiovascular system with modifications made to include LAA. In this model, the cardiovascular system consisting of the heart, the vessels and various organs is simplified as a large group of interconnected compartments; the transfer of the iodinated contrast medium among different compartment is governed by a large group of differential equations. A patient's clinical information, including age, gender, height and weight, are used to derive patient specific factors to adjust both the blood volume and the blood flow in the model. The iodine concentration of LAA at any time point is determined by solving the group of differential equations included in the model, and then the resulting HU enhancement is predicted by incorporating the physics of the CT scan process. A total of 20 LAA CT studies performed at our institution are included for evaluation of the proposed approach; the CT protocol included both a peak phase and a delayed phase. For all studies, no evidence of LAA thrombus was found by the interpreting physician teams. The predicted HU enhancements at both phases using the proposed approach are compared against the actual HU enhancements measured from the CT datasets. Results: For the peak phase, the errors of the predicted HU enhancements, compared to the actual enhancements, have a

mean value of -32 HU and a standard deviation of 32 HU. For the delayed phase, the errors of the predicted enhancements have a mean value of -31 HU and a standard deviation of 34 HU. In 75% of all comparisons, the deviation of the predicted enhancement from the actual enhancement is under 50 HU in magnitude. Conclusions: A numerical modeling approach is proposed to predict contrast enhancement of LAA CT with the input of both patient specific clinical information and the contrast injection protocol. The proposed approach has potential values in achieving image quality improvement in LAA CT through contrast protocol optimization

Emergency Medicine

Jaehne AK, Gill JK, Foster DM, and Rivers EP. Revisiting the impact of endotoxin clearance on survival in the euphrates trial. *Shock* 2020; 53:46.

Introduction: Sepsis is a diverse disease. The EUPHRATES TRIAL conducted in a subset of septic shock patients with elevated endotoxin activity levels (EAA) at baseline greater than 0.6 Units were randomized to receive Polymyxin B Hemoperfusion (PMXBHP) or a SHAM treatment. PMXBHP targets the reduction of circulating endotoxin, thought to be a continued trigger for a dysregulated host response. PMXBHP may aid reduction in EAA levels and treatment responders may have improved survival rates. Methods: This is a post hoc analysis of the EUPHRATES trial focusing on dynamic changes in EAA levels examined at time points (Baseline, Day 1, Day 2, and Day 3). To evaluate changes between the time points the endotoxin clearance (EAAC) was calculated [EAAC = (EAA Time1- EAA Time2)/ EAA Time1]. Values < 0% indicate increasing EAA values, values > 0% indicate reduction in measured EAA values. Chi2 test was used to compare mortality between increasing versus decreasing EAA values. P values of 0.05 were considered significant. Results: The primary end-point analysis of EUPHRATES did not show a mortality benefit with PMXBHP for all patients enrolled or patients with a Multiple Organ Dysfunction Syndrome (MODS) score of > 9. By using an EAAC assessments approach dynamic EAA changes can be observed. Positive EAAC indicates a response to PMXBHP from day 2 to day 3 and has a positive impact on survival. There is a significant 12.1% difference in mortality between the PMXBHP responders and PMXBHP non-responders. (Table 1) Increasing EAA (negative EAAC) has higher mortality in the PMXBHP and the Sham treated patients. PMXBHP treated patients with positive EAAC from day 2 to 3 have a 9.3% lower 28-day mortality compared to SHAM patients with positive EAAC. This difference in mortality is however not statistical significant with a Chi2 of 2.64 and a p-value of 0.10. Conclusions: All EUPHRATES trial patients regardless of MODS score, who responded to treatment with PMXBHP with reduction in EAA levels from day 2 to day 3, have an impactful mortality reduction of 12.1% over the non-responders treated with PMXBHP. The observed mortality benefit between PMXBHP and SHAM group with positive EAAC did not reach statistical significance and may be based on the small subgroup size. Future research should focus on optimization of EAA dynamics and optimization of EAA clearance rates do aid resolution of the dysregulated host response.

Internal Medicine

Abdelrahim E, Fuller B, Coriasso N, Alalwan Y, Hughes C, Aljamal A, Wang D, Pantelic M, Song T, Eng M, Frisoli T, Villablanca P, Wyman J, O'Neill W, and Lee J. Utility Of Standardized Pre-CTA Hydration Protocol On Patients Referred For Transcatheter Aortic Valve Replacement. *Journal of Cardiovascular Computed Tomography* 2020; 14(3):S37.

Introduction: ECG-gate computed tomography angiography (CTA) is the standard technique for pre-procedural planning prior to transcatheter aortic valve replacement (TAVR). CTA requires use of potentially nephrotoxic iodinated contrast, limiting use in patients with renal dysfunction. We evaluated the utility of a tiered hydration protocol in patients with renal dysfunction referred for TAVR. Methods: 258 patients (52.7% male, age 79 ± 8 years) who underwent TAVR between 1/1/18 and 12/30/18 were retrospectively evaluated. Pre-procedural CTA was performed per institutional protocols with weight based contrast dosing. Patients requiring hemodialysis prior to CTA were excluded. Patients with GFR <22ml/min did not receive CTA. Patients with GFR 22 - 40 ml/min underwent hydration protocol guidelines: Outpatients received normal saline (NS) at ≤3 mL/kg over one hour pre-procedure/test and 1 to 1.5 mL/kg/hour during and up to six hours post-procedure/test. Inpatients received normal saline for 1 mL/kg/hour for 6 to 12 hours pre-procedure/test, intra-procedure, and up to 12 hours post-procedure. Results: Total baseline creatinine was 1.08 ± 0.41 ng/dL. Hydration protocol patient creatinine levels were 1.67 ± 0.41 ng/dL. Upper quartile of creatinine was 1.91 ng/dL (range 0.79 - 2.65 ng/dL). Average CTA contrast dose was 100 ± 23 mL. 43 (17%) of patients received pre-CTA hydration protocol. Hydration protocol NS total infusion volumes were 490 ± 119 mL (range 40-100ml). Duration between CT and TAVR was 86 ± 155 days. Pre-TAVR creatinine was 1.09 ± 0.39, creatinine at discharge was 1.06 ± 0.73. 3 patients (1%) had ≥1 increase in CKD grade at discharge. No patients required dialysis prior to discharge or within 1 month of TAVR. No complications from hydration protocol were identified. Conclusions: Utilization of a routine pre-TAVR CT hydration protocol in patients at risk for contrast induced nephropathy is feasible and associated with no new renal dysfunction prior to TAVR, and low rates of new renal dysfunction post TAVR. In TAVR patients hydration carries risks and further study is needed to identify whether a more conservative hydration protocol can be utilized.

Internal Medicine

Alalwan Y, Coriasso N, Aljamal A, Hughes CL, Abdelrahim E, Dee Wang D, Pantelic M, Song T, Eng MH, Frisoli T, Villablanca P, Wyman JF, O'Neill WW, and Lee J. Targeted exclusion of proximal obstructive coronary disease on coronary computed tomography angiography for deferral of routine invasive coronary angiography prior to transcatheter aortic valve replacement. *Catheterization and Cardiovascular Interventions* 2020; 95:S115.

Background: Aortic stenosis is associated with coronary artery disease (CAD) and routine invasive coronary angiography (ICA) is performed prior to transcatheter aortic valve replacement (TAVR). Evaluation of CAD on computed tomography angiography (CTA) is limited due to coronary calcification, cardiac motion and absence of sublingual nitroglycerin but may be feasible for the exclusion of only proximal CAD. Methods: 339 patients (52% male, age 79 ± 27) who underwent TAVR between 5/1/18 and 12/20/18 were retrospectively studied. Routine pre-procedure ECG-gated CTA was performed with reconstruction phases in 10% increments. CTA evaluation of proximal CAD performed clinically on request from multidisciplinary heart team. CAD analysis performed on 3D workstations by experienced cardiologists and radiologists. Stenosis grades: 0=normal, 1=1-25%, 2=26-50%, 3=51-70%, 4=71-99%, 5=occluded, 8=absent, 9=uninterpretable. Results: Of 339 patients, 62 (18%) patients had CTA coronary analysis of which 49 (14%) also had ICA before or at time of TAVR. Of these patients, 21 (43%) patients had no stenosis more than 50% on CTA, and of those 21 patients, 19 (91%) also had no stenosis more than 50% on ICA. 28 patients who had both ICA and CTA had ≥50% stenosis in at least one coronary artery on CTA. Of these, 22 (79%) also had ≥50% stenosis on ICA. When excluding those with coronary artery bypass grafts (12 patients), 63% of patients had ≥50% stenosis on both CTA and ICA. 13 patients had CTA without follow up ICA. Overall including all patients with no CAD on ICA and those who were deferred ICA based on CTA results, 32 (52%) patients avoided or could have avoided ICA, leading to a total theoretical cost saving of \$155,000-310,000. No patients had acute coronary syndrome (ACS) at the time of discharge post TAVR. Conclusions: Exclusion of proximal obstructive CAD on routine pre-TAVR CTA is feasible and can decrease utilization of ICA with no increase in ACS at the time discharge post TAVR implantation. This strategy can decrease invasive procedures and potentially reduce cost. Further study is needed on longitudinal outcomes with this strategy.

Internal Medicine

Coriasso N, Alalwan Y, Aljamal A, Hughes C, Abdelrahim E, Pantelic M, Song T, Eng M, Frisoli T, Villablanca P, Wyman J, O'Neill W, Wang D, and Lee J. "Transcaval First" Alternative Access Strategy For Transcatheter Aortic Valve Replacement Guided By Computed Tomography Angiography. *Journal of Cardiovascular Computed Tomography* 2020; 14(3):S94.

Introduction: Patients with small caliber or otherwise hostile iliofemoral vasculature are at high risk for vascular injury when undergoing transcatheter aortic valve replacement (TAVR). Computed tomography angiography (CTA) guides alternative access feasibility including techniques such as transcaval access. Methods: 339 patients (51.6% male, 87.0% white, age 79 ± 1 years) who underwent TAVR at an urban tertiary care facility between 1/2/18 and 12/20/18 were retrospectively studied. Pre-procedure CTA of major vasculature was performed per institutional protocol. Femoral arteries with minimal luminal diameter (MLD) ≤5.5 mm triggered alternative access planning for transcaval, transcarotid, transaxillary, and transseptal anterograde routes. Decision for alternative access was made by a multidisciplinary heart team consensus utilizing a "transcaval first" strategy. Results: Of 339 patients, alternative access was used in 72 (21.2%) of patients with outcomes similar to transfemoral. Strategies were transcaval in 58 (17.1%), transcarotid in 10 (2.9%), transaxillary in 3 (0.9%), and transseptal anterograde in 1 (0.3%). Bilateral femoral arteries ≤5.5 mm were present in 25 (7.4%) of patients. Conclusions: CTA planning identifies patients who may benefit from transcaval access as a first line alternative access strategy.

Internal Medicine

Hughes CL, Lee J, Coriasso N, Alalwan Y, Aljamal A, Wang DD, Pantelic M, Song T, Eng MH, Frisoli T, Villablanca P, Wyman JF, O'Neill WW, and Abdelrahim E. Utility of ECG-gated computed tomography angiography for the improved diagnosis of bicuspid aortic valve disease prior to transcatheter aortic valve replacement. *Catheterization and Cardiovascular Interventions* 2020; 95:S118-S119.

Background: Diagnosis of a bicuspid aortic valve (BAV) morphology has important prognostic implications due to early valve degeneration and an associated aortopathy. Presence of a BAV also has technical implications for transcatheter aortic valve replacement (TAVR) procedural planning and implantation. BAV is often first identified on transthoracic echocardiography (TTE), but diagnosis may be limited by imaging windows, operator skill, and valve calcification. ECG-gated computed tomography angiography (CTA) may improve identification of BAV. Methods: 335 patients who underwent TAVR between 5/1/18 and 12/20/18 were retrospectively evaluated. Routine pre-procedure planning retrospectively ECG-gated CTA studies were performed with reconstruction phases at 10% increments through the R-R cycle. 50% or greater commissural fusion was categorized as a BAV. Valve morphology from the preprocedural TTE reports was also abstracted. Of 335 patients, 17 patients had prosthetic valves. Of the remaining 318 patients, 267 (52.4% male, age 79 ± 27) had TTE grading of aortic valve morphology. Results: BAV was

identified by TTE in 23 patients (8.6% of cohort, age 75 ± 20 years) whereas CTA identified 26 patients (9.7% of cohort, age 74 ± 21 years) with a bicuspid valve. Direct correlation between CTA and TTE was modest (R-value = 0.38). With CTA as the reference standard, TTE had a sensitivity, specificity, positive predictive value and negative predictive value of 88.5%, 100%, 100% and 98.8% respectively. The age of patients with tricuspid vs BAV was 80 ± 28 years vs 74 ± 21 years, respectively. Aortic size in tricuspid vs BAV patients was 34.2 ± 15 vs 37.9 ± 30 mm ($p=0.001$). In BAV patients, 82% of the patients had no aortic dilation greater than 40mm. Conclusions: In patients referred for TAVR, CTA is valuable tool for diagnosis of BAV and associated aortopathies, particularly when valve morphology cannot be characterized by TTE. In our cohort, BAV patients were older and rarely had significant aortopathy, suggesting an increased prevalence of degenerative valve fusion relative to congenital BAV disease. Further study is required to categorize and distinguish BAV sub-types and their effect on TAVR procedure results.

Internal Medicine

Isseh IN, Dagher C, Sharma S, Basir MB, and Parikh S. Escalation of temporary mechanical circulatory support in the setting of deteriorating cardiogenic shock. *Catheterization and Cardiovascular Interventions* 2020; 95:S178.

Background: Cardiogenic shock (CS) is a deadly condition and mechanical circulatory support (MCS) is frequently utilized. We evaluated the characteristics of CS patients who required escalation of MCS due to deteriorating shock. Methods: From 07/2016-07/2018 we identified consecutive CS patients with deteriorating shock requiring escalation of MCS. Deteriorating shock was defined as worsening hypotension, escalating doses of vasopressors or worsening end-organ hypoperfusion. MCS escalation was defined as adding or exchanging a MCS device to existing MCS. All statistical tests were performed with a two-sided P value=.05. Results: 81 CS patients ($61 \pm 14.2y$, 73% men) had deteriorating shock requiring MCS escalation. 23% presented with acute myocardial infarction, 72% with decompensated heart failure (non-ischemic cardiomyopathy 26% and ischemic cardiomyopathy 46%) and 5% undifferentiated. Distribution of CS per SCAI classification was stage C 7%, D 82% and E 11%. Survival to discharge was 32%. Survivors were younger (55 vs $65y$, $P=0.002$) and had lower BMI (29 vs 34 , $P=0.031$). Initial MCS was IABP ($n=32$), Impella 2.5 ($=4$), CP ($=32$), 5.0 ($=2$), TandemHeart ($=3$), ProtekDuo ($=3$), VVECMO ($=2$), VAECMO ($=2$) and ProtekDuo+Impella CP ($=1$). Patients were escalated to Impella 2.5 ($n=1$), CP ($=16$), 5.0 ($=10$), TandemHeart ($=6$), VAECMO ($=8$), VAECMO+(IABP, 2.5 or CP) ($=20$), ProtekDuo+(IABP, CP, 5.0 or TandemHeart) ($=13$), Impella CP+RP ($=2$), TandemHeart+Impella RP ($=1$), central VAECMO ($=3$) and LVAD ($=1$). Lactate levels pre and post escalation were lower in survivors compared to non-survivors (3.3 vs 6.9 , $P=0.02$) and (2 vs 4.4 , $P=0.01$). Non-survivor lactate levels did not significantly improve post escalation (6.9 vs 4.4 , $P=0.06$) and mean arterial pressure decreased (77.1 vs 66.8 , $P=0.002$) despite significant improvement in cardiac index (1.9 vs 3.4 , $P<0.001$) and cardiac power output (0.6 vs 1.1 , $P=0.0001$). Utilization of a PA catheter pre-escalation was associated with improved survival (40% vs 18% , $P=0.04$). Conclusions: CS patients requiring escalation of MCS due to deteriorating shock have low hospital survival (32%). Younger age, lower BMI, lower lactate levels and utilization of PA catheter pre-escalation were associated with increased survival.

Internal Medicine

Nona P, Dhillon D, Mawri S, Cowger J, Alaswad K, Khandelwal AK, O'Neill WW, and Basir MB. Inter-hospital transfers in acute myocardial infarction and cardiogenic shock. *Catheterization and Cardiovascular Interventions* 2020; 95:S180.

Background: Limited data exist on the use of "hub and spoke" models to transfer patients who present in cardiogenic shock. We sought to assess outcomes of patients transferred to our shock center within our network to those who presents from institutions out of our network. Methods: From January 2014 to June 2017, 110 patients transferred to our shock center with an admission diagnosis of acute myocardial infarction and cardiogenic shock (AMICS) based on ICD coding. Demographics, admission, procedural and clinical outcomes were obtained for all patients and compared. Statistical analysis was performed using two-sample t-tests, Wilcoxon rank sum tests, chi-square tests and Fisher exact tests. Results: 35 patients were transferred within our network and 75 patients presented out of our network. The average age of the cohort was 66.4 years. In-network patients were less likely to present with in-hospital cardiac arrest (12.1% vs. 35.7% , $p=0.013$). In-network patients presented with lower cardiac output (CO) (3.2 L/m \pm 0.7 vs 4.5 L/m \pm 1.0 ; $p=0.019$) but were less likely to be on vasopressors (42.3% vs 72.2% , $p=0.018$) upon transfer. Similarly, in-network patients had a lower cardiac output following initiation of mechanical circulatory support (3.9 L/m \pm 0.9 vs. 5.7 L/m \pm 2.3 , $p=0.010$), but higher SBP after initiation of MCS (124.7 mmHg \pm 28.2 vs. 105.5 mmHg \pm 25.2 , $p=0.006$). Overall, in-network patients had shorter delays from AMI onset to MCS when compared to out of network patients. In-network patients had improved survival to hospital discharge (62.9% vs 41.3% , $p=0.035$). Conclusions: Patients who presented to our shock center from an in-network hospital had improved survival to hospital discharge when compared to patients who presented from outside our network. Further system based processes are needed to best optimize care of patients transferred with acute myocardial and cardiogenic shock.

Internal Medicine

Vishwanath R, Iordanou J, Singh V, **Gorgis S, Papukhyan H, Hana A, and Ananthasubramaniam K.** Defining The Incidence And Patient Profile Of Incidental Coronary Artery Calcification On Non-cardiac Computed Tomography: An Opportunity To Identify Subclinical Coronary Atherosclerosis. *Journal of Cardiovascular Computed Tomography* 2020; 14(3):S54.

Introduction: Coronary artery calcification (CAC) is an independent predictor of cardiac events. The increased use of thoracic Computed Tomography (CT) has made coronary calcification a common incidental finding, although the frequency remains unknown. We aimed to identify the incidence of CAC found on routine non-ECG gated CT scans, and risk factors associated with these findings. Methods: A systematic review was conducted through literature search using predetermined search criteria. Applicable studies were screened by 3 investigators for eligibility. Data regarding indication for CT imaging, incidence of CAC, and cardiovascular risk factors was collected. Results: A total of 3,850 study subjects were included for review. CAC was found in 1,231 patients, with an incidence rate of 32%. Indications for CT imaging were; 33% lung cancer screening, 16% for intrapulmonary pathology, 13% for pulmonary thromboembolism, 33% for miscellaneous reasons. In patients with CAC, the average age was 59.4 years old, and 77.9% were male. Hypertension was present in 45.5% of patients, diabetes mellitus was recorded in 25%, and smoking was found in 41.5% of patients. Conclusions: In this systematic review of 6 studies, incidental CAC on non-ECG gated CT scans was found in 32% of patients. The majority of these patients were identified to have major risk factors for coronary artery disease. Incidental CAC should be routinely reported on non-ECG gated CT scans, as it presents opportunity for detecting subclinical atherosclerosis which can impact patient counselling and medical management.

Neurology

Singh J, and Ali A. Reversible cerebral vasoconstriction syndrome presenting with symptoms of intracranial hypotension. *Headache* 2020; 60:134.

Background: Headache associated with spontaneous intracranial hypotension typically presents as an orthostatic headache that is improved in the supine position. Conversely, RCVS, a transient intracerebral arteriopathy, is classically characterized by recurrent thunderclap headache. Methods: We report a 60 year old woman who presented to the emergency department with a sudden onset bilateral parietooccipital headache that developed after straining on the toilet. The headache was a throbbing, pounding sensation associated with neck stiffness, without photophobia, phonophobia, or nausea. CT head and MRI brain were unremarkable, and she was treated symptomatically. The headache persisted, and she also developed cognitive difficulty, prompting 2 additional ER visits the following week without additional testing. 2 weeks after symptom onset, a repeat MRI brain and CT Angiography were unremarkable at an ER visit. The patient was evaluated in our headache clinic 2.5 weeks after symptom onset. She would wake up symptom-free without head pain, and as the day progressed, would develop progressively worsening headache, cognitive, and memory symptoms. Given multiple negative neuroimaging studies, her current symptoms of position-dependent occipital headache, and cognitive impairment, there was concern for spontaneous intracranial hypotension. She was scheduled 2 days later for a diagnostic and therapeutic lumbar epidural blood patch. Just prior to the procedure, she described new onset vertigo and was taken to the ER for urgent evaluation. CT head revealed a hypodensity in the left posterior parietal lobe and follow up MRI brain confirmed an acute infarct. The following day she developed mild right upper extremity weakness, and a repeat CTH was stable, but CTA of the head and neck revealed numerous, bilateral, stenotic vessels intracranially. Given concern for RCVS, she was started on IV fluids and verapamil. Cerebral angiogram demonstrated findings consistent with RCVS LP for CSF studies was unremarkable. No clear etiology of her RCVS was identified. Results: The patient was discharged with verapamil 80 mg three times daily. At her 2 month follow up, the patient's headaches and neurologic deficits had resolved. Repeat CTA completed 3 months after presentation showed resolution of previously noted intracranial stenoses, and the patient's verapamil was tapered down to 20 mg three times daily. Conclusion: Although uncommon, RCVS may present with symptoms concerning for low CSF pressure headache. Both conditions can present with thunderclap headache, can occur following a Valsalva maneuver, and can be missed on initial neuroimaging studies.

Surgery

Bendix S, Rteil A, Potti C, Chamogeorgakis T, Lace B, Woodward A, and Kabbani L. Mycotic Aneurysm After Metallic Foreign Body Ingestion. *Journal of Vascular Surgery* 2020; 72(3):e304-e305.

Objective: The esophagus is a frequent foreign body impaction site. We present a case of foreign body ingestion complicated by erosion into the aorta, causing a mycotic aneurysm. Methods: We introduce the case of a 60-year-old man with abdominal pain, nausea, fatigue, and fevers. Blood cultures grew out gram-positive cocci. A computed tomography (CT) scan revealed a distal thoracic aortic saccular aneurysm, with a 2.8-cm linear metallic body penetrating the inferior border of the aneurysm, and intraluminal thrombus formation (Fig. A). CT of the abdomen revealed portal vein thrombosis and splenic and hepatic abscesses. Esophagogastroduodenoscopy was

unremarkable. Results: The patient was started on the appropriate antibiotic therapy. He was then taken to the operating room for an open thoracoabdominal aortic aneurysm repair with an interposition cryopreserved graft, with an intercostal muscle flap (Fig, B). A metal bristle was removed (Fig, C). He had an uneventful postoperative course and was discharged home on postoperative day 17. Follow-up CT angiography showed resolution of the infection and satisfactory repair (Fig, D). Postoperative esophagram showed no esophageal injury. Conclusions: We describe a case of a bristle from a metallic barbecue brush that was ingested. This penetrated the esophagus, causing a mycotic aneurysm with septic embolization to the spleen and liver. Our successful treatment approach involved open aortic repair with an interposition cryopreserved graft and an intercostal muscle flap.

Books and Book Chapters

Orthopaedics/Bone and Joint

Sassack B, and **Carrier JD**. "Anatomy, Back, Lumbar Spine". StatPearls. Treasure Island (FL), StatPearls Publishing Copyright © 2020, StatPearls Publishing LLC. Epub ahead of print. [Full Text](#)

Michigan State University College of Osteopathic Medicine
Henry Ford Health System

The lumbar spine comprises the lower end of the spinal column between the last thoracic vertebra (T12) and the first sacral vertebra (S1). The spinal cord in this region has protection from five durable and mobile vertebrae (L1-L5) that allow for the dispersion of axial forces. The spinal cord runs through the center of the vertebral column and terminates in the conus medullaris at the level of the L1-L2 vertebrae. The cauda equina, Latin for horse's tail, is a bundle of spinal nerve roots that begin at the termination of the spinal cord and descend through the remainder of the canal. The lumbar spine is comprised of bone, cartilage, ligaments, nerves, and muscle. Each of these components plays an integral role in the form and function of the lumbar spine.

Pulmonary and Critical Care Medicine

Agarwal AK, and **Huda N**. "Interstitial (Nonidiopathic) Pulmonary Fibrosis". StatPearls. Treasure Island (FL), StatPearls Publishing. Copyright © 2020, StatPearls Publishing LLC. Epub ahead of print. [Full Text](#)

Michigan State University
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Nonidiopathic interstitial pulmonary fibrosis (non-IPF) describes a group of interstitial lung diseases (ILD) that cause inflammation and fibrosis of the lung interstitium leading to impaired gas exchange due to a known cause. Depending on the specific disorder, it can also affect the trachea, bronchi, bronchioles, alveoli, and pleura. Most of these diseases are characterized by their clinical, radiographic, pathologic, and physiologic findings. The classic features often include progressive shortness of breath and cough, chest imaging abnormalities, and inflammatory and fibrotic changes on histology. A restrictive pattern with a decreased diffusing capacity for carbon monoxide (DLCO) is often seen in pulmonary function testing (PFT).

HFHS Publications on COVID-19

Cardiology/Cardiovascular Research

McCullough PA, Kelly RJ, Ruocco G, Lerma E, Tumlin J, Wheelan K, Katz N, Lepor NE, Vijay K, Carter H, Singh B, McCullough SP, Bhambi BK, Palazzuoli A, De Ferrari GM, Milligan G, Safder T, Tecson KM, **Wang DD, McKinnon JE, O'Neill WW, Zervos M**, and Risch HA. Pathophysiological Basis and Rationale for Early Outpatient Treatment of SARS-CoV-2 (COVID-19) Infection. *Am J Med* 2020; Epub ahead of print. PMID: 32771461. [Full Text](#)

Cardiology/Cardiovascular Research

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