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Henry Ford Health System Publication List – April 2021

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health System personnel. Searches were conducted in PubMed, Embase, and Web of Science during the month, and then imported into EndNote for formatting. There are **100 unique citations** listed this month, with **5 articles** and **1 conference abstract on COVID-19**. Articles are listed first, followed by conference abstracts, books and book chapters, and a bibliography of publications on COVID-19. Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health System authors.

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Articles

Conference Abstracts

Articles

Allergy and Immunology

Guarnieri KM, Slack IF, Gadoury-Lévesque V, **Eapen AA**, Andorf S, and Lierl MB. Peanut oral immunotherapy in a pediatric allergy clinic: patient factors associated with clinical outcomes. *Ann Allergy Asthma Immunol* 2021; Epub ahead of print. PMID: 33839246. Full Text

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Division of Allergy and Clinical Immunology, Henry Ford Health System, Detroit, MI.
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BACKGROUND: Additional information is needed to inform optimal patient selection, expected outcomes, and treatment endpoints for clinical peanut oral immunotherapy (OIT). OBJECTIVE: We analyzed a real-world peanut OIT cohort to provide insight into these questions. METHODS: Records were reviewed for 174 children undergoing peanut OIT at a pediatric allergy clinic. Patient age, peanut skin prick test, peanut-specific IgE (sIgE) results, and inclusion of additional foods in OIT were analyzed for correlations with OIT outcomes. RESULTS: To date, 144 patients have achieved maintenance dosing, 50 of whom transitioned to ad lib twice-weekly peanut ingestion. Thirty discontinued OIT. Fortyseven patients who underwent multi-food OIT had no significant difference in reactions or time to reach maintenance compared to those on peanut OIT alone. Age at initiation inversely correlated with achievement of maintenance: 92% of patients 0.5-<5 years, 81% of those 5-<11 years, and 70% of those 11-<18 years reached and continued maintenance (P=0.013). Baseline peanut-sIgE level positively correlated with number of reactions during updosing (P=0.0004) and maintenance (P=0.0048), though was not significantly different in patients achieving successful maintenance versus those who discontinued OIT (P=0.098). Sixty-six percent of patients experienced ≥1 adverse reaction during OIT. Of those on ad lib peanut ingestion, 2 reported mild reactions after lapses in peanut consumption. CONCLUSION: Clinical peanut OIT has similar outcomes to research protocols. OIT can be successful in older children and those with high peanut-sIgE levels, though these factors impact outcomes. Clinical and laboratory criteria can guide successful transition to intermittent ad lib peanut consumption.

Anesthesiology

Elsharkawy H, **Ahuja S**, Sessler DI, Maheshwari K, Mao G, Sakr Esa WA, Soliman LM, Ayad S, Khoshknabi D, Khan MZ, Raza S, DeGrande S, and Turan A. Subcostal Anterior Quadratus Lumborum Block Versus Epidural Block for Analgesia in Open Nephrectomy: A Randomized Clinical Trial. *Anesth Analg* 2021; 132(4):1138-1145. PMID: 33617181. Full Text

From the Department of Anesthesiology, Pain and Healing Center, Case Western Reserve University, MetroHealth, Cleveland, Ohio.
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BACKGROUND: Epidural block are often used for analgesia after open nephrectomy surgery. Subcostal anterior quadratus lumborum block may be an alternative. We therefore tested the hypothesis that the

continuous subcostal anterior quadratus lumborum block is noninferior to epidural block for analgesia in patients having open partial nephrectomies. METHODS: Adults having open partial nephrectomies were randomly allocated to epidural or unilateral subcostal anterior quadratus lumborum block. The joint primary outcomes were opioid consumption measured in morphine equivalents and pain measured on a numeric rating scale (0-10) from postanesthesia care unit (PACU) until 72 hours after surgery. The noninferiority deltas were 30% for opioid consumption and 1 point on a 0-10 scale for pain. Secondary outcomes included patient global assessment of pain management on the third postoperative day, the number of antiemetic medication doses through the third postoperative day, duration of PACU stay, and postoperative duration of hospitalization. RESULTS: Twenty-six patients were randomized to anterior quadratus lumborum block and 29 to epidural analgesia. Neither pain scores nor opioid consumption in the quadratus lumborum patients were noninferior to epidural analgesia. At 72 hours, mean ± standard deviation pain scores in subcoastal anterior quadratus lumborum block and epidural group were 4.7 ± 1.8 and 4.1 ± 1.7, with an estimated difference in pain scores of 0.62 (95% confidence interval [CI], 0.74-1.99; noninferiority P = .21). The median [Q1, Q3] opioid consumption was more than doubled in quadratus lumborum patients at 70 mg [43, 125] versus 30 mg [18, 75] in the epidural group with an estimated ratio of geometric means of 1.69 (95% CI, 0.66-4.33; noninferiority P = .80). Patient global assessment and duration of PACU and hospital stays did not differ significantly in the 2 groups. CONCLUSIONS: We were unable to show that subcostal anterior quadratus lumborum block are noninferior to epidural analgesia in terms of pain scores and opioid consumption for open partial nephrectomies. Effectiveness of novel blocks should be rigorously tested in specific surgical setting before widespread adoption.

Anesthesiology

Kalu R, **Boateng P**, **Carrier L**, **Garzon J**, **Tang A**, **Reickert C**, and **Stefanou A**. Effect of preoperative versus postoperative use of transversus abdominis plane block with plain 0.25 % bupivacaine on postoperative opioid use: a retrospective study. *BMC Anesthesiol* 2021; 21(1):114. PMID: 33845790. Full Text

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BACKGROUND: Enhanced recovery protocols optimize pain control via multimodal approaches that include transversus abdominis plane (TAP) block. The aim of this study was to evaluate the effect of preoperative vs. postoperative plain 0.25 % bupivacaine TAP block on postoperative opioid use after colorectal surgery. METHODS: A retrospective cohort study comparing postoperative opioid use in patients who received preoperative (n = 240) vs. postoperative (n = 22) plain 0.25 % bupivacaine TAP blocks. The study was conducted in a single tertiary care institution and included patients who underwent colorectal resections between August 2018 and January 2020. The primary outcome of the study was postoperative opioid use. Secondary outcomes included operative details, length of stay, reoperation, and readmission rates. RESULTS: Patients who received postoperative plain 0.25 % bupivacaine TAP blocks were less likely to require postoperative patient-controlled analgesia (PCA) (59.1 % vs. 83.3 %; p = 0.012) and opioid medications on discharge (6.4 % vs. 16.9 %; p = 0.004) relative to patients who received preoperative TAP. When needed, a significantly smaller amount of opioid was prescribed to the postoperative group (84.5 vs. 32.0 mg, p = 0.047). No significant differences were noted in the duration of postoperative PCA use, amount of oral opioid use, and length of stay. CONCLUSIONS: Plain 0.25 % bupivacaine TAP block administered postoperatively was associated with significantly lower need for postoperative PCA and discharge opioid medications. The overall hospital length of stay was not affected by the timing of TAP block. Because of the limited sample size in this study, conclusions cannot be generalized, and more research will be required.

Anesthesiology
Milne A, Teng JJ, **Vargas A**, Markley JC, and Collins A. Performance assessment of intravenous catheters for massive transfusion: A pragmatic in vitro study. *Transfusion* 2021; Epub ahead of print. PMID: 33846984. Full Text

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BACKGROUND: Rapid infusion of warmed blood products is the cornerstone of trauma resuscitation and treatment of surgical and obstetric massive hemorrhage. Integral to optimizing this delivery is selection of an intravenous (IV) catheter and use of a rapid infusion device (RID). We investigated which IV catheter and RID system enabled the greatest infusion rate of blood products and the governing catheter characteristics. STUDY DESIGN AND METHODS: The maximum flow rates of nine IV catheters were measured while infusing a mixture of packed red blood cells and fresh frozen plasma at a 1:1 ratio using a RID with and without a patient line extension. To account for IV catheters that achieved the RID's maximum 1000 ml/min, the conductance of each infusion circuit configuration was calculated. RESULTS: IV catheters of 7-Fr caliber or higher reached the maximum pressurized flow rate. The 9-Fr multi-lumen access catheter (MAC) achieved the greatest conductance, over sevenfold greater than the 18 g peripheral catheter (4.6 vs. 0.6 ml/min/mmHg, $p < .001$). Conductance was positively correlated with internal radius ($\beta = 1.098$, 95% CI 4.286-5.025, $p < .001$) and negatively correlated with length ($\beta = -0.495$, 95% CI -0.007 to 0.005, $p < .001$). Use of an extension line ($\beta = -0.094$, 95% CI -0.505 to -0.095, $p = .005$) was independently associated with reduced conductance in large caliber catheters. CONCLUSION: Short, large-diameter catheters provided the greatest infusion rates of massive transfusion blood products for the least pressure. For patients requiring the highest transfusion flow rates, extension tubing should be avoided when possible.

Anesthesiology
Navas-Blanco JR, and **Modak RK**. Perioperative care of heart transplant recipients undergoing non-cardiac surgery. *Ann Card Anaesth* 2021; 24(2):140-148. PMID: 33884968. Full Text

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The life expectancy of patients with end-stage heart disease undergoing Orthotopic Heart Transplantation (OHT) has increased significantly in the recent decades since its original introduction into the medical practice in 1967. Substantial advances in post-operative intensive care, surgical prophylaxis, and anti-rejection drugs have clearly impacted survivability after OHT, therefore the volume of patients presenting for non-cardiac surgical procedures is expected to continue to escalate in the upcoming years. There are a number of caveats associated with this upsurge of post-OHT patients requiring non-cardiac surgery, including presenting to healthcare facilities without the resources and technology necessary to manage potential perioperative complications or that may not be familiar with the care of these patients, facilities in which a cardiac anesthesiologist is not available, patients presenting for emergency procedures and so forth. The perioperative care of patients after OHT introduces several challenges to the anesthesiologist including preoperative risk assessments different to the general population and intraoperative management of a denervated organ with altered response to medications and drug-drug interactions. The present review aims to synopsize current data of patients presenting for non-cardiac surgery after OHT, surgical aspects of the transplant that may impact perioperative care, physiology of the transplanted heart as well as anesthetic considerations.

Behavioral Health Services/Psychiatry

Hecht LM, **Yeh HH**, **Braciszewski JM**, **Miller-Matero LR**, **Thakrar A**, **Patel S**, Simon GE, Lynch FL, Beck A, Owen-Smith AA, Rossom RC, Waitzfelder BE, Lu CY, Boggs JM, and **Ahmedani BK**. Weighing the Association Between BMI Change and Suicide Mortality. *Psychiatr Serv* 2021; Epub ahead of print. PMID: 33882679. Full Text

Henry Ford Health System Center for Health Policy and Health Services Research, Detroit (Hecht, Yeh, Braciszewski, Miller-Matero, Ahmedani); Henry Ford Health System Behavioral Health, Detroit (Hecht, Miller-Matero, Thakrar, Patel, Ahmedani); Kaiser Permanente Washington Health Research Institute, Seattle (Simon); Kaiser Permanente Northwest, Center for Health Research, Portland, Oregon (Lynch); Kaiser Permanente Colorado, Institute for Health Research, Denver (Beck, Boggs); Kaiser Permanente Georgia, Center for Research and Evaluation, Atlanta, and Department of Health Policy and Behavioral Sciences, Georgia State University School of Public Health, Atlanta (Owen-Smith); HealthPartners, Institute for Education and Research, Minneapolis (Rossom); Kaiser Permanente Hawaii, Center for Integrated Health Care Research, Honolulu (Waitzfelder); Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston (Lu).

OBJECTIVE: Suicide rates continue to rise, necessitating the identification of risk factors. Obesity and suicide mortality rates have been examined, but associations among weight change, death by suicide, and depression among adults in the United States remain unclear. METHODS: Data from 387 people who died by suicide in 2000-2015 with a recorded body mass index (BMI) in the first and second 6 months preceding their death ("index date") were extracted from the Mental Health Research Network. Each person was matched with five people in a control group (comprising individuals who did not die by suicide) by age, sex, index year, and health care site (N=1,935). RESULTS: People who died by suicide were predominantly male (71%), White (69%), and middle aged (mean age=57 years) and had a depression diagnosis (55%) and chronic health issues (57%) (corresponding results for the control group: 71% male, 66% White, 14% with depression diagnosis, and 43% with chronic health issues; mean age=56 years). Change in BMI within the year before the index date statistically significantly differed between those who died by suicide (mean change=-0.72±2.42 kg/m(2)) and the control group (mean change=0.06±4.99 kg/m(2)) ($p<0.001$, Cohen's $d=0.17$). A one-unit BMI decrease was associated with increased risk for suicide after adjustment for demographic characteristics, mental disorders, and Charlson comorbidity score (adjusted odds ratio=1.11, 95% confidence interval=1.05-1.18, $p<0.001$). For those without depression, a BMI change was significantly associated with suicide ($p<0.001$). CONCLUSIONS: An increased suicide mortality rate was associated with weight loss in the year before a suicide after analyses accounted for general and mental health indicators.

Cardiology/Cardiovascular Research

Birchak J, **Khan A**, and **Maskoun W**. A Plumbing and Electrical Problem: An Unusual Cause of Syncope. *Circulation* 2021; 143(15):1528-1532. PMID: 33844583. Full Text

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Cardiology/Cardiovascular Research

Cowger JA, Molina EJ, and Pagani FD. Intermacs: Evolving data capture to meet scientific needs. *Ann Thorac Surg* 2021; Epub ahead of print. PMID: 33891919. Full Text

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Cardiology/Cardiovascular Research

Guerrero M, Pursnani A, Narang A, Salinger M, **Wang DD**, Eleid M, Kodali SK, George I, Satler L, Waksman R, Meduri CU, Rajagopal V, Inglessis I, Palacios I, Reisman M, **Eng MH**, Russell HM, Pershad A, Fang K, Kar S, Makkar R, Saucedo J, Pearson P, Bokhary U, Kaptzan T, Lewis B, Tommaso C, Krause P, Thaden J, Oh J, Lang RM, Hahn RT, Leon MB, **O'Neill WW**, Feldman T, and Rihal C. Prospective Evaluation of Transseptal TMVR for Failed Surgical Bioprostheses: MITRAL Trial Valve-in-Valve Arm 1-Year Outcomes. *JACC Cardiovasc Interv* 2021; 14(8):859-872. PMID: 33888231. Full Text

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OBJECTIVES: The aim of this study was to assess 1-year clinical outcomes among high-risk patients with failed surgical mitral bioprostheses who underwent transseptal mitral valve-in-valve (MViV) with the SAPIEN 3 aortic transcatheter heart valve (THV) in the MITRAL (Mitral Implantation of Transcatheter Valves) trial. BACKGROUND: The MITRAL trial is the first prospective study evaluating transseptal MViV with the SAPIEN 3 aortic THV in high-risk patients with failed surgical mitral bioprostheses. METHODS: High-risk patients with symptomatic moderate to severe or severe mitral regurgitation (MR) or severe mitral stenosis due to failed surgical mitral bioprostheses were prospectively enrolled. The primary safety endpoint was technical success. The primary THV performance endpoint was absence of MR grade ≥2+ or mean mitral valve gradient ≥10 mm Hg (30 days and 1 year). Secondary endpoints included procedural success and all-cause mortality (30 days and 1 year). RESULTS: Thirty patients were enrolled between July 2016 and October 2017 (median age 77.5 years [interquartile range (IQR): 70.3 to 82.8 years], 63.3% women, median Society of Thoracic Surgeons score 9.4% [IQR: 5.8% to 12.0%], 80% in New York Heart Association functional class III or IV). The technical success rate was 100%. The primary performance endpoint in survivors was achieved in 96.6% (28 of 29) at 30 days and 82.8% (24 of 29) at 1 year. Thirty-day all-cause mortality was 3.3% and was unchanged at 1 year. The only death was due to airway obstruction after swallowing several pills simultaneously 29 days post-MViV. At 1-year follow-up, 89.3% of patients were in New York Heart Association functional class I or II, the median mean mitral valve gradient was 6.6 mm Hg (interquartile range: 5.5 to 8.9 mm Hg), and all patients had MR grade ≤1+. CONCLUSIONS: Transseptal MViV in high-risk patients was associated with 100% technical success, low procedural complication rates, and very low mortality at 1 year. The vast majority of patients experienced significant symptom alleviation, and THV performance remained stable at 1 year.

Cardiology/Cardiovascular Research

Guerrero M, **Wang DD**, Eleid MF, Pursnani A, Salinger M, Russell HM, Kodali SK, George I, Bapat VN, Dangas GD, Tang GHL, Inglesis I, Meduri CU, Palacios I, Reisman M, Whisenant BK, Jermihov A, Kaptzan T, Lewis BR, Tommaso C, Krause P, Thaden J, Oh JK, Douglas PS, Hahn RT, Leon MB, Rihal CS, Feldman T, and **O'Neill WW**. Prospective Study of TMVR Using Balloon-Expandable Aortic Transcatheter Valves in MAC: MITRAL Trial 1-Year Outcomes. *JACC Cardiovasc Interv* 2021; 14(8):830-845. PMID: 33888229. Full Text

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OBJECTIVES: The aim of this study was to evaluate 1-year outcomes of valve-in-mitral annular calcification (ViMAC) in the MITRAL (Mitral Implantation of Transcatheter Valves) trial. BACKGROUND: The MITRAL trial is the first prospective study evaluating the feasibility of ViMAC using balloon-expandable aortic transcatheter heart valves. METHODS: A multicenter prospective study was conducted, enrolling high-risk surgical patients with severe mitral annular calcification and symptomatic severe mitral valve dysfunction at 13 U.S. sites. RESULTS: Between February 2015 and December 2017, 31 patients were enrolled (median age 74.5 years [interquartile range (IQR): 71.3 to 81.0 years], 71% women, median Society of Thoracic Surgeons score 6.3% [IQR: 5.0% to 8.8%], 87.1% in New York Heart Association functional class III or IV). Access was transatrial (48.4%), transseptal (48.4%), or transapical (3.2%). Technical success was 74.2%. Left ventricular outflow tract obstruction (LVOTO) with hemodynamic compromise occurred in 3 patients (transatrial, n = 1; transseptal, n = 1; transapical, n = 1). After LVOTO occurred in the first 2 patients, pre-emptive alcohol septal ablation was implemented to decrease risk in high-risk patients. No intraprocedural deaths or conversions to open heart surgery occurred during the index procedures. All-cause mortality at 30 days was 16.7% (transatrial, 21.4%; transseptal, 6.7%; transapical, 100% [n = 1]; p = 0.33) and at 1 year was 34.5% (transatrial, 38.5%; transseptal, 26.7%; p = 0.69). At 1-year follow-up, 83.3% of patients were in New York Heart Association functional class I or II, the median mean mitral valve gradient was 6.1 mm Hg (IQR: 5.6 to 7.1 mm Hg), and all patients had ≤1+ mitral regurgitation. CONCLUSIONS: At 1 year, ViMAC was associated with symptom improvement and stable transcatheter heart valve performance. Pre-emptive alcohol septal ablation may prevent transcatheter mitral valve replacement-induced LVOTO in patients at risk. Thirty-day mortality of patients treated via transseptal access was lower than predicted by the Society of Thoracic Surgeons score. Further studies are needed to evaluate safety and efficacy of ViMAC.

Cardiology/Cardiovascular Research

Guerrero M, **Wang DD**, Pursnani A, Salinger M, Russell HM, Eleid M, Chakravarty T, **Eng MH**, Kodali SK, Meduri CU, Pershad A, Satler L, Waksman R, Palacios I, Smalling R, Reisman M, Gegenhuber M, Kaptzan T, Lewis B, Tommaso C, Krause P, Thaden J, Oh J, Douglas PS, Hahn RT, Kar S, Makkar R, Leon MB, Feldman T, Rihal C, and **O'Neill WW**. Prospective Evaluation of TMVR for Failed Surgical Annuloplasty Rings: MITRAL Trial Valve-in-Ring Arm 1-Year Outcomes. *JACC Cardiovasc Interv* 2021; 14(8):846-858. PMID: 33888230. Full Text

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OBJECTIVES: The authors report 1-year outcomes of high-risk patients with failed surgical annuloplasty rings undergoing transseptal mitral valve-in-ring (MViR) with the SAPIEN 3 aortic transcatheter heart valve (THV). BACKGROUND: The MITRAL (Mitral Implantation of Transcatheter Valves) trial is the first prospective study evaluating transseptal MViR with the SAPIEN 3 aortic THV in high-risk patients with failed surgical annuloplasty rings. METHODS: Prospective enrollment of high-risk patients with symptomatic moderate to severe or severe mitral regurgitation (MR) or severe mitral stenosis and failed annuloplasty rings at 13 U.S. sites. The primary safety endpoint was technical success. The primary THV performance endpoint was absence of MR grade ≥2+ or mean mitral valve gradient ≥10 mm Hg (30 days and 1 year). Secondary endpoints included procedural success and all-cause mortality (30 days and 1 year). RESULTS: Thirty patients were enrolled between January 2016 and October 2017 (median age 71.5 years [interquartile range: 67.0 to 76.8 years], 36.7% women, median Society of Thoracic Surgeons score 7.6% [interquartile range: 5.1% to 11.8%], 76.7% in New York Heart Association functional class III or IV). Technical success was 66.7% (driven primarily by need for a second valve in 6 patients). There was no intraprocedural mortality or conversion to surgery. The primary performance endpoint was achieved in 85.7% of survivors at 30 days (24 of 28) and 89.5% of patients alive at 1 year with echocardiographic data available (17 of 19). All-cause mortality at 30 days was 6.7% and at 1 year was 23.3%. Among survivors at 1-year follow-up, 84.2% were in New York Heart Association functional class I or II, the median mean mitral valve gradient was 6.0 mm Hg (interquartile range: 4.7 to 7.3 mm Hg), and all had ≤1+ MR. CONCLUSIONS: Transseptal MViR was associated with a 30-day mortality rate lower than predicted by the Society of Thoracic Surgeons score. At 1 year, transseptal MViR was associated with symptom improvement and stable THV performance.

Cardiology/Cardiovascular Research

Gupta K, Kalra R, Pate M, Nagalli S, Ather S, **Rajapreyar I**, Arora P, **Gupta A**, Zhou W, San Jose Estepar R, Di Carli M, Prabhu SD, and Bajaj NS. Relative Predictive Value of Circulating Immune Markers in US Adults Without Cardiovascular Disease: Implications for Risk Reclassification. *Mayo Clin Proc* 2021; Epub ahead of print. PMID: 33840521. Full Text

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OBJECTIVE: To investigate the relative predictive value of circulating immune cell markers for cardiovascular mortality in ambulatory adults without cardiovascular disease. METHODS: We analyzed data of participants enrolled in the National Health and Nutrition Examination Survey from January 1, 1999, to December 31, 2010, with the total leukocyte count within a normal range (4000-11,000 cells/μL [to convert to cells ×10(9)/L, multiply by 0.001]) and without cardiovascular disease. The relative predictive value of circulating immune cell markers measured at enrollment-including total leukocyte count, absolute neutrophil count, absolute lymphocyte count, absolute monocyte count, monocyte-lymphocyte ratio (MLR), neutrophil-lymphocyte ratio, and C-reactive protein-for cardiovascular mortality was evaluated. The marker with the best predictive value was added to the 10-year atherosclerotic cardiovascular disease (ASCVD) risk score to estimate net risk reclassification indices for 10-year cardiovascular mortality. RESULTS: Among 21,599 participants eligible for this analysis, the median age was 47 years (interquartile range, 34-63 years); 10,651 (49.2%) participants were women, and 10,713 (49.5%) were self-reported non-Hispanic white. During a median follow-up of 9.6 years (interquartile range, 6.8-13.1 years), there were 627 cardiovascular deaths. MLR had the best predictive value for cardiovascular mortality. The addition of elevated MLR (≥0.3) to the 10-year ASCVD risk score improved the classification by 2.7%±1.4% (P=.04). Elevated MLR had better predictive value than C-reactive protein and several components of the 10-year ASCVD risk score. CONCLUSION: Among ambulatory US adults without preexisting cardiovascular disease, we found that MLR had the best predictive value for cardiovascular mortality among circulating immune markers. The addition of MLR to the 10-year risk score significantly improved the risk classification of participants.

Cardiology/Cardiovascular Research

Haberman D, Estévez-Loureiro R, Benito-Gonzalez T, Denti P, Arzamendi D, Adamo M, Freixa X, Nombela-Franco L, **Villablanca P**, Krivoshei L, Fam N, Spargias K, Czarnecki A, Pascual I, Praz F, Sudarsky D, Kerner A, Ninios V, Gennari M, Beeri R, Perl L, Danenberg H, Poles L, Shimoni S, Goland S, Caneiro-Queija B, Scianna S, Moaraf I, Schiavi D, Scardino C, Corpataux N, Echarte-Morales J, Chrissoheris M, Fernández-Peregrina E, Di Pasquale M, Regueiro A, Vergara-Uzcategui C, Iñiguez-Romo A, Fernández-Vázquez F, Dvir D, Taramasso M, and Shuvy M. Safety and Feasibility of MitraClip Implantation in Patients with Acute Mitral Regurgitation after Recent Myocardial Infarction and Severe Left Ventricle Dysfunction. *J Clin Med* 2021; 10(9). PMID: 33921996. Full Text

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Patients with severe mitral regurgitation (MR) after myocardial infarction (MI) have an increased risk of mortality. Transcatheter mitral valve repair may therefore be a suitable therapy. However, data on clinical outcomes of patients in an acute setting are scarce, especially those with reduced left ventricle (LV) dysfunction. We conducted a multinational, collaborative data analysis from 21 centers for patients who were, within 90 days of acute MI, treated with MitraClip due to severe MR. The cohort was divided according to median left ventricle ejection fraction (LVEF)-35%. Included in the study were 105 patients. The mean age was 71 ± 10 years. Patients in the LVEF < 35% group were younger but with comparable Euroscore II, multivessel coronary artery disease, prior MI and coronary artery bypass graft surgery. Procedure time was comparable and acute success rate was high in both groups (94% vs. 90%, p = 0.728). MR grade was significantly reduced in both groups along with an immediate reduction in left atrial V-wave, pulmonary artery pressure and improvement in New York Heart Association (NYHA) class. In-hospital and 1-year mortality rates were not significantly different between the two groups (11% vs. 7%, p = 0.51 and 19% vs. 12%, p = 0.49) and neither was the 3-month re-hospitalization rate. In conclusion, MitraClip intervention in patients with acute severe functional mitral regurgitation (FMR) due to a recent

MI in an acute setting is safe and feasible. Even patients with severe LV dysfunction may benefit from transcatheter mitral valve intervention and should not be excluded.

Cardiology/Cardiovascular Research
Kunkel KJ, **Dabbagh MF**, **Zaidan M**, and **Alaswad K**. Mechanical Circulatory Support in High-Risk Percutaneous Coronary Intervention. *Interv Cardiol Clin* 2021; 10(2):207-219. PMID: 33745670. Full Text

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The use of mechanical circulatory devices to support high-risk elective percutaneous coronary intervention (PCI) has become more common as the group of patients considered inoperable or high risk for surgical revascularization has grown. Most of the data examining outcomes in high-risk PCI are observational and retrospective. Limited prospective randomized studies have been unable to show improved clinical outcomes with routine mechanical circulatory support (MCS) in patients with a high burden of coronary artery disease and reduced ejection fraction. The role for MCS in high-risk PCI continues to evolve as understanding of the appropriate groups for this therapy evolves.

Cardiology/Cardiovascular Research
Kunkel KJ, Fiorilli P, Kobayashi T, Desai ND, Anwaruddin S, and Herrmann HC. Snare-Assisted Valve Positioning of Self-Expanding Valves for Transcatheter Aortic Valve Replacement. *JACC: Case Reports* 2021; 3(4):658-662. PMID: Not assigned. Full Text

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We describe 4 cases in which technical challenges were anticipated in delivering a self-expanding TAVR valve due to challenging aortic anatomy or a previous placed surgical aortic valve. An upfront snare strategy is described which facilitates valve centralization and atraumatic valve delivery. (Level of Difficulty: Advanced.)

Cardiology/Cardiovascular Research
Lemor A, **Ya'qoub L**, and **Basir MB**. Mechanical Circulatory Support in Acute Myocardial Infarction and Cardiogenic Shock. *Interv Cardiol Clin* 2021; 10(2):169-184. PMID: 33745667. Full Text

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Mechanical circulatory support devices are increasingly used for the treatment of acute myocardial infarction complicated by cardiogenic shock. These devices provide different levels of univentricular and biventricular support, have different mechanisms of actions, and provide different physiologic effects. Institutions require expert teams to safely implant and manage these devices. This article reviews the mechanism of action, physiologic effects, and data as they relate to the utilization of these devices.

Cardiology/Cardiovascular Research
Megaly M, Morcos R, Khalil C, Garcia S, **Basir M**, Maini B, Khalili H, Burke MN, **Alaswad K**, and Brilakis ES. Complications and failure modes of coronary embolic protection devices: Insights from the MAUDE database. *Catheter Cardiovasc Interv* 2021; Epub ahead of print. PMID: 33876860. Full Text

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BACKGROUND: There is limited data on complications associated with the use of coronary embolic protection devices (EPDs). METHODS: We queried the Manufacturer and User Facility Device Experience database between November 2010 and November 2020 for reports on coronary EPDs: Spider FX (Medtronic, Minneapolis, MN) and Filterwire EZ (Boston Scientific, Natick, MA). RESULTS: We retrieved 119 reports on coronary EPD failure (Spider FX n = 33 and Filterwire EZ n = 86), most of which (78.2%) occurred during saphenous vein graft interventions. The most common failure mode was inability to retrieve the EPD (49.6%), with the filter trapped against stent struts in 76.2% of the cases. Other device complications included filter fracture (28.6%), failure to cross (7.6%), failure to deploy (7.6%), and failure to recapture the filter (3.4%). Filter fracture (54.5 vs. 29.1%) and failure to recapture (9.1 vs. 2.1%) were more commonly reported, while failure to deploy the filter (0 vs. 10.5%) was less commonly reported with the Spider-FX. CONCLUSIONS: The most common modes of failure of coronary EPDs are the failure of retrieval (49.6%), followed by the filter fracture (28.6%). When using EPDs, careful attention to the technique is essential to avoid failures and subsequent complications.

Cardiology/Cardiovascular Research
O'Neill B. Mechanical Circulatory Support. *Interv Cardiol Clin* 2021; 10(2):xiii. PMID: 33745677. Full Text

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Cardiology/Cardiovascular Research
Singh G, and **Greenberg JC**. Reply to the Editor-Cardiac implantable electronic devices and phone interaction. *Heart Rhythm* 2021; Epub ahead of print. PMID: 33892204. Full Text

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Cardiology/Cardiovascular Research
Singh H, Mehta RH, **O'Neill W**, Kapur NK, Lalonde T, Ohman M, Ghiu I, Chen-Hsing Y, Dutcheshen K, Schreiber T, Rosman H, and Kaki A. Clinical Features and Outcomes in Patients with Cardiogenic Shock Complicating Acute Myocardial Infarction: Early versus Recent Experience with Impella. *Am Heart J* 2021; Epub ahead of print. PMID: 33848505. Full Text

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Abiomed Inc.

OBJECTIVES: To compare clinical features and outcomes in patients with acute myocardial infarction complicated by cardiogenic shock (AMICS) treated in the early experience with Impella percutaneous ventricular assist device and patients treated recently. BACKGROUND: Since pre-market approval (PMA) of Impella device as treatment for AMICS, use of the device has grown considerably. METHODS: We retrospectively analyzed 649 AMICS patients treated with perioperative Impella, with 291 patients treated from 2008 to 2014 comprising the early experience cohort and 358 patients treated from 2017 to 2019 comprising the recent experience cohort. The primary end point was risk adjusted in-hospital mortality.

RESULTS: Mean age and gender distribution of patients was similar in the two cohorts. The recent cohort had more invasive hemodynamic monitoring (64% vs 46%; p<0.001) and less use of an intra-aortic balloon pump prior to Impella (15% vs 41%; p<0.001). Recently treated patients were significantly more likely to receive Impella support prior to PCI (58% vs 44%; p=0.005). In-hospital mortality was lower in the recent cohort (48% versus 56%; p=0.043). This difference was however no longer significant after risk adjustment (adjusted OR 0.89, 95% CI 0.59-1.34, p=0.59). Rates of acute kidney injury, major bleeding, and vascular complications requiring surgery were also significantly lower in the recent cohort. CONCLUSIONS: Use of Impella for AMICS during recent years is associated with lower unadjusted in-hospital mortality, which may reflect better patient selection, earlier device implantation, and improved management algorithms. In-depth understanding of these factors may inform the development of future treatment protocols.

Cardiology/Cardiovascular Research

Sparrow R, Sanjoy S, Choi YH, Elgendy IY, Jneid H, **Villablanca PA**, Holmes DR, Pershad A, Alraies C, Sposato LA, Mamas MA, and Bagur R. Racial, ethnic and socioeconomic disparities in patients undergoing left atrial appendage closure. *Heart* 2021; Epub ahead of print. PMID: 33795381. Full Text

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OBJECTIVE: This manuscript aims to explore the impact of race/ethnicity and socioeconomic status on in-hospital complication rates after left atrial appendage closure (LAAC). METHODS: The US National Inpatient Sample was used to identify hospitalisations for LAAC between 1 October 2015 to 31 December 2018. These patients were stratified by race/ethnicity and quartiles of median neighbourhood income. The primary outcome was the occurrence of in-hospital major adverse events, defined as a composite of postprocedural bleeding, cardiac and vascular complications, acute kidney injury and ischaemic stroke. RESULTS: Of 6478 unweighted hospitalisations for LAAC, 58% were male and patients of black, Hispanic and 'other' race/ethnicity each comprised approximately 5% of the cohort. Adjusted by the older Americans population, the estimated number of LAAC procedures was 69.2/100 000 for white individuals, as compared with 29.5/100 000 for blacks, 47.2/100 000 for Hispanics and 40.7/100 000 for individuals of 'other' race/ethnicity. Black patients were ~5 years younger but had a higher comorbidity burden. The primary outcome occurred in 5% of patients and differed significantly between racial/ethnic groups (p<0.001) but not across neighbourhood income quartiles (p=0.88). After multilevel modelling, the overall rate of in-hospital major adverse events was higher in black patients as compared with whites (OR: 1.60, 95% CI 1.22 to 2.10, p<0.001); however, the incidence of acute kidney injury was higher in Hispanics (OR: 2.19, 95% CI 1.52 to 3.17, p<0.001). No significant differences were found in adjusted overall in-hospital complication rates between income quartiles. CONCLUSION: In this study assessing racial/ethnic disparities in patients undergoing LAAC, minorities are under-represented, specifically patients of black race/ethnicity. Compared with whites, black patients had higher comorbidity burden and higher rates of in-hospital complications. Lower socioeconomic status was not associated with complication rates.

Cardiology/Cardiovascular Research

Valdez-Lowe C, **Parikh S**, and **Kenel KL**. Running a cardiology consult service during a pandemic: Experiences from the front lines. *J Am Assoc Nurse Pract* 2021; Epub ahead of print. PMID: 33927158. Full Text

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Millions of deaths worldwide have been attributed to the novel coronavirus (COVID-19). As case counts increased in the United States and resurgence occurred in Europe, health care systems across the country prepared for the influx of acutely ill patients. In response to this, our cardiology consult service was called to aid in the management of COVID-19 patients. We describe our experiences and the changes that were implemented.

Cardiology/Cardiovascular Research

Villablanca P, **Nona P**, **Lemor A**, **Qintar M**, **O'Neill B**, **Lee J**, **Frisoli T**, **Wang DD**, **Eng MH**, and **O'Neill WW**. Mechanical Circulatory Support in Cardiogenic Shock due to Structural Heart Disease. *Interv Cardiol Clin* 2021; 10(2):221-234. PMID: 33745671. Full Text

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Despite advances in cardiovascular care, managing cardiogenic shock caused by structural heart disease is challenging. Patients with cardiogenic shock are critically ill upon presentation and require early disease recognition and rapid escalation of care. Temporary mechanical circulatory support provides a higher level of care than current medical therapies such as vasopressors and inotropes. This review article focuses on the role of hemodynamic monitoring, mechanical circulatory support, and device selection in patients who present with cardiogenic shock due to structural heart disease. Early initiation of appropriate mechanical circulatory support may reduce morbidity and mortality.

Center for Health Policy and Health Services Research

Havewala M, Bowker JC, Smith KA, Rose-Krasnor L, Booth-LaForce C, Laursen B, **Felton JW**, and Rubin KH. Peer Influence during Adolescence: The Moderating Role of Parental Support. *Children (Basel)* 2021; 8(4). PMID: 33920622. Full Text

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Although many studies show that peers influence the development of adolescent internalizing and externalizing difficulties, few have considered both internalizing and externalizing difficulties in the same study, and fewer have considered the contributions of parents. Using a longitudinal sample of 385 adolescents, the contributions of best friends' internalizing and externalizing difficulties (as assessed in Grade 6; G6: M(age) = 13.64 years; 53% female; 40% ethnic or racial minority) were examined as they predicted subsequent adolescent internalizing and externalizing difficulties (at G8); in addition, the moderating role of both maternal and paternal support (at G6) was explored. Structural equation modelling revealed that best friend internalizing difficulties predicted decreases, but that best friend

externalizing difficulties predicted increases in adolescents' externalizing difficulties over time. Significant interactions involving both maternal and paternal support revealed that the negative impact of a G6 best friend having internalizing problems on later G8 adolescent externalizing problems was stronger at low levels of maternal and paternal support. The findings highlight the complex, and interactive, influences of friends and parents on the development of internalizing and externalizing symptomatology during adolescence, and underscore the importance of targeting both sources of social influence in research and clinical work.

Center for Health Policy and Health Services Research
Hecht LM, **Yeh HH**, **Braciszewski JM**, **Miller-Matero LR**, **Thakrar A**, **Patel S**, Simon GE, Lynch FL, Beck A, Owen-Smith AA, Rossom RC, Waitzfelder BE, Lu CY, Boggs JM, and **Ahmedani BK**. Weighing the Association Between BMI Change and Suicide Mortality. *Psychiatr Serv* 2021; Epub ahead of print. PMID: 33882679. Full Text

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OBJECTIVE: Suicide rates continue to rise, necessitating the identification of risk factors. Obesity and suicide mortality rates have been examined, but associations among weight change, death by suicide, and depression among adults in the United States remain unclear. METHODS: Data from 387 people who died by suicide in 2000-2015 with a recorded body mass index (BMI) in the first and second 6 months preceding their death ("index date") were extracted from the Mental Health Research Network. Each person was matched with five people in a control group (comprising individuals who did not die by suicide) by age, sex, index year, and health care site (N=1,935). RESULTS: People who died by suicide were predominantly male (71%), White (69%), and middle aged (mean age=57 years) and had a depression diagnosis (55%) and chronic health issues (57%) (corresponding results for the control group: 71% male, 66% White, 14% with depression diagnosis, and 43% with chronic health issues; mean age=56 years). Change in BMI within the year before the index date statistically significantly differed between those who died by suicide (mean change=-0.72±2.42 kg/m(2)) and the control group (mean change=0.06±4.99 kg/m(2)) ($p<0.001$, Cohen's $d=0.17$). A one-unit BMI decrease was associated with increased risk for suicide after adjustment for demographic characteristics, mental disorders, and Charlson comorbidity score (adjusted odds ratio=1.11, 95% confidence interval=1.05-1.18, $p<0.001$). For those without depression, a BMI change was significantly associated with suicide ($p<0.001$). CONCLUSIONS: An increased suicide mortality rate was associated with weight loss in the year before a suicide after analyses accounted for general and mental health indicators.

Center for Health Policy and Health Services Research
Nerenz DR, Austin JM, Deutscher D, Maddox KEJ, Nuccio EJ, Teigland C, Weinhandl E, and Glance LG. Adjusting Quality Measures For Social Risk Factors Can Promote Equity In Health Care. *Health Aff (Millwood)* 2021; 40(4):637-644. PMID: 33819097. Full Text

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Eric Weinhandl is a senior epidemiologist in the Chronic Disease Research Group at the Hennepin Healthcare Research Institute, in Minneapolis, Minnesota.
Laurent G. Glance is vice chair for research and a professor in the Department of Anesthesiology and Perioperative Medicine, University of Rochester School of Medicine, in Rochester, New York.

Risk adjustment of quality measures using clinical risk factors is widely accepted; risk adjustment using social risk factors remains controversial. We argue here that social risk adjustment is appropriate and necessary in defined circumstances and that social risk adjustment should be the default option when there are valid empirical arguments for and against adjustment for a given measure. Social risk adjustment is an important way to avoid exacerbating inequity in the health care system.

Dermatology
Boothby-Shoemaker W, **Lim HW**, **Kohli I**, and **Ozog DM**. Changes in Google search for "sunburn" during the COVID-19 pandemic. *Photodermatol Photoimmunol Photomed* 2021; Epub ahead of print. PMID: 33830570. Full Text

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Dermatology
Friedman BJ. Pitfall regarding expression of ETS-related gene (ERG) in fibrohistiocytic neoplasms. *J Cutan Pathol* 2021; Epub ahead of print. PMID: 33837979. Full Text

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Dermatology
Liu T, **Wang J**, **Subedi K**, **Yi Q**, **Zhou L**, and **Mi QS**. MicroRNA-155 Regulates MAIT1 and MAIT17 Cell Differentiation. *Front Cell Dev Biol* 2021; 9:670531. PMID: 33898469. Full Text

Department of Dermatology, Center for Cutaneous Biology and Immunology Research, Henry Ford Health System, Detroit, MI, United States.
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Mucosal-associated invariant T (MAIT) cells are innate-like T cells that develop in the thymus through three maturation stages to acquire effector function and differentiate into MAIT1 (T-bet(+)) and MAIT17 (RORγt(+)) subsets. Upon activation, MAIT cells release IFN-γ and IL-17, which modulate a broad spectrum of diseases. Recent studies indicate defective MAIT cell development in microRNA deficient mice, however, few individual miRNAs have been identified to regulate MAIT cells. MicroRNA-155 (miR-155) is a key regulator of numerous cellular processes that affect some immune cell development, but its role in MAIT cell development remains unclear. To address whether miR-155 is required for MAIT cell development, we performed gain-of-function and loss-of-function studies. We first generated a CD4Cre.miR-155 knock-in mouse model, in which miR-155 is over-expressed in the T cell lineage. We found that overexpression of miR-155 significantly reduced numbers and frequencies of MAIT cells in all immune organs and lungs and blocked thymic MAIT cell maturation through downregulating PLZF

expression. Strikingly, upregulated miR-155 promoted MAIT1 differentiation and blocked MAIT17 differentiation, and timely inducible expression of miR-155 functionally inhibited peripheral MAIT cells secreting IL-17. miR-155 overexpression also increased CD4(-)CD8(+) subset and decreased CD4(-)CD8(-) subset of MAIT cells. We further analyzed MAIT cells in conventional miR-155 knockout mice and found that lack of miR-155 also promoted MAIT1 differentiation and blocked MAIT17 differentiation but without alteration of their overall frequency, maturation and function. Overall, our results indicate that adequate miR-155 expression is required for normal MAIT1 and MAIT17 cell development and function.

Dermatology

McMahon DE, Amerson E, Rosenbach M, Lipoff JB, Moustafa D, Tyagi A, Desai SR, French LE, **Lim HW**, Thiers BH, Hruza GJ, Blumenthal KG, Fox LP, and Freeman EE. Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: A registry-based study of 414 cases. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 33838206. Full Text

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BACKGROUND: Cutaneous reactions after messenger RNA (mRNA)-based COVID-19 vaccines have been reported but are not well characterized. OBJECTIVE: To evaluate the morphology and timing of cutaneous reactions after mRNA COVID-19 vaccines. METHODS: A provider-facing registry-based study collected cases of cutaneous manifestations after COVID-19 vaccination. RESULTS: From December 2020 to February 2021, we recorded 414 cutaneous reactions to mRNA COVID-19 vaccines from Moderna (83%) and Pfizer (17%). Delayed large local reactions were most common, followed by local injection site reactions, urticarial eruptions, and morbilliform eruptions. Forty-three percent of patients with first-dose reactions experienced second-dose recurrence. Additional less common reactions included pernio/chilblains, cosmetic filler reactions, zoster, herpes simplex flares, and pityriasis rosea-like reactions. LIMITATIONS: Registry analysis does not measure incidence. Morphologic misclassification is possible. CONCLUSIONS: We report a spectrum of cutaneous reactions after mRNA COVID-19 vaccines. We observed some dermatologic reactions to Moderna and Pfizer vaccines that mimicked SARS-CoV-2 infection itself, such as pernio/chilblains. Most patients with first-dose reactions did not have a second-dose reaction and serious adverse events did not develop in any of the patients in the registry after the first or second dose. Our data support that cutaneous reactions to COVID-19 vaccination are generally minor and self-limited, and should not discourage vaccination.

Dermatology

Stein Gold L, and Dirschka T. Why We Should Consider Evidence-Based Treatment Options for Truncal Acne. *Dermatol Ther (Heidelb)* 2021; Epub ahead of print. PMID: 33871801. Full Text

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Dermatology
Tisack A, Fotouhi A, **Fidai C**, **Friedman BJ**, **Ozog D**, and **Veenstra J**. A Clinical and Biologic Review of Keratoacanthoma. *Br J Dermatol* 2021; Epub ahead of print. PMID: 33864244. Full Text

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Keratoacanthoma (KA) is a common skin tumor that remains controversial regarding classification, epidemiology, diagnosis, prognosis, and management. Classically, a KA manifests as a rapidly growing, well-differentiated, squamoid lesion with a predilection for sun-exposed sites in the elderly and a tendency to spontaneously regress. Historically, KAs have been considered a variant of cutaneous squamous cell carcinoma (cSCC) and are often reported as KA-type cSCC. However, the penchant for regression has led many to categorize KAs as biologically benign tumors with distinct pathophysiological mechanisms than malignant cSCC. The clinical and histopathological similarities between KA and cSCC, particularly the well-differentiated variant of cSCC, have made definitive differentiation difficult or impossible in many cases. The ambiguity between entities has led to the general recommendation for surgical excision of KA to ensure a potentially malignant cSCC is not left untreated. This current standard creates unnecessary surgical morbidity and financial strain for patients, especially the at-risk elderly population. There have been no reports of death from a definitive KA to date, while cSCC has an approximate mortality rate of 1.5%. Reliably distinguishing cSCC from KA would shift management strategies for KAs toward less-invasive treatment modalities, prevent unnecessary surgical morbidity, and likely reduce associated healthcare costs. Herein, we review the pathophysiology and clinical characteristics of KA, and conclude on the balance of current evidence that KA is a benign and distinct lesion from cSCC.

Dermatology
Veenstra J, **Dimitrion P**, **Yao Y**, **Zhou L**, **Ozog D**, and **Mi QS**. Research Techniques Made Simple: Use of Imaging Mass Cytometry for Dermatological Research and Clinical Applications. *J Invest Dermatol* 2021; 141(4):705-712.e701. PMID: 33752807. Full Text

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Traditional immunohistochemistry (IHC) is inherently limited by its ability to analyze only several markers within a histological tissue section at a given time, which hinders in-depth characterization and phenotyping of tissues. Imaging mass cytometry (IMC), which combines IHC using metal-labeled antibodies with laser ablation and detection using mass cytometry by time-of-flight, overcomes this limitation with the capability to simultaneously analyze up to 40 protein markers to generate high-dimensional images from a single tissue section. IMC analysis preserves tissue architecture and spatial cellular relationships that would otherwise be lost or significantly altered in applications requiring tissue dissociation, such as flow cytometry or single-cell RNA sequencing. Resulting high-dimensional

histological images permit spatially conserved analysis to identify unique cell populations, cellular interactions and avoidances, and insight into activation and behavioral status based on tissue location. IMC can be performed on both frozen and formalin-fixed paraffin-embedded tissue, allowing for previously banked samples to be analyzed and correlated with known clinical outcomes. Expectedly, IMC will change the landscape of investigative pathology, particularly when used in coordination with multiomic platforms to combine transcriptomic and proteomic data at a single-cell resolution. Here, we aim to highlight the potential utility of IMC within dermatologic research and clinical applications.

Dermatology

Vellaichamy G, **Dimitrion P**, **Zhou L**, **Ozog D**, **Lim HW**, Liao W, **Hamzavi IH**, and **Mi QS**. Insights from γ-Secretase: Functional Genetics of Hidradenitis Suppurativa. *J Invest Dermatol* 2021; Epub ahead of print. PMID: 33836848. Full Text

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Hidradenitis suppurativa (HS) is a chronic, relapsing, and remitting inflammatory disease of the skin with significant heritability and racial disposition. The pathogenesis of HS remains enigmatic, but occlusion of the terminal hair follicle and dysregulation of the local innate immune response may contribute to pathogenesis. Genetic predisposition might also contribute to disease susceptibility and phenotypic heterogeneity because mutations in γ-secretase have been found to underlie a minor but characteristic subset of patients with HS. In this review, we synthesized the current data on γ-secretase in HS, evaluated its importance in the context of disease pathobiology, and discussed avenues of future studies.

Diagnostic Radiology

Mohamed GA, **Aboul Nour H**, Nogueira RG, Mohammaden MH, Haussen DC, Al-Bayati AR, Nguyen TN, Abdalkader M, Kaliaev A, Ma A, Fifi J, Morey J, Yavagal DR, Saini V, Ortega-Gutierrez S, Farooqui M, Zevallos CB, Quispe-Orozco D, **Schultz L**, **Kole M**, **Miller D**, Mayer SA, **Marin H**, and **Bou Chebl A**. Repeated Mechanical Endovascular Thrombectomy for Recurrent Large Vessel Occlusion: A Multicenter Experience. *Stroke* 2021; Epub ahead of print. PMID: 33910367. Full Text

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BACKGROUND AND PURPOSE: Mechanical thrombectomy (MT) is now the standard of care for large vessel occlusion (LVO) stroke. However, little is known about the frequency and outcomes of repeat MT (rMT) for patients with recurrent LVO. METHODS: This is a retrospective multicenter cohort of patients who underwent rMT at 6 tertiary institutions in the United States between March 2016 and March 2020. Procedural, imaging, and outcome data were evaluated. Outcome at discharge was evaluated using the modified Rankin Scale. RESULTS: Of 3059 patients treated with MT during the study period, 56 (1.8%) underwent at least 1 rMT. Fifty-four (96%) patients were analyzed; median age was 64 years. The median time interval between index MT and rMT was 2 days; 35 of 54 patients (65%) experienced recurrent LVO during the index hospitalization. The mechanism of stroke was cardioembolism in 30 patients (56%), intracranial atherosclerosis in 4 patients (7%), extracranial atherosclerosis in 2 patients (4%), and other causes in 18 patients (33%). A final TICI recanalization score of 2b or 3 was achieved in all 54 patients during index MT (100%) and in 51 of 54 patients (94%) during rMT. Thirty-two of 54 patients (59%) experienced recurrent LVO of a previously treated artery, mostly the pretreated left MCA (23 patients, 73%). Fifty of the 54 patients (93%) had a documented discharge modified Rankin Scale after rMT: 15 (30%) had minimal or no disability (modified Rankin Scale score ≤2), 25 (50%) had moderate to severe disability (modified Rankin Scale score 3-5), and 10 (20%) died. CONCLUSIONS: Almost 2% of patients treated with MT experience recurrent LVO, usually of a previously treated artery during the same hospitalization. Repeat MT seems to be safe and effective for attaining vessel recanalization, and good outcome can be expected in 30% of patients.

Diagnostic Radiology

Morris ED, **Ghanem AI**, **Zhu S**, Dong M, **Pantelic MV**, and Glide-Hurst CK. Quantifying inter-fraction cardiac substructure displacement during radiotherapy via magnetic resonance imaging guidance. *Physics and Imaging in Radiation Oncology* 2021; 18:34-40. PMID: Not assigned. Full Text

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Emerging evidence suggests cardiac substructures are highly radiosensitive during radiation therapy for cancer treatment. However, variability in substructure position after tumor localization has not been well characterized. This study quantifies inter-fraction displacement and planning organ at risk volumes (PRVs) of substructures by leveraging the excellent soft tissue contrast of magnetic resonance imaging (MRI). Eighteen retrospectively evaluated patients underwent radiotherapy for intrathoracic tumors with a 0.35 T MRI-guided linear accelerator. Imaging was acquired at a 17–25 s breath-hold (resolution 1.5 × 1.5 × 3 mm3). Three to four daily MRIs per patient (n = 71) were rigidly registered to the planning MRI-simulation based on tumor matching. Deep learning or atlas-based segmentation propagated 13 substructures (e.g., chambers, coronary arteries, great vessels) to daily MRIs and were verified by two radiation oncologists. Daily centroid displacements from MRI-simulation were quantified and PRVs were calculated. Across substructures, inter-fraction displacements for 14% in the left–right, 18% in the anterior-posterior, and 21% of fractions in the superior-inferior were > 5 mm. Due to lack of breath-hold compliance, ~4% of all structures shifted > 10 mm in any axis. For the chambers, median displacements were 1.8, 1.9, and 2.2 mm in the left–right, anterior-posterior, and superior-inferior axis, respectively. Great vessels demonstrated larger displacements (> 3 mm) in the superior-inferior axis (43% of shifts) and were only 25% (left–right) and 29% (anterior-posterior) elsewhere. PRVs from 3 to 5 mm were determined as anisotropic substructure-specific margins. This exploratory work derived substructure-specific safety margins to ensure highly effective cardiac sparing. Findings require validation in a larger cohort for robust margin derivation and for applications in prospective clinical trials.

Diagnostic Radiology

Zintsmaster MP, and **Myers DT**. Patients avoided important care during the early weeks of the coronavirus pandemic: diverticulitis patients were more likely to present with an abscess on CT. *Emerg Radiol* 2021; 28(2):279-282. PMID: 32979139. Full Text

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PURPOSE: To evaluate the frequency with which patients with an urgent health concern, specifically diverticulitis, avoided appropriate medical care during the early weeks of the coronavirus pandemic of 2020 and to study the consequences of the resultant delay in care, the incidence of an associated abscess. METHODS: This study was institutional review board approved. Reports for CT studies with findings of newly diagnosed diverticulitis within Henry Ford Health System during the early weeks of the coronavirus pandemic of 2020 were reviewed and compared with the same time period in 2019. Total cases of diverticulitis on CT were compared, as well as the prevalence of an associated abscess. A chi-squared analysis was performed to determine the statistical significance of the percentage of patients presenting with an abscess in each year. RESULTS: During the early weeks of the coronavirus pandemic, 120 patients were identified with CT findings of newly diagnosed diverticulitis with 11.7% of those patients (14 patients) presenting with an associated abscess. During the same time period in 2019, many more CT studies with newly diagnosed diverticulitis were obtained (339), and, compared to 2020, less than half the percentage of those patients had an associated abscess (4.4% or 15 patients). CONCLUSION: Patients with urgent health concerns avoided appropriate and necessary care during the early weeks of the coronavirus pandemic. While non-COVID-19 emergency visits were diminished, patients who did present with diverticulitis were more likely to present with greater disease severity as manifested by an associated abscess. Patients must be encouraged to seek care when appropriate and need reassurance that hospitals and their emergency departments are safe to visit. Furthermore, emergency physicians and radiologists in particular should be vigilant during times when emergency volumes are low, such as a future surge in coronavirus patients, other pandemics, snow storms, and holidays as the patients who do present for care are more likely to present at later stages and with serious complications.

Emergency Medicine

McDonald L, **Illg Z**, **Dow A**, and **Gunaga S**. Maternity Experiences and Perceptions of Emergency Medicine Physicians. *Spartan Med Res J* 2021; 6(1):22009. PMID: 33870004. Full Text

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INTRODUCTION: Postpartum employment has been recognized as a significant obstacle to breastfeeding continuation rates in the general population. Multiple additional factors can influence emergency medicine (EM) physician mothers' ability to continue breastfeeding upon return to work. These include the unpredictable nature of emergency room volumes and acuity, absence of protected lactation time or facilities, and varying levels of support from colleagues. This study investigated a sample of female EM physicians' current perceptions and experiences regarding breastfeeding practices and identified modifiable work-place factors affecting their decision to wean. The authors hypothesized that EM physician mothers would have excellent breastfeeding initiation rates but be largely unable to maintain breastfeeding practices upon returning to work. METHODS: A 34-item survey questionnaire evaluated demographics, perceptions, and experiences with breastfeeding with a convenience sample of EM attending and resident physicians from two Michigan academic community hospitals. RESULTS: Thirty-nine surveys were completed, representing a participant response rate of 88.6%. Breastfeeding had been initiated by all respondent mothers, all of whom returned to full-time employment after delivery. Upon return to work, 15 (75%) respondents continued to exclusively breastfeed. The goal of participants was to breastfeed for an average of 7.1 months (± 4.1 months), although the average duration children were exclusively breastfed was 5.8 months (± 4.0 months). CONCLUSIONS: Based on these results, the reasons for decreased breastfeeding after return to work in an EM residency program setting are

multifactorial and include some modifiable interpersonal and institutional influences. These findings support the implementation of work-place strategies and policies to promote successful breastfeeding practices among EM resident and attending physician mothers returning to work.

Emergency Medicine

Mikhjian G, **Elghoroury A**, **Cronovich K**, **Brody K**, and Jarski R. Using Quantitative D-Dimer to Determine the Need for Pulmonary CT Angiography in COVID-19 Patients. *Spartan Med Res J* 2021; 6(1):18652. PMID: 33870000. Full Text

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INTRODUCTION: COVID-19 has been frequently cited as a condition causing a pro-inflammatory state leading to hypercoagulopathy and increased risk for venous thromboembolism. This condition has thus prompted prior studies and screening models that utilize D-dimer for pulmonary embolism (PE) into question. The limited research to date has failed to provide tools or guidance regarding what COVID-19 positive patients should receive pulmonary CT angiography screening. This knowledge gap has led to missed diagnoses, CT overutilization, and increased morbidity and mortality. OBJECTIVE: The purpose of this study was to examine the utility of the quantitative D-dimer lab marker in a convenience sample of 426 COVID-19 positive patients to assist providers in determining the utility of pulmonary CT angiography. METHODS: The authors conducted a retrospective analysis on all COVID-19 positive patients within the Henry Ford Medical System between March 1st, 2020 through April 30th, 2020 who received pulmonary CT angiography and had a quantitative D-dimer lab drawn within 24 hours of CT imaging. RESULTS: Our sampling criteria yielded a total of n = 426 patients, of whom 347 (81.5%) were negative for PE and 79 (18.5%) were positive for PE. The average D-dimer in the negative PE group was 2.95 µg./mL. (SD 4.26), significantly different than the 9.15 µg./mL. (SD 6.80) positive PE group ($P < 0.05$; 95% CI -7.8, -4.6). Theoretically, applying the traditional ≤ 0.5 µg./mL. D-dimer cut-off to our data would yield a sensitivity of 100% and specificity of 7.49% for exclusion of PE. Based on these results, the authors would be able to increase the D-dimer threshold to < 0.89 µg./mL. to maintain their sensitivity to 100% and raise the specificity to 27.95%. Observing a D-dimer cut-off value of ≤ 1.28 µg./mL. would reduce sensitivity to 97.47% but increase the specificity to 57.93%. CONCLUSIONS: These study results support the utilization of alternative D-dimer thresholds to exclude PE in COVID-19 patients. Based on these findings, providers may be able to observe increased D-dimer cut-off values to reduce unnecessary pulmonary CT angiography scans.

Emergency Medicine

Stein PD, Matta F, Hughes PG, Gerstner BJ, Hatoum Z, Berens N, Hanover KR, **Kakish EJ**, and Hughes MJ. Usefulness of ancillary findings on CT pulmonary angiograms that are negative for pulmonary embolism. *Thromb Res* 2021; 200:48-50. PMID: 33540291. Full Text

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Endocrinology and Metabolism

Galindo RJ, Parkin CG, Aleppo G, Carlson AL, **Kruger DF**, Levy CJ, Umpierrez GE, and McGill JB. What's Wrong with This Picture? A Critical Review of Current Centers for Medicare & Medicaid Services Coverage Criteria for Continuous Glucose Monitoring. *Diabetes Technol Ther* 2021; Epub ahead of print. PMID: 33844588. Request Article

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Numerous studies have demonstrated the clinical value of continuous glucose monitoring (CGM) in type 1 diabetes and type 2 diabetes populations. However, the eligibility criteria for CGM coverage required by the Centers for Medicare & Medicaid Services (CMS) ignore conclusive evidence that supports CGM use in various diabetes populations that are currently deemed ineligible. This article discusses the limitations and inconsistencies of the CMS eligibility criteria relative to current scientific evidence and proposes workable solutions to address this issue and improve the safety and care of all individuals with diabetes.

Family Medicine

Mikhjian G, **Elghoroury A**, **Cronovich K**, **Brody K**, and Jarski R. Using Quantitative D-Dimer to Determine the Need for Pulmonary CT Angiography in COVID-19 Patients. *Spartan Med Res J* 2021; 6(1):18652. PMID: 33870000. Full Text

Henry Ford Macomb.
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INTRODUCTION: COVID-19 has been frequently cited as a condition causing a pro-inflammatory state leading to hypercoagulopathy and increased risk for venous thromboembolism. This condition has thus prompted prior studies and screening models that utilize D-dimer for pulmonary embolism (PE) into question. The limited research to date has failed to provide tools or guidance regarding what COVID-19 positive patients should receive pulmonary CT angiography screening. This knowledge gap has led to missed diagnoses, CT overutilization, and increased morbidity and mortality. OBJECTIVE: The purpose of this study was to examine the utility of the quantitative D-dimer lab marker in a convenience sample of 426 COVID-19 positive patients to assist providers in determining the utility of pulmonary CT angiography. METHODS: The authors conducted a retrospective analysis on all COVID-19 positive patients within the Henry Ford Medical System between March 1st, 2020 through April 30th, 2020 who

received pulmonary CT angiography and had a quantitative D-dimer lab drawn within 24 hours of CT imaging. RESULTS: Our sampling criteria yielded a total of n = 426 patients, of whom 347 (81.5%) were negative for PE and 79 (18.5%) were positive for PE. The average D-dimer in the negative PE group was 2.95 µg./mL. (SD 4.26), significantly different than the 9.15 µg./mL. (SD 6.80) positive PE group (P < 0.05; 95% CI -7.8, -4.6). Theoretically, applying the traditional ≤ 0.5 µg./mL. D-dimer cut-off to our data would yield a sensitivity of 100% and specificity of 7.49% for exclusion of PE. Based on these results, the authors would be able to increase the D-dimer threshold to < 0.89 µg./mL. to maintain their sensitivity to 100% and raise the specificity to 27.95%. Observing a D-dimer cut-off value of ≤ 1.28 µg./mL. would reduce sensitivity to 97.47% but increase the specificity to 57.93%. CONCLUSIONS: These study results support the utilization of alternative D-dimer thresholds to exclude PE in COVID-19 patients. Based on these findings, providers may be able to observe increased D-dimer cut-off values to reduce unnecessary pulmonary CT angiography scans.

Gastroenterology

Gonzalez HC, **Trudeau S**, and **Gordon SC**. Editorial: Changing trends in the US prevalence of hepatitis B core antibody provide important perspectives into future screening and vaccination strategies. *J Infect Dis* 2021; Epub ahead of print. PMID: 33903913. Full Text

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Gastroenterology

Shen B, Kochhar GS, Navaneethan U, Cross RK, Farraye FA, Iacucci M, Schwartz DA, Gonzalez-Lama Y, **Schairer J**, Kiran RP, Kotze PG, Kobayashi T, Bortlik M, Liu X, Levy AN, González Suárez B, Tang SJ, Coelho-Prabhu N, Lukas M, Bruining DH, El-Hachem S, Charles RJ, Chen Y, Sood A, Mao R, Loras C, Dulai PS, Picoraro JA, Chiorean M, Lukas M, Shergill A, Silverberg MS, Sandborn WJ, and Bernstein CN. Endoscopic evaluation of surgically altered bowel in inflammatory bowel disease: a consensus guideline from the Global Interventional Inflammatory Bowel Disease Group. *Lancet Gastroenterol Hepatol* 2021; Epub ahead of print. PMID: 33872568. Request Article

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The majority of patients with Crohn's disease and a proportion of patients with ulcerative colitis will ultimately require surgical treatment despite advances in diagnosis, therapy, and endoscopic interventions. The surgical procedures that are most commonly done include bowel resection with anastomosis, strictureplasty, faecal diversion, and ileal pouch. These surgical treatment modalities result in substantial alterations in bowel anatomy. In patients with inflammatory bowel disease, endoscopy plays a key role in the assessment of disease activity, disease recurrence, treatment response, dysplasia surveillance, and delivery of endoscopic therapy. Endoscopic evaluation and management of surgically altered bowel can be challenging. This consensus guideline delineates anatomical landmarks and endoscopic assessment of these landmarks in diseased and surgically altered bowel.

Global Health Initiative

Quirós RE, **Bardossy AC**, Angeleri P, Zurita J, Aleman Espinoza WR, Carneiro M, Guerra S, Medina J, Castañeda Luquerna X, Guerra A, Vega S, Cuellar Ponce de Leon LE, Munita J, Escobar ED, **Maki G**, **Prentiss T**, and **Zervos M**. Antimicrobial stewardship programs in adult intensive care units in Latin America: Implementation, assessments, and impact on outcomes. *Infect Control Hosp Epidemiol* 2021; Epub ahead of print. PMID: 33829982. Full Text

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Wayne State University School of Medicine, Detroit, Michigan, United States.

OBJECTIVE: To assess the impact of antimicrobial stewardship programs (ASPs) in adult medical-surgical intensive care units (MS-ICUs) in Latin America. DESIGN: Quasi-experimental prospective with continuous time series. SETTING: The study included 77 MS-ICUs in 9 Latin American countries. PATIENTS: Adult patients admitted to an MS-ICU for at least 24 hours were included in the study. METHODS: This multicenter study was conducted over 12 months. To evaluate the ASPs, representatives from all MS-ICUs performed a self-assessment survey (0-100 scale) at the beginning and end of the study. The impact of each ASP was evaluated monthly using the following measures: antimicrobial consumption, appropriateness of antimicrobial treatments, crude mortality, and multidrug-resistant microorganisms in healthcare-associated infections (MDRO-HAIs). Using final stewardship program quality self-assessment scores, MS-ICUs were stratified and compared among 3 groups: ≤25th percentile, >25th to <75th percentile, and ≥75th percentile. RESULTS: In total, 77 MS-ICU from 9 Latin American countries completed the study. Twenty MS-ICUs reached at least the 75th percentile at the end of the study in comparison with the same number who remain within the 25th percentile (score, 76.1 ± 7.5 vs 28.0 ± 7.3; P < .0001). Several indicators performed better in the MS-ICUs in the 75th versus 25th percentiles: antimicrobial consumption (143.4 vs 159.4 DDD per 100 patient days; P < .0001), adherence to clinical guidelines (92.5% vs 59.3%; P < .0001), validation of prescription by pharmacist (72.0% vs 58.0%; P < .0001), crude mortality (15.9% vs 17.7%; P < .0001), and MDRO-HAIs (9.45 vs 10.96 cases per 1,000 patient days; P = .004). CONCLUSION: MS-ICUs with more comprehensive ASPs showed significant improvement in antimicrobial utilization.

Hematology-Oncology

Gadgeel SM. Patient-Reported Outcomes in the Era of Immunotherapy Trials. *J Thorac Oncol* 2021; 16(4):516-518. PMID: 33781441. Full Text

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Hematology-Oncology

Nhean S, **Kostoff D**, **Yang JJ**, **Vogel V**, and **Rybkin, II**. Impact of Oral Chemotherapy Management Program on Capecitabine Toxicity Management. *JCO Oncol Pract* 2021; Epub ahead of print. PMID: 33900803. Request Article

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PURPOSE: Increasing use of oral chemotherapy has created unique challenges related to patient safety and compliance. To address this issue, the Henry Ford Cancer Institute at Henry Ford Health System developed and implemented a system-wide, multidisciplinary program named the Oral Chemotherapy Management Program (OCMP). The purpose of this study was to evaluate the impact of OCMP on patient outcomes in those receiving capecitabine. METHODS: This was a retrospective, quasi-experimental study that compared outcomes in patients receiving capecitabine before and after OCMP implementation. The co-primary outcomes were incidence(s) of grade 1-4 and grade 3-4 adverse effects (AEs) associated with capecitabine. Secondary outcomes were emergency department (ED) visits, hospitalizations because of toxicity, and adherence rate. RESULTS: OCMP patients had significantly lower overall incidence of AE of any grade (58.9% v 70.3%; 95% CI, 0.39 to 0.94; P = .03). OCMP implementation significantly lowered incidence of any grade and grade 3-4 nausea, vomiting, and/or diarrhea, and grade 3-4 hand-foot syndrome. It resulted in the decreased number of ED visits (8.9% v 18.9%; P = .005) and hospitalizations (6.3% v 17.1%; P = .002), as well as improved medication adherence rates (0.94 v 0.97; P = .03). CONCLUSION: Most patients who developed capecitabine-related AE required intervention by OCMP. Implementation of OCMP reduced the incidence of high-grade AE, decreased the number of ED visits and hospitalizations because of AE, and improved the medication adherence rate.

Hematology-Oncology

Qin A, Zhao S, Miah A, Wei L, Patel S, Johns A, Grogan M, Bertino EM, He K, Shields PG, Kalemkerian GP, **Gadgeel SM**, Ramnath N, Schneider BJ, Hassan KA, Szerlip N, Chopra Z, Journey S, Waninger J, Spakowicz D, Carbone DP, Presley CJ, Otterson GA, Green MD, and Owen DH. Bone Metastases, Skeletal-Related Events, and Survival in Patients With Metastatic Non-Small Cell Lung Cancer Treated With Immune Checkpoint Inhibitors. *J Natl Compr Canc Netw* 2021; Epub ahead of print. PMID: 33878726. Request Article

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BACKGROUND: Bone metastases and skeletal-related events (SREs) are a frequent cause of morbidity in patients with metastatic non-small cell lung cancer (mNSCLC). Data are limited on bone metastases and SREs in patients with mNSCLC treated using immune checkpoint inhibitors (ICIs), and on the efficacy of bone-modifying agents (BMAs) in this setting. Here we report the incidence, impact on survival, risk factors for bone metastases and SREs, and impact of BMAs in patients with mNSCLC treated with ICIs in a multi-institutional cohort. PATIENTS AND METHODS: We conducted a retrospective study of patients with mNSCLC treated with ICIs at 2 tertiary care centers from 2014 through 2017. Overall survival (OS) was compared between patients with and without baseline bone metastases using a log-rank test. A Cox regression model was used to evaluate the association between OS and the presence of bone metastases at ICI initiation, controlling for other confounding factors. RESULTS: We identified a cohort of 330 patients who had received ICIs for metastatic disease. Median patient age was 63 years, most patients were treated in the second line or beyond (n=259; 78%), and nivolumab was the most common ICI (n=211; 64%). Median OS was 10 months (95% CI, 8.4-12.0). In our cohort, 124 patients (38%) had baseline bone metastases, and 43 (13%) developed SREs during or after ICI treatment. Patients with bone metastases had a higher hazard of death after controlling for performance status, histology, line of therapy, and disease burden (hazard ratio, 1.57; 95% CI, 1.19-2.08; P=.001). Use of BMAs was not associated with OS or a decreased risk of SREs. CONCLUSIONS: Presence of bone metastases at baseline was associated with a worse prognosis for patients with mNSCLC treated with ICI after controlling for multiple clinical characteristics. Use of BMAs was not associated with reduced SREs or a difference in survival.

Hospital Medicine

Cramer-Bour C, Peterson J, Walsh B, and Klings ES. Common Complications of Sickle Cell Disease: A Simulation-Based Curriculum. *MedEdPORTAL* 2021; 17:11139. PMID: 33851012. Full Text

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INTRODUCTION: Sickle cell disease (SCD), the most common autosomal recessive genetic disorder worldwide, affects nearly every organ of the body and results in accelerated mortality. Nationally, internal medicine physicians lack a complete understanding of morbidity and mortality in this population leading to health care disparities. METHODS: We created a 2-hour curriculum consisting of three SCD case vignettes representing common disease complications (acute stroke, acute chest syndrome, and septic shock) with the goal to increase medicine house staff knowledge and confidence in patient management. Residents completed a pretest to assess baseline knowledge and were divided into groups of four to five.

Three simulation cases were completed by each group; learners needed to work through a differential diagnosis and describe key management steps. Each group was graded on achieving the 10 critical actions for each case. Following each case, there was a faculty-led debriefing session. Residents repeated the pretest 30 days after completion of the curriculum (posttest). RESULTS: Thirty-six second year internal medicine residents participated in this curriculum. After completing this curriculum, residents improved their test score from 33% (SD = 12%) to 57% (SD = 18%) ($p < .0001$). Additionally, self-reported confidence in management scores increased from 2.6 (SD = 0.8) in the pretest to 3.5 (SD = 0.4) in the posttest ($p = .02$) on a 5-point Likert scale (1 = not very confident, 5 = very confident). DISCUSSION: Use of a simulation curriculum increased knowledge and confidence of internal medicine residents in the management of critical illness in patients with SCD.

Hospital Medicine

Schaefer JK, Errickson J, Li Y, Kong X, Alexandris-Souphis T, Ali MA, Decamillo D, Haymart B, **Kaatz S**, Kline-Rogers E, Kozlowski JH, **Krol GD**, Shankar SR, Sood SL, Froehlich JB, and Barnes GD. Adverse Events Associated With the Addition of Aspirin to Direct Oral Anticoagulant Therapy Without a Clear Indication. *JAMA Intern Med* 2021; Epub ahead of print. PMID: 33871544. Full Text

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Department of Cardiovascular Medicine, Huron Valley Sinai Hospital, Commerce Township, Michigan.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan.

IMPORTANCE: It is unclear how many patients treated with a direct oral anticoagulant (DOAC) are using concomitant acetylsalicylic acid (ASA, or aspirin) and how this affects clinical outcomes. OBJECTIVE: To evaluate the frequency and outcomes of prescription of concomitant ASA and DOAC therapy for patients with atrial fibrillation (AF) or venous thromboembolic disease (VTE). DESIGN, SETTING, AND PARTICIPANTS: This registry-based cohort study took place at 4 anticoagulation clinics in Michigan from January 2015 to December 2019. Eligible participants were adults undergoing treatment with a DOAC for AF or VTE, without a recent myocardial infarction (MI) or history of heart valve replacement, with at least 3 months of follow-up. EXPOSURES: Use of ASA concomitant with DOAC therapy. MAIN OUTCOMES AND MEASURES: Rates of bleeding (any, nonmajor, major), rates of thrombosis (stroke, VTE, MI), emergency department visits, hospitalizations, and death. RESULTS: Of the study cohort of 3280 patients (1673 [51.0%] men; mean [SD] age 68.2 [13.3] years), 1107 (33.8%) patients without a clear indication for ASA were being treated with DOACs and ASA. Two propensity score-matched cohorts, each with 1047 patients, were analyzed (DOAC plus ASA and DOAC only). Patients were followed up for a mean (SD) of 20.9 (19.0) months. Patients taking DOAC and ASA experienced more bleeding events compared with DOAC monotherapy (26.0 bleeds vs 31.6 bleeds per 100 patient years, $P = .01$). Specifically, patients undergoing combination therapy had significantly higher rates of nonmajor bleeding (26.1 bleeds vs 21.7 bleeds per 100 patient years, $P = .02$) compared with DOAC monotherapy. Major bleeding rates were similar between the 2 cohorts. Thrombotic event rates were also similar between the cohorts (2.5 events vs 2.3 events per 100 patient years for patients treated with DOAC and ASA compared with DOAC monotherapy, $P = .80$). Patients were more often hospitalized while undergoing combination therapy (9.1 vs 6.5 admissions per 100 patient years, $P = .02$). CONCLUSION AND RELEVANCE: Nearly one-third of patients with AF and/or VTE who were treated with a DOAC received ASA without a clear indication. Compared with DOAC monotherapy, concurrent DOAC and ASA use was associated with increased bleeding and hospitalizations but similar observed thrombosis rate. Future research should identify and deprescribe ASA for patients when the risk exceeds the anticipated benefit.

Hospital Medicine

Sheikh MA, Kong X, Haymart B, **Kaatz S**, **Krol G**, Kozlowski J, Dahu M, Ali M, Almany S, Alexandris-Souphis T, Kline-Rogers E, Froehlich JB, and Barnes GD. Comparison of temporary interruption with continuation of direct oral anticoagulants for low bleeding risk procedures. *Thromb Res* 2021; 203:27-32. PMID: 33906063. Full Text

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INTRODUCTION: Limited data is available on the rates of bleeding and thromboembolic events for patients undergoing low bleeding risk procedures while taking direct oral anticoagulants (DOAC). METHODS: Adults taking DOAC in the Michigan Anticoagulation Quality Improvement Initiative (MAQI(2)) database who underwent a low bleeding risk procedure between May 2015 and Sep 2019 were included. Thirty-day bleeding (of any severity), thromboembolic events, and death were compared between DOAC temporarily interrupted and continued uninterrupted groups. Adverse event rates were compared using an inverse probability weighting propensity score. RESULTS: There were 820 patients who underwent 1412 low risk procedures. DOAC therapy was temporarily interrupted in 371 (45.2%) patients (601 [42.6%] procedures) and continued uninterrupted in 449 (54.8%) patients (811 [57.4%] procedures). DOAC patients with temporary interruptions were more likely to have diabetes, prior stroke or TIA, prior bleeding, higher CHA2DS2-VASc, and higher modified HAS-BLED scores. DOAC interruption was common for gastrointestinal endoscopy, electrophysiology device implantation, and cardiac catheterization while it was less common for cardioversion, dermatologic procedures, and subcutaneous injection. After propensity score adjustment, bleeding risk was lower in the DOAC temporary interruption group (OR 0.62, 95% CI 0.41-0.95) as compared to the group with continuous DOAC use. Rates of thromboembolic events and death did not differ significantly between the two groups. CONCLUSIONS: DOAC-treated patients undergoing low bleeding risk procedures may experience lower rates of bleeding when DOAC is temporarily interrupted. Prospective studies focused on low bleeding risk procedures are needed to identify the safety DOAC management strategy.

Hypertension and Vascular Research

Roy B, and **Palaniyandi SS**. Tissue-specific role and associated downstream signaling pathways of adiponectin. *Cell Biosci* 2021; 11(1):77. PMID: 33902691. Full Text

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According to the World Health Organization, metabolic syndrome (MetS) can be defined as a pathological condition characterized by abdominal obesity, insulin resistance, hypertension, and hyperlipidemia. The incidence of MetS keeps rising, as at least 35% of the USA population suffers from MetS. One of the worst comorbidities of metabolic syndrome are cardiovascular diseases that significantly amplifies the mortality associated with this syndrome. There is an urgent need to understand the pathophysiology of MetS to find novel diagnosis, treatment and management to mitigate the MetS and associated complications. Altered circulatory adiponectin levels have been implicated in MetS. Adiponectin has numerous biologic functions including antioxidative, anti-nitrative, anti-inflammatory, and cardioprotective

effects. Being a pleiotropic hormone of multiple tissues, tissue-specific key signaling pathways of adiponectin will help finding specific target/s to blunt the pathophysiology of metabolic syndrome and associated disorders. The purpose of this review is to elucidate tissue-specific signaling pathways of adiponectin and possibly identify potential therapeutic targets for MetS as well as to evaluate the potential of adiponectin as a biomarker/therapeutic option in MetS.

Infectious Diseases

Quirós RE, **Bardossy AC**, Angeleri P, Zurita J, Aleman Espinoza WR, Carneiro M, Guerra S, Medina J, Castañeda Luquerna X, Guerra A, Vega S, Cuellar Ponce de Leon LE, Munita J, Escobar ED, **Maki G**, **Prentiss T**, and **Zervos M**. Antimicrobial stewardship programs in adult intensive care units in Latin America: Implementation, assessments, and impact on outcomes. *Infect Control Hosp Epidemiol* 2021; Epub ahead of print. PMID: 33829982. Full Text

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Wayne State University School of Medicine, Detroit, Michigan, United States.

OBJECTIVE: To assess the impact of antimicrobial stewardship programs (ASPs) in adult medical-surgical intensive care units (MS-ICUs) in Latin America. DESIGN: Quasi-experimental prospective with continuous time series. SETTING: The study included 77 MS-ICUs in 9 Latin American countries. PATIENTS: Adult patients admitted to an MS-ICU for at least 24 hours were included in the study. METHODS: This multicenter study was conducted over 12 months. To evaluate the ASPs, representatives from all MS-ICUs performed a self-assessment survey (0-100 scale) at the beginning and end of the study. The impact of each ASP was evaluated monthly using the following measures: antimicrobial consumption, appropriateness of antimicrobial treatments, crude mortality, and multidrug-resistant microorganisms in healthcare-associated infections (MDRO-HAIs). Using final stewardship program quality self-assessment scores, MS-ICUs were stratified and compared among 3 groups: ≤25th percentile, >25th to <75th percentile, and ≥75th percentile. RESULTS: In total, 77 MS-ICU from 9 Latin American countries completed the study. Twenty MS-ICUs reached at least the 75th percentile at the end of the study in comparison with the same number who remain within the 25th percentile (score, 76.1 ± 7.5 vs 28.0 ± 7.3; P < .0001). Several indicators performed better in the MS-ICUs in the 75th versus 25th percentiles: antimicrobial consumption (143.4 vs 159.4 DDD per 100 patient days; P < .0001), adherence to clinical guidelines (92.5% vs 59.3%; P < .0001), validation of prescription by pharmacist (72.0% vs 58.0%; P < .0001), crude mortality (15.9% vs 17.7%; P < .0001), and MDRO-HAIs (9.45 vs 10.96 cases per 1,000 patient days; P = .004). CONCLUSION: MS-ICUs with more comprehensive ASPs showed significant improvement in antimicrobial utilization.

Internal Medicine

Gupta K, Kalra R, Pate M, Nagalli S, Ather S, **Rajapreyar I**, Arora P, **Gupta A**, Zhou W, San Jose Estepar R, Di Carli M, Prabhu SD, and Bajaj NS. Relative Predictive Value of Circulating Immune Markers in US Adults Without Cardiovascular Disease: Implications for Risk Reclassification. *Mayo Clin Proc* 2021; Epub ahead of print. PMID: 33840521. Full Text

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OBJECTIVE: To investigate the relative predictive value of circulating immune cell markers for cardiovascular mortality in ambulatory adults without cardiovascular disease. METHODS: We analyzed data of participants enrolled in the National Health and Nutrition Examination Survey from January 1, 1999, to December 31, 2010, with the total leukocyte count within a normal range (4000-11,000 cells/μL [to convert to cells ×10(9)/L, multiply by 0.001]) and without cardiovascular disease. The relative predictive value of circulating immune cell markers measured at enrollment-including total leukocyte count, absolute neutrophil count, absolute lymphocyte count, absolute monocyte count, monocyte-lymphocyte ratio (MLR), neutrophil-lymphocyte ratio, and C-reactive protein-for cardiovascular mortality was evaluated. The marker with the best predictive value was added to the 10-year atherosclerotic cardiovascular disease (ASCVD) risk score to estimate net risk reclassification indices for 10-year cardiovascular mortality. RESULTS: Among 21,599 participants eligible for this analysis, the median age was 47 years (interquartile range, 34-63 years); 10,651 (49.2%) participants were women, and 10,713 (49.5%) were self-reported non-Hispanic white. During a median follow-up of 9.6 years (interquartile range, 6.8-13.1 years), there were 627 cardiovascular deaths. MLR had the best predictive value for cardiovascular mortality. The addition of elevated MLR (≥0.3) to the 10-year ASCVD risk score improved the classification by 2.7%±1.4% (P=.04). Elevated MLR had better predictive value than C-reactive protein and several components of the 10-year ASCVD risk score. CONCLUSION: Among ambulatory US adults without preexisting cardiovascular disease, we found that MLR had the best predictive value for cardiovascular mortality among circulating immune markers. The addition of MLR to the 10-year risk score significantly improved the risk classification of participants.

Internal Medicine

Schaefer JK, Errickson J, Li Y, Kong X, Alexandris-Souphis T, Ali MA, Decamillo D, Haymart B, **Kaatz S**, Kline-Rogers E, Kozlowski JH, **Krol GD**, Shankar SR, Sood SL, Froehlich JB, and Barnes GD. Adverse Events Associated With the Addition of Aspirin to Direct Oral Anticoagulant Therapy Without a Clear Indication. *JAMA Intern Med* 2021; Epub ahead of print. PMID: 33871544. Full Text

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Internal Medicine

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INTRODUCTION: Limited data is available on the rates of bleeding and thromboembolic events for patients undergoing low bleeding risk procedures while taking direct oral anticoagulants (DOAC). METHODS: Adults taking DOAC in the Michigan Anticoagulation Quality Improvement Initiative (MAQI(2)) database who underwent a low bleeding risk procedure between May 2015 and Sep 2019 were included. Thirty-day bleeding (of any severity), thromboembolic events, and death were compared between DOAC temporarily interrupted and continued uninterrupted groups. Adverse event rates were compared using an inverse probability weighting propensity score. RESULTS: There were 820 patients who underwent 1412 low risk procedures. DOAC therapy was temporarily interrupted in 371 (45.2%) patients (601 [42.6%] procedures) and continued uninterrupted in 449 (54.8%) patients (811 [57.4%] procedures). DOAC patients with temporary interruptions were more likely to have diabetes, prior stroke or TIA, prior bleeding, higher CHA2DS2-VASc, and higher modified HAS-BLED scores. DOAC interruption was common for

gastrointestinal endoscopy, electrophysiology device implantation, and cardiac catheterization while it was less common for cardioversion, dermatologic procedures, and subcutaneous injection. After propensity score adjustment, bleeding risk was lower in the DOAC temporary interruption group (OR 0.62, 95% CI 0.41-0.95) as compared to the group with continuous DOAC use. Rates of thromboembolic events and death did not differ significantly between the two groups. CONCLUSIONS: DOAC-treated patients undergoing low bleeding risk procedures may experience lower rates of bleeding when DOAC is temporarily interrupted. Prospective studies focused on low bleeding risk procedures are needed to identify the safety DOAC management strategy.

Nephrology

Flamm SL, Brown K, Wadei HM, Brown RS, Jr., Kugelmas M, **Samaniego-Picota M**, Burra P, Poordad F, and Saab S. The Current Management of Hepatorenal Syndrome-Acute Kidney Injury in the United States and the Potential of Terlipressin. *Liver Transpl* 2021; Epub ahead of print. PMID: 33848394. Full Text

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Acute kidney injury in the setting of cirrhosis (hepatorenal syndrome-acute kidney injury [HRS-AKI]) is a severe and often fatal complication of end-stage liver disease. The goals of treatment are to reverse renal failure and prolong survival in critically ill patients. However, interventions have limited efficacy, and mortality rates remain high. In the US, the mainstay of pharmacologic therapy consists of the off-label use of vasoconstrictive agents in combination with plasma expanders, a strategy that produces modest effects. Liver transplantation is the ultimate solution but is only an option in a minority of patients since contraindications to transplantation are common and organ availability is limited. Renal replacement therapy is a temporary option but is known to confer an extremely poor, short-term prognosis in patients with HRS-AKI and, at best, serves as a bridge to liver transplantation for the minority of patients who are transplantation candidates. The high mortality rate associated with HRS-AKI in the US is a reflection of the suboptimal standard of care. Improved therapeutic options to treat HRS-AKI are sought. Terlipressin is a drug approved in Europe for treatment of HRS-AKI and supported by recommendations for first-line therapy by some liver societies and experts around the world. This review article will discuss the substantial unmet medical need associated with HRS-AKI and the potential benefits if terlipressin was approved in the US.

Nephrology

Joseph MS, **Tinney F**, Naik A, Parasuraman R, **Samaniego-Picota M**, and Bhave NM. Right Ventricular Dysfunction and Adverse Outcomes after Renal Transplantation. *Cardiorenal Med* 2021; 11(2):109-118. PMID: 33853060. Full Text

Division of Cardiovascular Medicine, Department of Internal Medicine, University of Michigan Medical School and Michigan Medicine, Ann Arbor, Michigan, USA.

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INTRODUCTION: Pulmonary hypertension is common among patients with end-stage renal disease, although data regarding the impact of right ventricular (RV) failure on postoperative outcomes remain limited. We hypothesized that echocardiographic findings of RV dilation and dysfunction are associated with adverse clinical outcomes after renal transplant. METHODS: A retrospective review of adult renal transplant recipients at a single institution from January 2008 to June 2010 was conducted. Patients with transthoracic echocardiograms (TTEs) within 1 year leading up to transplant were included. The primary end point was a composite of delayed graft function, graft failure, and all-cause mortality. RESULTS: Eighty patients were included. Mean follow-up time was 9.4 ± 0.8 years. Eight patients (100%) with qualitative RV dysfunction met the primary end point, while 39/65 patients (60.0%) without RV dysfunction met the end point ($p = 0.026$). Qualitative RV dilation was associated with a significantly shorter time to all-cause graft failure ($p = 0.03$) and death ($p = 0.048$). RV systolic pressure was not measurable in 45/80 patients (56%) and was not associated with outcomes in the remaining patients. CONCLUSION: RV dilation and dysfunction are associated with adverse outcomes after renal transplant. TTE assessment of RV size and function should be a standard part of the pre-kidney transplant cardiovascular risk assessment.

Nephrology

Singh N, Friedewald J, Bloom R, Dadhania D, Parsons RF, Kaplan B, **Samaniego M**, Qazi Y, Doshi M, McNatt G, Naseer MS, Pesavento T, and Wiseman A. Transplant administration-A survey of the roles and responsibilities of kidney and pancreas medical directors of US transplant centers. *Clin Transplant* 2021; e14305. Epub ahead of print. PMID: 33797134. Full Text

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The current American Society of Transplantation (AST) accredited transplant fellowship programs in the United States provide no structured formal training in leadership and administration which is essential for successfully running a transplant program. We conducted a survey of medical directors of active adult kidney and kidney-pancreas transplant programs in the United States about their demographics, training pathways, and roles and responsibilities. The survey was emailed to 183 medical directors, and 123 (67.2%) completed the survey. A majority of respondents were older than 50 years (61%), males (80%), and holding that position for more than 10 years (47%). Only 51% of current medical directors had taken that position after completing a one-year transplant fellowship, and 58% took on the role with no prior administrative or leadership experience. The medical directors reported spending a median 50%-75% of time in clinical responsibilities, 25%-50% of time in administration, and 0%-25% time in research. The survey also captured various administrative roles of medical directors vis-à-vis other transplant leaders. The study, designed to be the starting point of an improvement initiative of the AST, provided important

insight into the demographics, training pathways, roles and responsibilities, job satisfaction, education needs, and training gaps of current medical directors.

Nephrology

Wheeler DC, Toto RD, Stefansson BV, Jongs N, Chertow GM, Greene T, Hou FF, McMurray JJV, Pecoits-Filho R, Correa-Rotter R, Rossing P, Sjöström CD, **Umanath K**, Langkilde AM, and Heerspink HJL. A pre-specified analysis of the DAPA-CKD trial indicates effects of dapagliflozin on major adverse kidney events in patients with IgA nephropathy. *Kidney Int* 2021; Epub ahead of print. PMID: 33878338. Full Text

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Immunoglobulin A (IgA) nephropathy is a common form of glomerulonephritis, which despite use of renin-angiotensin-aldosterone-system blockers and immunosuppressants, often progresses to kidney failure. In the Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease trial, dapagliflozin reduced risk of kidney failure and prolonged survival in participants with chronic kidney disease with and without type 2 diabetes, including those with IgA nephropathy. Here we randomized participants with estimated glomerular filtration rate (eGFR) 25-75 mL/min/1.73m(2) and urinary albumin-to-creatinine ratio 200-5000 mg/g (22.6-565 mg/mol) to dapagliflozin 10mg or placebo, as adjunct to standard care The primary composite endpoint was a sustained decline in eGFR of 50% or more, end-stage kidney disease, or death from a kidney disease-related or cardiovascular cause. Of 270 participants with IgA nephropathy (254 [94%] confirmed by previous biopsy), 137 were randomized to dapagliflozin and 133 to placebo, and followed for median 2.1 years. Overall, mean age was 51.2 years; mean eGFR, 43.8 mL/min/1.73m(2); and median urinary albumin-to-creatinine ratio, 900 mg/g. The primary outcome occurred in six (4%) participants on dapagliflozin and 20 (15%) on placebo (hazard ratio, 0.29; 95% confidence interval, 0.12, 0.73). Mean rates of eGFR decline with dapagliflozin and placebo were -3.5 and -4.7 mL/min/1.73m(2)/year, respectively. Dapagliflozin reduced the urinary albumin-to-creatinine ratio by 26% relative to placebo. Adverse events leading to study drug discontinuation were similar with dapagliflozin and placebo. There were fewer serious adverse events with dapagliflozin. It had no new safety findings in this population. Thus, in participants with IgA nephropathy, dapagliflozin reduced the risk of chronic kidney disease progression with a favorable safety profile.

Neurology

Fang J, **Chopp M**, **Xin H**, **Zhang L**, **Wang F**, **Golembieski W**, **Zhang ZG**, He L, and **Liu Z**. Plasminogen deficiency causes reduced angiogenesis and behavioral recovery after stroke in mice. *J Cereb Blood Flow Metab* 2021; Epub ahead of print. PMID: 33853408. Full Text

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Plasminogen is involved in the process of angiogenesis; however, the underlying mechanism is unclear. Here, we investigated the potential contribution of plasmin/plasminogen in mediating angiogenesis and thereby contributing to functional recovery post-stroke. Wild-type plasminogen naive (Plg(+/+)) mice and plasminogen knockout (Plg(-/-)) mice were subjected to unilateral permanent middle cerebral artery occlusion (MCAo). Blood vessels were labeled with FITC-dextran. Functional outcomes, and cerebral vessel density were compared between Plg(+/+) and Plg(-/-) mice at different time points after stroke. We found that Plg(-/-) mice exhibited significantly reduced functional recovery, associated with significantly decreased vessel density in the peri-infarct area in the ipsilesional cortex compared with Plg(+/+) mice. In vitro, cerebral endothelial cells harvested from Plg(-/-) mice exhibited significantly reduced angiogenesis assessed using tube formation assay, and migration, as evaluated using Scratch assays, compared to endothelial cells harvested from Plg(+/+) mice. In addition, using Western blots, expression of thrombospondin (TSP)-1 and TSP-2 were increased after MCAo in the Plg(-/-) group compared to Plg(+/+) mice, especially in the ipsilesional side of brain. Taken together, our data suggest that plasmin/plasminogen down-regulates the expression level of TSP-1 and TSP-2, and thereby promotes angiogenesis in the peri-ischemic brain tissue, which contributes to functional recovery after ischemic stroke.

Neurology

Mohamed GA, **Aboul Nour H**, Nogueira RG, Mohammaden MH, Haussen DC, Al-Bayati AR, Nguyen TN, Abdalkader M, Kaliaev A, Ma A, Fifi J, Morey J, Yavagal DR, Saini V, Ortega-Gutierrez S, Farooqui M, Zevallos CB, Quispe-Orozco D, **Schultz L**, **Kole M**, **Miller D**, Mayer SA, **Marin H**, and **Bou Chebl A**. Repeated Mechanical Endovascular Thrombectomy for Recurrent Large Vessel Occlusion: A Multicenter Experience. *Stroke* 2021; Epub ahead of print. PMID: 33910367. Full Text

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Department of Interventional Radiology, Henry Ford Hospital, Detroit, MI. (H.M.).

BACKGROUND AND PURPOSE: Mechanical thrombectomy (MT) is now the standard of care for large vessel occlusion (LVO) stroke. However, little is known about the frequency and outcomes of repeat MT (rMT) for patients with recurrent LVO. METHODS: This is a retrospective multicenter cohort of patients who underwent rMT at 6 tertiary institutions in the United States between March 2016 and March 2020. Procedural, imaging, and outcome data were evaluated. Outcome at discharge was evaluated using the modified Rankin Scale. RESULTS: Of 3059 patients treated with MT during the study period, 56 (1.8%) underwent at least 1 rMT. Fifty-four (96%) patients were analyzed; median age was 64 years. The median time interval between index MT and rMT was 2 days; 35 of 54 patients (65%) experienced recurrent LVO during the index hospitalization. The mechanism of stroke was cardioembolism in 30 patients (56%), intracranial atherosclerosis in 4 patients (7%), extracranial atherosclerosis in 2 patients (4%), and other causes in 18 patients (33%). A final TICI recanalization score of 2b or 3 was achieved in all 54 patients during index MT (100%) and in 51 of 54 patients (94%) during rMT. Thirty-two of 54 patients (59%) experienced recurrent LVO of a previously treated artery, mostly the pretreated left MCA

(23 patients, 73%). Fifty of the 54 patients (93%) had a documented discharge modified Rankin Scale after rMT: 15 (30%) had minimal or no disability (modified Rankin Scale score ≤2), 25 (50%) had moderate to severe disability (modified Rankin Scale score 3-5), and 10 (20%) died. CONCLUSIONS: Almost 2% of patients treated with MT experience recurrent LVO, usually of a previously treated artery during the same hospitalization. Repeat MT seems to be safe and effective for attaining vessel recanalization, and good outcome can be expected in 30% of patients.

Neurology

Nagaraja TN, **Elmghirbi R**, **Brown SL**, Rey JA, **Schultz L**, **Mukherjee A**, **Cabral G**, **Panda S**, **Lee IY**, Sarntinoranont M, **Keenan KA**, **Knight RA**, and **Ewing JR**. Imaging acute effects of bevacizumab on tumor vascular kinetics in a preclinical orthotopic model of U251 glioma. *NMR Biomed* 2021; e4516. Epub ahead of print. PMID: 33817893. Full Text

Department of Neurosurgery, Henry Ford Hospital, Detroit, Michigan, USA.
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The effect of a human vascular endothelial growth factor antibody on the vasculature of human tumor grown in rat brain was studied. Using dynamic contrast-enhanced magnetic resonance imaging, the effects of intravenous bevacizumab (Avastin; 10 mg/kg) were examined before and at postadministration times of 1, 2, 4, 8, 12 and 24 h (N = 26; 4-5 per time point) in a rat model of orthotopic, U251 glioblastoma (GBM). The commonly estimated vascular parameters for an MR contrast agent were: (i) plasma distribution volume (v(p)), (ii) forward volumetric transfer constant (K(trans)) and (iii) reverse transfer constant (k(ep)). In addition, extracellular distribution volume (V(D)) was estimated in the tumor (V(D-tumor)), tumor edge (V(D-edge)) and the mostly normal tumor periphery (V(D-peri)), along with tumor blood flow (TBF), peri-tumoral hydraulic conductivity (K) and interstitial flow (Flux) and tumor interstitial fluid pressure (TIFP). Studied as % changes from baseline, the 2-h post-treatment time point began showing significant decreases in v(p) , V(D-tumor,) V(D-edge) and V(D-peri) , as well as K, with these changes persisting at 4 and 8 h in v(p) , K, V(D-tumor, -edge) and (-peri) (t-tests; $p < 0.05$-0.01). Decreases in K(trans) were observed at the 2- and 4-h time points ($p < 0.05$), while interstitial volume fraction (v(e) ; = K(trans) /k(ep)) showed a significant decrease only at the 2-h time point ($p < 0.05$). Sustained decreases in Flux were observed from 2 to 24 h ($p < 0.01$) while TBF and TIFP showed delayed responses, increases in the former at 12 and 24 h and a decrease in the latter only at 12 h. These imaging biomarkers of tumor vascular kinetics describe the short-term temporal changes in physical spaces and fluid flows in a model of GBM after Avastin administration.

Neurosurgery

Asmaro K, **Fadel HA**, **Haider SA**, **Pawloski J**, **Telemi E**, **Mansour TR**, Chandra A, **Bazydlo M**, **Robin AM**, **Lee IY**, **Air EL**, **Rock JP**, **Kalkanis SN**, and **Schwalb JM**. Reducing Superfluous Opioid Prescribing Practices After Brain Surgery: It Is Time to Talk About Drugs. *Neurosurgery* 2021; Epub ahead of print. PMID: 33862632. Full Text

Department of Neurosurgery, Henry Ford Health System, Detroit, Michigan, USA.
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BACKGROUND: Opioids are prescribed routinely after cranial surgery despite a paucity of evidence regarding the optimal quantity needed. Overprescribing may adversely contribute to opioid abuse, chronic use, and diversion. OBJECTIVE: To evaluate the effectiveness of a system-wide campaign to reduce opioid prescribing excess while maintaining adequate analgesia. METHODS: A retrospective cohort study of patients undergoing a craniotomy for tumor resection with home disposition before and after a 2-mo educational intervention was completed. The educational initiative was composed of directed didactic

seminars targeting senior staff, residents, and advanced practice providers. Opioid prescribing patterns were then assessed for patients discharged before and after the intervention period. RESULTS: A total of 203 patients were discharged home following a craniotomy for tumor resection during the study period: 98 who underwent surgery prior to the educational interventions compared to 105 patients treated post-intervention. Following a 2-mo educational period, the quantity of opioids prescribed decreased by 52% (median morphine milligram equivalent per day [interquartile range], 32.1 [16.1, 64.3] vs 15.4 [0, 32.9], P < .001). Refill requests also decreased by 56% (17% vs 8%, P = .027) despite both groups having similar baseline characteristics. There was no increase in pain scores at outpatient follow-up (1.23 vs 0.85, P = .105). CONCLUSION: A dramatic reduction in opioids prescribed was achieved without affecting refill requests, patient satisfaction, or perceived analgesia. The use of targeted didactic education to safely improve opioid prescribing following intracranial surgery uniquely highlights the ability of simple, evidence-based interventions to impact clinical decision making, lessen potential patient harm, and address national public health concerns.

Neurosurgery

Datta I, **Noushmehr H**, **Brodie C**, and **Poisson LM**. Expression and regulatory roles of lncRNAs in G-CIMP-low vs G-CIMP-high Glioma: an in-silico analysis. *J Transl Med* 2021; 19(1):182. PMID: 33926464.
Full Text

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BACKGROUND: Clinically relevant glioma subtypes, such as the glioma-CpG island methylator phenotype (G-CIMP), have been defined by epigenetics. In this study, the role of long non-coding RNAs in association with the poor-prognosis G-CMIP-low phenotype and the good-prognosis G-CMIP-high phenotype was investigated. Functional associations of lncRNAs with mRNAs and miRNAs were examined to hypothesize influencing factors of the aggressive phenotype. METHODS: RNA-seq data on 250 samples from TCGA's Pan-Glioma study, quantified for lncRNA and mRNAs (GENCODE v28), were analyzed for differential expression between G-CIMP-low and G-CIMP-high phenotypes. Functional interpretation of the differential lncRNAs was performed by Ingenuity Pathway Analysis. Spearman rank order correlation estimates between lncRNA, miRNA, and mRNA nominated differential lncRNA with a likely miRNA sponge function. RESULTS: We identified 4371 differentially expressed features (mRNA = 3705; lncRNA = 666; FDR ≤ 5%). From these, the protein-coding gene TP53 was identified as an upstream regulator of differential lncRNAs PANDAR and PVT1 (p = 0.0237) and enrichment was detected in the "development of carcinoma" (p = 0.0176). Two lncRNAs (HCG11, PART1) were positively correlated with 342 mRNAs, and their correlation estimates diminish after adjusting for either of the target miRNAs: hsa-miR-490-3p, hsa-miR-129-5p. This suggests a likely sponge function for HCG11 and PART1. CONCLUSIONS: These findings identify differential lncRNAs with oncogenic features that are associated with G-CIMP phenotypes. Further investigation with controlled experiments is needed to confirm the molecular relationships.

Neurosurgery

Lim S, and **Chang V**. Commentary: Single-Position Surgery: Prone Lateral Lumbar Interbody Fusion: 2-Dimensional Operative Video. *Oper Neurosurg (Hagerstown)* 2021; 20(5):E373-e375. PMID: 33646295.
Full Text

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Neurosurgery

Mohamed GA, **Aboul Nour H**, Nogueira RG, Mohammaden MH, Haussen DC, Al-Bayati AR, Nguyen TN, Abdalkader M, Kaliaev A, Ma A, Fifi J, Morey J, Yavagal DR, Saini V, Ortega-Gutierrez S, Farooqui M, Zevallos CB, Quispe-Orozco D, **Schultz L**, **Kole M**, **Miller D**, Mayer SA, **Marin H**, and **Bou Chebl A**. Repeated Mechanical Endovascular Thrombectomy for Recurrent Large Vessel Occlusion: A Multicenter Experience. *Stroke* 2021; Epub ahead of print. PMID: 33910367. Full Text

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Neurosurgery

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The effect of a human vascular endothelial growth factor antibody on the vasculature of human tumor grown in rat brain was studied. Using dynamic contrast-enhanced magnetic resonance imaging, the effects of intravenous bevacizumab (Avastin; 10 mg/kg) were examined before and at postadministration times of 1, 2, 4, 8, 12 and 24 h (N = 26; 4-5 per time point) in a rat model of orthotopic, U251 glioblastoma (GBM). The commonly estimated vascular parameters for an MR contrast agent were: (i) plasma distribution volume (v(p)), (ii) forward volumetric transfer constant (K(trans)) and (iii) reverse transfer constant (k(ep)). In addition, extracellular distribution volume (V(D)) was estimated in the tumor (V(D-tumor)), tumor edge (V(D-edge)) and the mostly normal tumor periphery (V(D-peri)), along with tumor blood flow (TBF), peri-tumoral hydraulic conductivity (K) and interstitial flow (Flux) and tumor interstitial fluid pressure (TIFP). Studied as % changes from baseline, the 2-h post-treatment time point began showing significant decreases in v(p) , V(D-tumor,) V(D-edge) and V(D-peri) , as well as K, with these changes persisting at 4 and 8 h in v(p) , K, V(D-tumor, -edge) and (-peri) (t-tests; $p < 0.05$-0.01). Decreases in K(trans) were observed at the 2- and 4-h time points ($p < 0.05$), while interstitial volume fraction (v(e) ; = K(trans) /k(ep)) showed a significant decrease only at the 2-h time point ($p < 0.05$). Sustained decreases in Flux were observed from 2 to 24 h ($p < 0.01$) while TBF and TIFP showed delayed responses, increases in the former at 12 and 24 h and a decrease in the latter only at 12 h. These imaging biomarkers of tumor vascular kinetics describe the short-term temporal changes in physical spaces and fluid flows in a model of GBM after Avastin administration.

Neurosurgery

Tesileanu CMS, van den Bent MJ, Sanson M, Wick W, Brandes AA, Clement PM, Erridge SC, Vogelbaum MA, Nowak AK, Baurain JF, Mason WP, Wheeler H, Chinot OL, Gill S, Griffin M, Rogers L, Taal W, Rudà R, Weller M, McBain C, van Linde ME, **Sabedot TS**, Hoogstrate Y, von Deimling A, de Heer I, van IWFJ, Brouwer RWW, Aldape K, Jenkins RB, Dubbink HJ, Kros JM, Wesseling P, Cheung KJ, Golfinopoulos V, Baumert BG, Gorlia T, Noushmehr H, and French PJ. Prognostic significance of genome-wide DNA methylation profiles within the randomised, phase 3, EORTC CATNON trial on non-1p/19q deleted anaplastic glioma. *Neuro Oncol* 2021; Epub ahead of print. PMID: 33914057. Full Text

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Neuro-Oncology Department, University of Turin, Turin, Italy.
Neurology Department, University Hospital of Zurich, Zurich, Switzerland.
Clinical Oncology Department, The Christie NHS FT, Manchester, UK.
Medical Oncology Department, Amsterdam UMC, Amsterdam, the Netherlands.
Neurosurgery Department, Henry Ford Health System, Detroit, MI, USA.
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Biomics Center, Erasmus MC, Rotterdam, the Netherlands.
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BACKGROUND: Survival in patients with IDH1/2 mutant (mt) anaplastic astrocytomas is highly variable. We have used the prospective phase 3 CATNON trial to identify molecular factors related to outcome in IDH1/2mt anaplastic astrocytoma patients. METHODS: The CATNON trial randomized 751 adult patients with newly diagnosed 1p/19q non-codeleted anaplastic glioma to 59.4 Gy radiotherapy +/- concurrent and/or adjuvant temozolomide. The presence of necrosis and/or microvascular proliferation was scored at central pathology review. Infinium MethylationEPIC BeadChip arrays were used for genome-wide DNA methylation analysis and the determination of copy number variations (CNV). Two DNA methylation-based tumour classifiers were used for risk stratification. Next-generation sequencing (NGS) was performed using one of two glioma-tailored NGS panels. The primary endpoint was overall survival measured from date of randomization. RESULTS: Full analysis (genome-wide DNA methylation and NGS) was successfully performed on 654 tumours. Of these, 432 tumours were IDH1/2mt anaplastic astrocytomas. Both epigenetic classifiers identified poor prognosis patients that partially overlapped. A predictive prognostic Cox proportional hazards model identified that independent prognostic factors for IDH1/2mt anaplastic astrocytoma patients included; age, mini-mental state examination score, treatment with concurrent and/or adjuvant temozolomide, the epigenetic classifiers, PDGFRA amplification, CDKN2A/B homozygous deletion, PI3K mutations and total CNV load. Independent recursive partitioning analysis highlights the importance of these factors for patient prognostication. CONCLUSION: Both clinical and molecular factors identify IDH1/2mt anaplastic astrocytoma patients with worse outcome. These results will further refine the current WHO criteria for glioma classification.

Obstetrics, Gynecology and Women's Health Services

Pitts DS, Treadwell MC, and O'Brien LM. Fetal Heart Rate Decelerations in Women with Sleep-Disordered Breathing. *Reprod Sci* 2021; Epub ahead of print. PMID: 33847976. Request Article

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Emerging literature has shown that women with sleep-disordered breathing (SDB) have increased risk for gestational hypertension/preeclampsia and gestational diabetes. Case reports suggest an association between maternal apnea and fetal heart rate deceleration but data are lacking on how maternal sleep impacts fetal health. Since decelerations may be associated with adverse outcomes, we sought to determine whether fetal heart rate decelerations were associated with SDB. A cohort study of third trimester pregnant women with a singleton fetus was conducted. Participants underwent a home sleep test with continuous portable electronic fetal monitoring. SDB was defined as a respiratory disturbance index (RDI)≥10 events/hour. The temporality between a respiratory event and fetal heart rate decelerations was determined to be present if a deceleration occurred < 30 s after a respiratory event. Forty women were included with mean (±SD) age, BMI, and gestational age of 32.0±5.5 years, 37.1±8.0 kg/m(2), and 34.6±2.4 weeks respectively. Overall, n=23 (57.5%) women had SDB. Thirty-seven late decelerations were observed in 18 women; of these, 84% were temporally associated with a respiratory event. Nine of the 18 women (50%) had SDB. Ten prolonged decelerations were observed in 6 women of which nine (90%) were temporally associated with a respiratory event. Five of the six women (83%) had an RDI≥10. These initial data suggest that, in this population, the majority of both late and prolonged fetal heart rate decelerations occur with a maternal respiratory event. Since respiratory events are characteristic of maternal SDB, this raises the possibility that SDB may influence fetal well-being.

Ophthalmology and Eye Care Services
Vazquez-Galvan AJ. Ophthalmic Photographers' Society Exhibit, May 2020: Category: Fluorescein Angiography, 1st Place. *J Cataract Refract Surg* 2021; 47(4):551. PMID: 33901122. Full Text

Henry Ford Health System Detroit, Michigan, USA.

Ophthalmology and Eye Care Services
Zhang F. Re: Modi et al.: Visual and patient-reported outcomes of a diffractive trifocal intraocular lens compared with those of a monofocal intraocular lens (Ophthalmology. 2021;128:197-207). *Ophthalmology* 2021; Epub ahead of print. PMID: 33849730. Full Text

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Orthopedics/Bone and Joint Center
Bernstein DN, **Koolmees D**, **Hester J**, **Yedulla N**, and **Makhni EC**. Pain is the Primary Factor Associated with Satisfaction with Symptoms for New Patients Presenting to the Orthopaedic Clinic. *Arthroscopy* 2021; Epub ahead of print. PMID: 33878419. Full Text

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PURPOSE: The purpose of the current study was to: (1) determine the percentage of new orthopaedic patients reporting their symptoms to be acceptable at presentation, as measured by the Patient Acceptable Symptom State (PASS) question and (2) evaluate whether patient-reported outcome measures (PROMs), including Patient-Reported Outcome Measurement Information System (PROMIS) Physical Function (PF) or Upper Extremity (UE), Pain Interference (PI), and Depression (D), or sociodemographic factors are associated with acceptable symptoms at presentation. METHODS: Between 2/7/2020-3/16/2020, new orthopaedic patients who completed PROMs were identified. Patient records were reviewed for those who also completed the patient acceptable symptom state (PASS) question, a yes/no question about whether a patient's current symptom state is satisfactory. Bivariate analysis was conducted to compare patient characteristics, such as area deprivation index (ADI), between those reporting acceptable symptoms and those who did not. Multivariable logistic regression models were used to determine factors associated with acceptable symptoms at presentation. RESULTS: A total of 570 patients were included, with one quarter (n = 143 [25%]) reporting acceptable symptoms at presentation. In multivariable regression analysis, only pain, as measured by the PROMIS PI, was associated with acceptable symptoms at presentation (Non-Upper Extremity Patient Regression: PROMIS PI (OR: 0.84 (95% CI: 0.79 to 0.90), p<0.01); Upper Extremity Patient Regression: PROMIS PI (OR: 0.91 (95% CI: 0.85 to 0.98), p<0.01)). In both multivariable regression analyses, insurance type (private, Medicare, Medicaid, other), visit subspecialty (sports, hand, joints, foot and ankle, spine, other), PROMIS PF, PROMIS D, and national ADI were not associated with acceptable symptoms at presentation (all p>0.05). CONCLUSIONS: One quarter of new orthopaedic patients reported their symptoms to be acceptable at presentation. Of those who considered their symptom state unsatisfactory, pain - not functional status, mental health, or sociodemographic factors - was the primary determinant. LEVEL OF EVIDENCE: Diagnostic, III.

Orthopedics/Bone and Joint Center
Jildeh TR, Ference DA, **Abbas MJ**, **Jiang EX**, and Okoroha KR. Scapulothoracic Dyskinesis: A Concept Review. *Curr Rev Musculoskelet Med* 2021; Epub ahead of print. PMID: 33822304. Full Text

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PURPOSE OF REVIEW: Scapulothoracic dyskinesis (SD) occurs when there is a noticeable disruption in typical position and motion of the scapula, which can result in debilitating pain. The purpose of this review is to describe the current knowledge regarding the diagnosis and management of scapulothoracic dyskinesis by providing an evidence-based overview of clinical exams and treatment modalities available for orthopedic surgeons and provide insight into which treatment modalities require further investigation. RECENT FINDINGS: SD is highly prevalent in athletes, particularly those participating in overhead activities (e.g., baseball, tennis, and swimming) and can coexist with several shoulder pathologies. A holistic approach in the diagnosis of SD has been supported in the literature; however, it is important to recognize that diagnosis is currently limited to the absence of a quantitative SD clinical assessment. The main goal of the treatment of SD is to regain proper scapular positioning and dynamics. The standard of care for the management of SD is conservative interventions aimed at optimizing scapular kinematics. Surgical intervention is only considered in the presence of concomitant pathology requiring surgery. Due to the complexity of coordinated movement of the shoulder girdle, recent literature has begun to move away from the use of traditional orthopedic tests, in favor of a more system-based approach for the diagnosis of SD. We present a concise review of clinical exams and treatment modalities available for orthopedic surgeons in the management of SD.

Orthopedics/Bone and Joint Center

Shaw JH, Wesemann LD, Ayooluwa AS, Les CM, **Charters MA**, and **North WT**. Comparison of Area Deprivation Index, Socioeconomic Parameters, and Preoperative Demographics With Postoperative Emergency Department Visits After Total Knee Arthroplasty. *J Arthroplasty* 2021; Epub ahead of print. PMID: 33902984. Full Text

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BACKGROUND: This study aims to determine if socioeconomic (SE) parameters, primarily area deprivation index (ADI), relate to postoperative emergency department (ED) visits after total knee arthroplasty (TKA). METHODS: We retrospectively reviewed 2655 patients who underwent TKA in a health system of 4 hospitals. The primary outcome was an ED visit within 90 days, which was divided into those with and without readmission. SE parameters including ADI as well as preoperative demographics were analyzed. Univariable and multiple logistic regressions were performed determining risk of 90-day postoperative ED visits, as well as once in the ED, risks for readmission. RESULTS: 436 patients (16.4%) presented to the ED within 90 days. ADI was not a risk factor. The multiple logistic regression demonstrated men, Medicare or Medicaid, and preoperative ED visits were consistently risk factors for a postoperative ED visit with and without readmission. Preoperative anticoagulation was only a risk factor for ED visits with readmission. Among patients who visited the ED, if the patient was Caucasian, a lower BMI, or higher American Society of Anesthesiologists score, they were likely to be readmitted. CONCLUSION: The study demonstrated that the percentage of early ED returns after TKA was high and that ADI was not a predictor for 90-day postoperative ED visit. The only SE factor that may contribute to this phenomenon was insurance type. Once in the ED, race, preoperative ED visits, preoperative anticoagulation, BMI, gender, and preoperative American Society of Anesthesiologists score contributed to a risk of readmission. The study supports hospitals' mission to provide equal access health care.

Otolaryngology – Head and Neck Surgery

Husain S, **Lohia S**, Petkov V, Blackwell T, Swisher-McClure S, Mizrachi A, Morris LG, Cohen MA, Wong RJ, and Roman BR. Disparities and guideline adherence for HPV testing among patients with oropharyngeal squamous cell carcinoma, NCDB, and SEER. *Head Neck* 2021; Epub ahead of print. PMID: 33851469. Full Text

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BACKGROUND: Human papilloma virus testing for oropharyngeal squamous-cell carcinoma has been recommended by the National Comprehensive Cancer Network since 2012. We examine disparities, reported rates of human papillomavirus (HPV) testing, and the impact on these findings of limitations with the variable in database registries. METHODS: The HPV variable was queried for patients with oropharyngeal squamous carcinoma (OPSCC) from 2013 to 2016 in National Cancer Data Base (NCDB) and Surveillance, Epidemiology, and End Results (SEER). Multivariable regression was used to identify disparities based on sociodemographic variables. Sensitivity analyses were used to investigate limitations of the variable. RESULTS: Despite limitations in the HPV variable in the databases, there was less than 100% adherence to recommended testing, and there were significant disparities in multiple sociodemographic variables. For example, in NCDB 70% of white versus 60.4% of black patients were tested (odds ratio [OR] 0.75, confidence interval [CI] 0.66-0.85, $p \leq 0.0001$); in SEER 59.8% of white and 47.6% of black patients were tested (OR 0.73, CI 0.67-0.81; $p \leq 0.0001$). CONCLUSIONS: Disparities exist among patients undergoing testing for HPV-associated OPSCC and adherence to guideline recommended HPV testing has been suboptimal. In addition, the HPV variable definition, especially as it relates to p16 positivity, and use in these two registries should be improved.

Otolaryngology – Head and Neck Surgery
Momin S. Burning Mouth Syndrome-A Frustrating Problem. *JAMA Otolaryngol Head Neck Surg* 2021; Epub ahead of print. PMID: 33830201. Full Text

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Otolaryngology – Head and Neck Surgery
Turfe Z, Zhao K, Palmer JN, and **Craig JR**. Computational fluid dynamic modelling of maxillary sinus irrigation after maxillary antrostomy and modified endoscopic medial maxillectomy. *J Laryngol Otol* 2021;1-5. Epub ahead of print. PMID: 33875024. Full Text

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OBJECTIVE: For recalcitrant chronic maxillary sinusitis, modified endoscopic medial maxillectomy has been shown to be clinically beneficial after failed maxillary antrostomy as endoscopic medial maxillectomy may offer improved topical therapy delivery. This study compared irrigation patterns after maxillary antrostomy versus endoscopic medial maxillectomy, using computational fluid dynamic modelling. CASE REPORT: A 54-year-old female with left chronic maxillary sinusitis underwent maxillary antrostomy, followed by endoscopic medial maxillectomy. Computational fluid dynamic models were created after each surgery and used to simulate irrigations. RESULTS: After maxillary antrostomy, irrigation penetrated the maxillary sinus at 0.5 seconds, initially contacting the posterior wall. The maxillary sinus was half-filled at 2 seconds, and completely filled at 4 seconds. After endoscopic medial maxillectomy, irrigation penetrated the maxillary sinus at 0.5 seconds and immediately contacted all maxillary sinus walls. The maxillary sinus was completely filled by 2 seconds. CONCLUSION: Computational fluid dynamic modelling demonstrated that endoscopic medial maxillectomy allowed faster, more forceful irrigation to all maxillary sinus walls compared with maxillary antrostomy.

Otolaryngology – Head and Neck Surgery

Wu VF, and Malloy KM. Sentinel Node Biopsy for Head and Neck Cutaneous Melanoma. *Otolaryngol Clin North Am* 2021; 54(2):281-294. PMID: 33743887. Full Text

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Sentinel lymph node biopsy is the most precise and accurate staging technique for malignant melanoma. This resulted from international collaborations and technical innovations across subspecialties and systematic and methodical study of real-time clinical problems. This article describes sentinel node biopsy from conception to current techniques. Indications for the procedure and evidence of its prognostic value are discussed. Controversies surrounding results of Multicenter Selective Lymphadenectomy Trial I and II and German Dermatologic Cooperative Oncology Group Selective Lymphadenectomy trial are reviewed. Head and neck melanoma is presented as a unique subsite for performing sentinel node biopsy and when considering completion cervical lymphadenectomy.

Pathology and Laboratory Medicine

Cloutier JM, Charville GW, Mertens F, Sukov W, Fritchie K, **Perry KD**, Edgar M, Rowsey RA, and Folpe AL. "Inflammatory Leiomyosarcoma" and "Histiocyte-rich Rhabdomyoblastic Tumor": a clinicopathological, immunohistochemical and genetic study of 13 cases, with a proposal for reclassification as "Inflammatory Rhabdomyoblastic Tumor". *Mod Pathol* 2021; 34(4):758-769. PMID: 33318583. Full Text

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Inflammatory leiomyosarcoma (ILMS), defined as "a malignant neoplasm showing smooth muscle differentiation, a prominent inflammatory infiltrate, and near-haploidization", is a very rare soft tissue tumor with a generally favorable prognosis. The morphologic features of "histiocyte-rich rhabdomyoblastic tumor" (HRRMT) are similar to those of ILMS, although this lesion shows by definition a skeletal muscle phenotype. Recent gene expression profiling and immunohistochemical studies have also suggested that ILMS and HRRMT may be related. We studied the clinicopathologic, immunohistochemical and genetic features of four cases previously classified as ILMS and nine classified as HRRMT. Tumors from both groups tended to occur in the deep soft tissues of the extremities of young to middle-aged males and exhibited indolent behavior. Morphologically, all were well-circumscribed, often encapsulated, and showed a striking histiocyte-rich inflammatory infiltrate admixed with variably pleomorphic tumor cells showing spindled and epithelioid to rhabdoid morphology, eosinophilic cytoplasm, and prominent nucleoli, but few, if any, mitotic figures. Immunohistochemically, the tumor cells expressed desmin, alpha-smooth muscle actin, and the rhabdomyoblastic markers PAX7, MyoD1, and myogenin. H-caldesmon expression was absent in all cases, using the specific h-CD antibody. Karyotypic study (1 HRRMT) and genome-wide copy number analysis (7 HRRMT, OncoScan SNP assay), revealed near-haploidization in four cases, with subsequent genome doubling in one, an identical phenotype to that seen in ILMS. We propose reclassification of ILMS and HRRMT as "inflammatory rhabdomyoblastic tumor", a name which accurately describes the salient morphologic and immunohistochemical features of this distinctive tumor, as well as its intermediate (rarely metastasizing) clinical behavior.

Pathology and Laboratory Medicine

Nagaraja TN, **Elmghirbi R**, **Brown SL**, Rey JA, **Schultz L**, **Mukherjee A**, **Cabral G**, **Panda S**, **Lee IY**, Sarntinoranont M, **Keenan KA**, **Knight RA**, and **Ewing JR**. Imaging acute effects of bevacizumab on tumor vascular kinetics in a preclinical orthotopic model of U251 glioma. *NMR Biomed* 2021;e4516. Epub ahead of print. PMID: 33817893. Full Text

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The effect of a human vascular endothelial growth factor antibody on the vasculature of human tumor grown in rat brain was studied. Using dynamic contrast-enhanced magnetic resonance imaging, the effects of intravenous bevacizumab (Avastin; 10 mg/kg) were examined before and at postadministration times of 1, 2, 4, 8, 12 and 24 h (N = 26; 4-5 per time point) in a rat model of orthotopic, U251 glioblastoma (GBM). The commonly estimated vascular parameters for an MR contrast agent were: (i) plasma distribution volume (v(p)), (ii) forward volumetric transfer constant (K(trans)) and (iii) reverse transfer constant (k(ep)). In addition, extracellular distribution volume (V(D)) was estimated in the tumor (V(D-tumor)), tumor edge (V(D-edge)) and the mostly normal tumor periphery (V(D-peri)), along with tumor blood flow (TBF), peri-tumoral hydraulic conductivity (K) and interstitial flow (Flux) and tumor interstitial fluid pressure (TIFP). Studied as % changes from baseline, the 2-h post-treatment time point began showing significant decreases in v(p) , V(D-tumor,) V(D-edge) and V(D-peri) , as well as K, with these changes persisting at 4 and 8 h in v(p) , K, V(D-tumor, -edge) and (-peri) (t-tests; $p < 0.05$-0.01). Decreases in K(trans) were observed at the 2- and 4-h time points ($p < 0.05$), while interstitial volume fraction (v(e) ; = K(trans) /k(ep)) showed a significant decrease only at the 2-h time point ($p < 0.05$). Sustained decreases in Flux were observed from 2 to 24 h ($p < 0.01$) while TBF and TIFP showed delayed responses, increases in the former at 12 and 24 h and a decrease in the latter only at 12 h. These imaging biomarkers of tumor vascular kinetics describe the short-term temporal changes in physical spaces and fluid flows in a model of GBM after Avastin administration.

Pathology and Laboratory Medicine

Tsogbadrakh B, Kunaviktikul W, Akkadechanunt T, Wichaikhum OA, Gaalan K, Badamdorj O, and **Stark A**. Development and psychometric testing of quality nursing care scale in Mongolia. *BMC Nurs* 2021; 20(1):68. PMID: 33910559. Full Text

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BACKGROUND: Quality Nursing Care (QNC) is fundamental to the profession of nursing practice. Perception of QNC differ across the globe because of differences in social norms, cultural values and political ambiance and economy. This study aimed to develop a QNC instrument congruent with the Mongolian (QNCS-M) healthcare system and cultural values and societal norms. METHODS: Exploratory sequential mixed-method design was implemented to develop and assess performance of QNCS-M. First, we focused on developing the components of QNCS-M and their operational definitions. Second, we dedicated to ascertaining psychometric performance of QNCS-M. The field testing consisted of assessing the construct validity and internal consistency reliability. Correlation between QNCS-M and the criterion

tool, Quality of Nursing Care Questionnaire-Registered Nurse was evaluated. RESULTS: The initial version of QNCS-M contained 66 items of which 7 (I-CVI < .78) were deleted after item-content validity assessment. The total-item correlation analysis yielded to exclusion of another 3 items (<.3). Additional 12 items were excluded after inter-item correlation (<.3, >.7). Results from Spearman rank-order correlation analysis of the remaining 44 items indicated relationship between social desirability and 6 items (r = -.09 to r = .11). These items were excluded to reduce the likelihood of potential information bias. A total of 38 items remained for exploratory factor analysis. Results from exploratory factor analysis yielded eigenvalues > 1.0 for the 9 domains. Three domains contained items fewer than 3. These domains and 2 items (factor loading <.4) were eliminated, yielding to 6 domains with 36-item. Results from internal consistency reliability yielded an overall Cronbach's α = .92; the coefficient values for the 6 domains ranging between .72 and .85 and Pearson correlation for stability reliability yielded an acceptable (r = .82, P < .001). CONCLUSION: Improving the quality of healthcare services delivered by nurses is a priority for the Mongolian government. The development of QNCS-M is a major stride in addressing this concern. The final version of QNCS-M which contains 36 items, loaded into 6 domains, was morphed to the specifics of the Mongolian healthcare systems and cultural values and societal norms. QNCS-M demonstrates a high level of content and construct validity with acceptable reliability.

Pharmacy

Nhean S, **Kostoff D**, **Yang JJ**, **Vogel V**, and **Rybkin, II**. Impact of Oral Chemotherapy Management Program on Capecitabine Toxicity Management. *JCO Oncol Pract* 2021; Epub ahead of print. PMID: 33900803. Request Article

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PURPOSE: Increasing use of oral chemotherapy has created unique challenges related to patient safety and compliance. To address this issue, the Henry Ford Cancer Institute at Henry Ford Health System developed and implemented a system-wide, multidisciplinary program named the Oral Chemotherapy Management Program (OCMP). The purpose of this study was to evaluate the impact of OCMP on patient outcomes in those receiving capecitabine. METHODS: This was a retrospective, quasi-experimental study that compared outcomes in patients receiving capecitabine before and after OCMP implementation. The co-primary outcomes were incidence(s) of grade 1-4 and grade 3-4 adverse effects (AEs) associated with capecitabine. Secondary outcomes were emergency department (ED) visits, hospitalizations because of toxicity, and adherence rate. RESULTS: OCMP patients had significantly lower overall incidence of AE of any grade (58.9% v 70.3%; 95% CI, 0.39 to 0.94; P = .03). OCMP implementation significantly lowered incidence of any grade and grade 3-4 nausea, vomiting, and/or diarrhea, and grade 3-4 hand-foot syndrome. It resulted in the decreased number of ED visits (8.9% v 18.9%; P = .005) and hospitalizations (6.3% v 17.1%; P = .002), as well as improved medication adherence rates (0.94 v 0.97; P = .03). CONCLUSION: Most patients who developed capecitabine-related AE required intervention by OCMP. Implementation of OCMP reduced the incidence of high-grade AE, decreased the number of ED visits and hospitalizations because of AE, and improved the medication adherence rate.

Plastic Surgery

Ivanics T, **Zimnicki K**, **Ahmad H**, **Saab I**, Liu V, **Tepper D**, and **Siddiqui A**. Fat grafting: A novel technique for difficult ostomy management. *Surgery* 2021; Epub ahead of print. PMID: 33820652. Full Text

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Plastic Surgery

Luker J, Tajran J, Marquette L, Tepper D, **Carlin A**, Darian V, and **Siddiqui A**. Long-Term Weight Loss with Body Contour Surgery After Roux-en-Y Gastric Bypass. *Obes Surg* 2021; Epub ahead of print. PMID: 33851305. Full Text

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BACKGROUND: Bariatric surgery is accepted as an evidence-based treatment for morbid obesity. Many patients seek out body contour surgery afterwards to correct acquired deformities. This study seeks to better define the impact of body contour surgery on long-term weight loss. METHODS: This study is a single-center retrospective review of 78 patients who underwent body contouring surgery post-Roux-en-Y gastric bypass compared with 221 matched control patients who underwent Roux-en-Y gastric bypass only. Data was collected for patients at least 7 years post-Roux-en-Y gastric bypass. RESULTS: Patients who underwent both bariatric surgery and body contour surgery maintained mean long-term weight loss of 58 kg. The matched control group mean weight loss over the same time interval was 42 kg. The difference was statistically and clinically significant ($p = 0.005$). Change in body mass index, percent total weight loss, and percent excess body mass index loss were all statistically significant between the 2 groups. CONCLUSION: Patients who underwent body contour surgery better maintained long-term weight reduction in comparison to those who only had gastric bypass. Further understanding of the etiology of this association is important for patients contemplating body contouring surgery.

Public Health Sciences

Jansen EC, **She R**, Rukstalis M, and Alexander GL. Changes in fruit and vegetable consumption in relation to changes in sleep characteristics over a 3-month period among young adults. *Sleep Health* 2021; Epub ahead of print. PMID: 33840631. Full Text

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OBJECTIVE: To evaluate whether increases in fruit and vegetable (FV) consumption were associated with concomitant changes in insomnia symptoms, sleep duration, and quality. DESIGN: Secondary longitudinal analysis of a randomized trial, baseline to 3 months. SETTING: Integrated health care systems in Detroit, Michigan and Danville, Pennsylvania. PARTICIPANTS: About 1165 young adults who were low consumers of FV (<3 servings/day) at baseline. INTERVENTION: Online 3-arm program designed to increase FV consumption. MEASUREMENTS: We categorized FV changes into 4 categories: no change or decrease, 1 serving increase, 2 serving increase, and 3 or more serving increase. We then compared the changes in chronic insomnia classification (yes or no), sleep duration, quality, and time to fall asleep (all self-reported) across the FV change categories. Analyses were both overall and stratified by gender, adjusting for potential confounders (depression, physical activity, education, children, and study site). RESULTS: Average age ± SD was 26 ± 2.8 years (71% women). At 3-month follow-up, participants on average increased FV intake by 1.2 ± 1.4 servings. Women who increased FV intake by 3+ servings showed improvements in insomnia symptoms (2-fold higher odds of improvement; 95% CI 1.1 to 3.6), sleep quality (0.2-point higher sleep quality score; 95% CI -0.01, 0.3), and time to fall asleep (4.2 minutes; 95% CI -8, 0) compared to women who did not change or decreased their FV intake. Associations were not as apparent among men. CONCLUSION: Young women with low consumption of

FV may experience improvements in insomnia-related sleep difficulties by increasing their consumption of FV.

Public Health Sciences

Gonzalez HC, **Trudeau S**, and **Gordon SC**. Editorial: Changing trends in the US prevalence of hepatitis B core antibody provide important perspectives into future screening and vaccination strategies. *J Infect Dis* 2021; Epub ahead of print. PMID: 33903913. Full Text

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Public Health Sciences

Kalu R, **Boateng P**, **Carrier L**, **Garzon J**, **Tang A**, **Reickert C**, and **Stefanou A**. Effect of preoperative versus postoperative use of transversus abdominis plane block with plain 0.25 % bupivacaine on postoperative opioid use: a retrospective study. *BMC Anesthesiol* 2021; 21(1):114. PMID: 33845790. Full Text

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BACKGROUND: Enhanced recovery protocols optimize pain control via multimodal approaches that include transversus abdominis plane (TAP) block. The aim of this study was to evaluate the effect of preoperative vs. postoperative plain 0.25 % bupivacaine TAP block on postoperative opioid use after colorectal surgery. METHODS: A retrospective cohort study comparing postoperative opioid use in patients who received preoperative (n = 240) vs. postoperative (n = 22) plain 0.25 % bupivacaine TAP blocks. The study was conducted in a single tertiary care institution and included patients who underwent colorectal resections between August 2018 and January 2020. The primary outcome of the study was postoperative opioid use. Secondary outcomes included operative details, length of stay, reoperation, and readmission rates. RESULTS: Patients who received postoperative plain 0.25 % bupivacaine TAP blocks were less likely to require postoperative patient-controlled analgesia (PCA) (59.1 % vs. 83.3 %; p = 0.012) and opioid medications on discharge (6.4 % vs. 16.9 %; p = 0.004) relative to patients who received preoperative TAP. When needed, a significantly smaller amount of opioid was prescribed to the postoperative group (84.5 vs. 32.0 mg, p = 0.047). No significant differences were noted in the duration of postoperative PCA use, amount of oral opioid use, and length of stay. CONCLUSIONS: Plain 0.25 % bupivacaine TAP block administered postoperatively was associated with significantly lower need for postoperative PCA and discharge opioid medications. The overall hospital length of stay was not affected by the timing of TAP block. Because of the limited sample size in this study, conclusions cannot be generalized, and more research will be required.

Public Health Sciences

Datta I, **Noushmehr H**, **Brodie C**, and **Poisson LM**. Expression and regulatory roles of lncRNAs in G-CIMP-low vs G-CIMP-high Glioma: an in-silico analysis. *J Transl Med* 2021; 19(1):182. PMID: 33926464. Full Text

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BACKGROUND: Clinically relevant glioma subtypes, such as the glioma-CpG island methylator phenotype (G-CIMP), have been defined by epigenetics. In this study, the role of long non-coding RNAs in association with the poor-prognosis G-CMIP-low phenotype and the good-prognosis G-CMIP-high phenotype was investigated. Functional associations of lncRNAs with mRNAs and miRNAs were examined to hypothesize influencing factors of the aggressive phenotype. METHODS: RNA-seq data on 250 samples from TCGA's Pan-Glioma study, quantified for lncRNA and mRNAs (GENCODE v28), were analyzed for differential expression between G-CIMP-low and G-CIMP-high phenotypes. Functional interpretation of the differential lncRNAs was performed by Ingenuity Pathway Analysis. Spearman rank order correlation estimates between lncRNA, miRNA, and mRNA nominated differential lncRNA with a likely miRNA sponge function. RESULTS: We identified 4371 differentially expressed features (mRNA = 3705; lncRNA = 666; FDR ≤ 5%). From these, the protein-coding gene TP53 was identified as an upstream regulator of differential lncRNAs PANDAR and PVT1 ($p = 0.0237$) and enrichment was detected in the "development of carcinoma" ($p = 0.0176$). Two lncRNAs (HCG11, PART1) were positively correlated with 342 mRNAs, and their correlation estimates diminish after adjusting for either of the target miRNAs: hsa-miR-490-3p, hsa-miR-129-5p. This suggests a likely sponge function for HCG11 and PART1. CONCLUSIONS: These findings identify differential lncRNAs with oncogenic features that are associated with G-CIMP phenotypes. Further investigation with controlled experiments is needed to confirm the molecular relationships.

Public Health Sciences

Asmaro K, **Fadel HA**, **Haider SA**, **Pawloski J**, **Telemi E**, **Mansour TR**, Chandra A, **Bazydlo M**, **Robin AM**, **Lee IY**, **Air EL**, **Rock JP**, **Kalkanis SN**, and **Schwalb JM**. Reducing Superfluous Opioid Prescribing Practices After Brain Surgery: It Is Time to Talk About Drugs. *Neurosurgery* 2021; Epub ahead of print. PMID: 33862632. Full Text

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BACKGROUND: Opioids are prescribed routinely after cranial surgery despite a paucity of evidence regarding the optimal quantity needed. Overprescribing may adversely contribute to opioid abuse, chronic use, and diversion. OBJECTIVE: To evaluate the effectiveness of a system-wide campaign to reduce opioid prescribing excess while maintaining adequate analgesia. METHODS: A retrospective cohort study of patients undergoing a craniotomy for tumor resection with home disposition before and after a 2-mo educational intervention was completed. The educational initiative was composed of directed didactic seminars targeting senior staff, residents, and advanced practice providers. Opioid prescribing patterns were then assessed for patients discharged before and after the intervention period. RESULTS: A total of 203 patients were discharged home following a craniotomy for tumor resection during the study period: 98 who underwent surgery prior to the educational interventions compared to 105 patients treated post-intervention. Following a 2-mo educational period, the quantity of opioids prescribed decreased by 52% (median morphine milligram equivalent per day [interquartile range], 32.1 [16.1, 64.3] vs 15.4 [0, 32.9], $P < .001$). Refill requests also decreased by 56% (17% vs 8%, $P = .027$) despite both groups having similar baseline characteristics. There was no increase in pain scores at outpatient follow-up (1.23 vs 0.85, $P = .105$). CONCLUSION: A dramatic reduction in opioids prescribed was achieved without affecting refill requests, patient satisfaction, or perceived analgesia. The use of targeted didactic education to safely improve opioid prescribing following intracranial surgery uniquely highlights the ability of simple, evidence-based interventions to impact clinical decision making, lessen potential patient harm, and address national public health concerns.

Pulmonary and Critical Care Medicine

Zhang Y, **Simoff MJ**, Ost D, Wagner OJ, Lavin J, Nauman B, Hsieh MC, Wu XC, Pettiford B, and Shi L. Understanding the patient journey to diagnosis of lung cancer. *BMC Cancer* 2021; 21(1):402. PMID: 33853552. Full Text

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OBJECTIVE: This research describes the clinical pathway and characteristics of two cohorts of patients. The first cohort consists of patients with a confirmed diagnosis of lung cancer while the second consists of patients with a solitary pulmonary nodule (SPN) and no evidence of lung cancer. Linked data from an electronic medical record and the Louisiana Tumor Registry were used in this investigation. MATERIALS AND METHODS: REACHnet is one of 9 clinical research networks (CRNs) in PCORnet®, the National Patient-Centered Clinical Research Network and includes electronic health records for over 8 million patients from multiple partner health systems. Data from Ochsner Health System and Tulane Medical Center were linked to Louisiana Tumor Registry (LTR), a statewide population-based cancer registry, for analysis of patient's clinical pathways between July 2013 and 2017. Patient characteristics and health services utilization rates by cancer stage were reported as frequency distributions. The Kaplan-Meier product limit method was used to estimate the time from index date to diagnosis by stage in lung cancer cohort. RESULTS: A total of 30,559 potentially eligible patients were identified and 2929 (9.58%) had primary lung cancer. Of these, 1496 (51.1%) were documented in LTR and their clinical pathway to diagnosis was further studied. Time to diagnosis varied significantly by cancer stage. A total of 24,140 patients with an SPN were identified in REACHnet and 15,978 (66.6%) had documented follow up care for 1 year. 1612 (10%) had no evidence of any work up for their SPN. The remaining 14,366 had some evidence of follow up, primarily office visits and additional chest imaging. CONCLUSION: In both cohorts multiple biopsies were evident in the clinical pathway. Despite clinical workup, 70% of patients in the lung cancer cohort had stage III or IV disease. In the SPN cohort, only 66% were identified as receiving a diagnostic work-up.

Radiation Oncology

Nagaraja TN, **Elmghirbi R**, **Brown SL**, Rey JA, **Schultz L**, **Mukherjee A**, **Cabral G**, **Panda S**, **Lee IY**, Sarntinoranont M, **Keenan KA**, **Knight RA**, and **Ewing JR**. Imaging acute effects of bevacizumab on tumor vascular kinetics in a preclinical orthotopic model of U251 glioma. *NMR Biomed* 2021;e4516. Epub ahead of print. PMID: 33817893. Full Text

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The effect of a human vascular endothelial growth factor antibody on the vasculature of human tumor grown in rat brain was studied. Using dynamic contrast-enhanced magnetic resonance imaging, the effects of intravenous bevacizumab (Avastin; 10 mg/kg) were examined before and at postadministration times of 1, 2, 4, 8, 12 and 24 h (N = 26; 4-5 per time point) in a rat model of orthotopic, U251 glioblastoma

(GBM). The commonly estimated vascular parameters for an MR contrast agent were: (i) plasma distribution volume (v(p)), (ii) forward volumetric transfer constant (K(trans)) and (iii) reverse transfer constant (k(ep)). In addition, extracellular distribution volume (V(D)) was estimated in the tumor (V(D-tumor)), tumor edge (V(D-edge)) and the mostly normal tumor periphery (V(D-peri)), along with tumor blood flow (TBF), peri-tumoral hydraulic conductivity (K) and interstitial flow (Flux) and tumor interstitial fluid pressure (TIFP). Studied as % changes from baseline, the 2-h post-treatment time point began showing significant decreases in v(p) , V(D-tumor,) V(D-edge) and V(D-peri) , as well as K, with these changes persisting at 4 and 8 h in v(p) , K, V(D-tumor, -edge) and (-peri) (t-tests; $p < 0.05$-0.01). Decreases in K(trans) were observed at the 2- and 4-h time points ($p < 0.05$), while interstitial volume fraction (v(e) ; = K(trans) /k(ep)) showed a significant decrease only at the 2-h time point ($p < 0.05$). Sustained decreases in Flux were observed from 2 to 24 h ($p < 0.01$) while TBF and TIFP showed delayed responses, increases in the former at 12 and 24 h and a decrease in the latter only at 12 h. These imaging biomarkers of tumor vascular kinetics describe the short-term temporal changes in physical spaces and fluid flows in a model of GBM after Avastin administration.

Radiation Oncology

Morris ED, **Ghanem AI**, **Zhu S**, Dong M, **Pantelic MV**, and Glide-Hurst CK. Quantifying inter-fraction cardiac substructure displacement during radiotherapy via magnetic resonance imaging guidance. *Physics and Imaging in Radiation Oncology* 2021; 18:34-40. PMID: Not assigned. Full Text

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Emerging evidence suggests cardiac substructures are highly radiosensitive during radiation therapy for cancer treatment. However, variability in substructure position after tumor localization has not been well characterized. This study quantifies inter-fraction displacement and planning organ at risk volumes (PRVs) of substructures by leveraging the excellent soft tissue contrast of magnetic resonance imaging (MRI). Eighteen retrospectively evaluated patients underwent radiotherapy for intrathoracic tumors with a 0.35 T MRI-guided linear accelerator. Imaging was acquired at a 17–25 s breath-hold (resolution 1.5 × 1.5 × 3 mm3). Three to four daily MRIs per patient (n = 71) were rigidly registered to the planning MRI-simulation based on tumor matching. Deep learning or atlas-based segmentation propagated 13 substructures (e.g., chambers, coronary arteries, great vessels) to daily MRIs and were verified by two radiation oncologists. Daily centroid displacements from MRI-simulation were quantified and PRVs were calculated. Across substructures, inter-fraction displacements for 14% in the left–right, 18% in the anterior-posterior, and 21% of fractions in the superior-inferior were > 5 mm. Due to lack of breath-hold compliance, ~4% of all structures shifted > 10 mm in any axis. For the chambers, median displacements were 1.8, 1.9, and 2.2 mm in the left–right, anterior-posterior, and superior-inferior axis, respectively. Great vessels demonstrated larger displacements (> 3 mm) in the superior-inferior axis (43% of shifts) and were only 25% (left–right) and 29% (anterior-posterior) elsewhere. PRVs from 3 to 5 mm were determined as anisotropic substructure-specific margins. This exploratory work derived substructure-specific safety margins to ensure highly effective cardiac sparing. Findings require validation in a larger cohort for robust margin derivation and for applications in prospective clinical trials.

Radiation Oncology

Prasanna PG, Citrin DE, Hildesheim J, Ahmed MM, Venkatachalam S, Riscuta G, Xi D, Zheng G, van Deursen J, Goronzy J, Kron SJ, Anscher MS, Sharpless NE, Campisi J, **Brown SL**, Niedernhofer LJ, O'Loghlen A, Georgakilas AG, Paris F, Gius D, Gewirtz DA, Schmitt CA, Abazeed ME, Kirkland JL, Richmond A, Romesser PB, Lowe SW, Gil J, Mendonca MS, Burma S, Zhou D, and Coleman CN. Therapy-Induced Senescence: Opportunities to Improve Anti-Cancer Therapy. *J Natl Cancer Inst* 2021; Epub ahead of print. PMID: 33792717. Full Text

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Cellular senescence is an essential tumor suppressive mechanism that prevents the propagation of oncogenically activated, genetically unstable, and/or damaged cells. Induction of tumor cell senescence is also one of the underlying mechanisms by which cancer therapies exert antitumor activity. However, an increasing body of evidence from preclinical studies demonstrates that radiation and chemotherapy cause accumulation of senescent cells (SnCs) both in tumor and normal tissue. SnCs in tumors can, paradoxically, promote tumor relapse, metastasis, and resistance to therapy, in part, through expression of the senescence-associated secretory phenotype. In addition, SnCs in normal tissue can contribute to certain radiation- and chemotherapy-induced side effects. Because of its multiple roles, cellular senescence could serve as an important target in the fight against cancer. This commentary provides a summary of the discussion at the National Cancer Institute Workshop on Radiation, Senescence, and Cancer (August 10-11, 2020, National Cancer Institute, Bethesda, MD) regarding the current status of senescence research, heterogeneity of therapy-induced senescence, current status of senotherapeutics and molecular biomarkers, a concept of "one-two punch" cancer therapy (consisting of therapeutics to induce tumor cell senescence followed by selective clearance of SnCs), and its integration with personalized adaptive tumor therapy. It also identifies key knowledge gaps and outlines future directions in this emerging field to improve treatment outcomes for cancer patients.

Research Administration

Peeri H, Shalev N, Vinayaka AC, Nizar R, Kazimirsky G, Namdar D, Anil SM, Belausov E, **Brodie C**, and Koltai H. Specific Compositions of Cannabis sativa Compounds Have Cytotoxic Activity and Inhibit Motility and Colony Formation of Human Glioblastoma Cells In Vitro. *Cancers (Basel)* 2021; 13(7). PMID: 33916466. Full Text

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Glioblastoma multiforme (GBM) is the most lethal subtype of glioma. Cannabis sativa is used for the treatment of various medical conditions. Around 150 phytocannabinoids have been identified in C. sativa, among them Δ-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) that trigger GBM cell death. However, the optimal combinations of cannabis molecules for anti-GBM activity are unknown. Chemical composition was determined using high-performance liquid chromatography (HPLC) and gas chromatography mass spectrometry (GC/MS). Cytotoxic activity was determined by XTT and lactate dehydrogenase (LDH) assays and apoptosis and cell cycle by fluorescence-activated cell sorting (FACS). F-actin structures were observed by confocal microscopy, gene expression by quantitative PCR, and cell migration and invasion by scratch and transwell assays, respectively. Fractions of a high-THC cannabis strain extract had significant cytotoxic activity against GBM cell lines and glioma stem cells derived from tumor specimens. A standard mix (SM) of the active fractions F4 and F5 induced apoptosis and expression of endoplasmic reticulum (ER)-stress associated-genes. F4 and F5 inhibited cell migration and invasion, altered cell cytoskeletons, and inhibited colony formation in 2 and 3-dimensional models. Combinations of cannabis compounds exert cytotoxic, anti-proliferative, and anti-migratory effects and should be examined for efficacy on GBM in pre-clinical studies and clinical trials.

Sleep Medicine

Kalmbach DA, **Cheng P**, and **Drake CL**. A pathogenic cycle between insomnia and cognitive arousal fuels perinatal depression: exploring the roles of nocturnal cognitive arousal and perinatal-focused rumination. *Sleep* 2021; Epub ahead of print. PMID: 33830248. Full Text

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STUDY OBJECTIVES: Depression is among the most prevalent perinatal complications, yet modifiable risk factors remain elusive. Over half of perinatal women endorse clinical insomnia symptoms, which are etiologically implicated in depression in nonperinatal samples. Yet, prospective data on perinatal insomnia and depression are mixed. We sought to clarify temporal associations of insomnia and depression during peripartum, and to investigate cognitive arousal as a potential mechanism facilitating this relationship. METHODS: Seventy pregnant women completed sociodemographic information and baseline sleep and mood symptoms between gestational weeks 25 and 30. Beginning at gestational week 30, participants completed 17 weekly online surveys assessing insomnia, depression, and three cognitive arousal indices (nocturnal cognitive arousal, perseverative thinking, and perinatal-focused rumination). Mixed effects models were conducted to test hypotheses. RESULTS: Women were at risk for depression when experiencing insomnia (odds ratio [OR] = 2.36, 95% confidence interval [CI] = 1.28 to 4.35), nocturnal cognitive arousal (OR = 3.05, 95% CI = 1.60 to 5.79), perinatal-focused rumination (OR = 2.05, 95% CI = 1.11 to 3.79), and perseverative thinking (OR = 7.48, 95% CI = 3.90 to 14.32). Prospective analyses revealed bidirectional effects between insomnia and cognitive arousal, and both predicted future depression. Nocturnal cognitive arousal mediated 23-43% of the effect of insomnia on depression. Insomnia mediated 12%-18% of the effect of nocturnal cognitive arousal on depression. A similar pattern was observed with perinatal-focused rumination. Depression did not predict insomnia. CONCLUSION: Nocturnal cognitive arousal, including ruminating on perinatal concerns while trying to fall asleep, fuels insomnia. In turn, lying awake at night provides an opportunity for nocturnal cognitive arousal. This cycle feeds perinatal depression. Daytime cognitive arousal may indirectly disrupt sleep as perseverating during the day persists into the night.

Surgery

Varban OA, Bonham AJ, Stricklen AL, Ross R, **Carlin AM**, Finks JF, and Ghaferi AA. Am I on Track? Evaluating Patient-Specific Weight Loss After Bariatric Surgery Using an Outcomes Calculator. *Obes Surg* 2021; Epub ahead of print. PMID: 33825152. Full Text

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PURPOSE: Individual weight loss outcomes after bariatric surgery can vary considerably. As a result, identifying and assisting patients who are not on track to reach their weight loss goals can be challenging. MATERIALS AND METHODS: Using a bariatric surgery outcomes calculator, which was formulated using a state-wide bariatric-specific data registry, predicted weight loss at 1 year after surgery was calculated on 658 patients who underwent bariatric surgery at 35 different bariatric surgery programs between 2015 and 2017. Patient characteristics, postoperative complications, and weight loss trajectories were compared between patients who met or exceeded their predicted weight loss calculation to those who did not based on observed to expected weight loss ratio (O:E) at 1 year after surgery. RESULTS: Patients who did not meet their predicted weight loss at 1 year (n = 237, 36%) had a mean O:E of 0.71, while patients who met or exceeded their prediction (n = 421, 63%) had a mean O:E = 1.14. At 6 months, there was a significant difference in the percent of the total amount of predicted weight loss between the groups (88% of total predicted weight loss for those that met their 1-year prediction vs 66% for those who did not, $p < 0.0001$). Age, gender, procedure type, and risk-adjusted complication rates were similar between groups. CONCLUSION: Using a bariatric outcomes calculator can help set appropriate weight-loss expectations after surgery and also identify patients who may benefit from additional therapy prior to reaching their weight loss nadir.

Surgery
Macias BR, Ferguson CR, Patel N, Gibson C, Samuels BC, Laurie SS, Lee SMC, Ploutz-Snyder R, Kramer L, Mader TH, Brunstetter T, Alferova IV, Hargens AR, Ebert DJ, **Dulchavsky SA**, and Stenger MB. Changes in the Optic Nerve Head and Choroid Over 1 Year of Spaceflight. *JAMA Ophthalmol* 2021; Epub ahead of print. PMID: 33914020. Full Text

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University of Alabama at Birmingham, Birmingham.
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IMPORTANCE: While 6-month data are available regarding spaceflight-associated neuro-ocular syndrome, manned missions for 1 year and beyond are planned, warranting evaluation for spaceflight-associated neuro-ocular syndrome beyond 6 months. OBJECTIVE: To determine if the manifestation of spaceflight-associated neuro-ocular syndrome worsens during International Space Station missions exceeding the present 4- to 6-month duration. DESIGN, SETTING, AND PARTICIPANTS: The One-Year Mission Study used quantitative imaging modalities to investigate changes in ocular structure in 2 crew members who completed a 1-year-long spaceflight mission. This study investigated the ocular structure of crew members before, during, and after their mission on the International Space Station. Two crew members participated in this study from March 2015 to September 2016. Analysis began in March 2015 and ended in May 2020. EXPOSURES: Crew members were tested before, during, and up to 1 year after spaceflight. MAIN OUTCOMES AND MEASURES: This study compares ocular changes (peripapillary retinal edema, axial length, anterior chamber depth, and refraction) in two 1-year spaceflight mission crew

members with cohort crew members from a 6-month mission (n = 11). Minimum rim width (the shortest distance between Bruch membrane opening and the internal limiting membrane) and peripapillary total retinal thickness were measured using optical coherence tomography. RESULTS: Both crew members were men. Minimum rim width and total retinal thickness increased in both participants throughout the duration of spaceflight exposure to the maximal observed change from preflight (minimum rim width: participant 1, 561 [+149 from preflight] μm at flight day 270; participant 2, 539 [+56 from preflight] μm at flight day 270; total retinal thickness: participant 1, 547 [+135 from preflight] μm at flight day 90; participant 2, 528 [+45 from preflight] μm at flight day 210). Changes in peripapillary choroid engorgement, axial length, and anterior chamber depth appeared similar between the 1-year mission participants and a 6-month mission cohort. CONCLUSIONS AND RELEVANCE: This report documents the late development of mild optic disc edema in 1 crew member and the progressive development of choroidal folds and optic disc edema in another crew member over the duration of 1 year in low Earth orbit aboard the International Space Station. Previous reports characterized the ocular risk associated with 4 to 6 months of spaceflight. As future spaceflight missions are planned to increase in duration and extend beyond low Earth orbit, further observation of astronaut ocular health on spaceflight missions longer than 6 months in duration may be warranted.

Surgery

Martins PN, **Rizzari MD**, Ghinolfi D, Jochmans I, Attia M, Jalan R, and Friend PJ. Design, Analysis, and Pitfalls of Clinical Trials Using Ex Situ Liver Machine Perfusion: The International Liver Transplantation Society Consensus Guidelines. *Transplantation* 2021; 105(4):796-815. PMID: 33760791. Full Text

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BACKGROUND: Recent trials in liver machine perfusion (MP) have revealed unique challenges beyond those seen in most clinical studies. Correct trial design and interpretation of data are essential to avoid drawing conclusions that may compromise patient safety and increase costs. METHODS: The International Liver Transplantation Society, through the Special Interest Group "DCD, Preservation and Machine Perfusion," established a working group to write consensus statements and guidelines on how future clinical trials in liver perfusion should be designed, with particular focus on relevant clinical endpoints and how different techniques of liver perfusion should be compared. Protocols, abstracts, and full published papers of clinical trials using liver MP were reviewed. The use of a simplified Grading of Recommendations Assessment, Development, and Evaluation working group (GRADE) system was attempted to assess the level of evidence. The working group presented its conclusions at the International Liver Transplantation Society consensus conference "DCD, Liver Preservation, and Machine Perfusion" held in Venice, Italy, on January 31, 2020. RESULTS: Twelve recommendations were proposed with the main conclusions that clinical trials investigating the effect of MP in liver transplantation should (1) make the protocol publicly available before the start of the trial, (2) be adequately powered, and (3) carefully consider timing of randomization in function of the primary outcome. CONCLUSIONS: There are issues with using accepted primary outcomes of liver transplantation trials in the context of MP trials, and no ideal endpoint could be defined by the working group. The setup of an international registry was considered vital by the working group.

Surgery

Kalu R, **Boateng P**, **Carrier L**, **Garzon J**, **Tang A**, **Reickert C**, and **Stefanou A**. Effect of preoperative versus postoperative use of transversus abdominis plane block with plain 0.25 % bupivacaine on postoperative opioid use: a retrospective study. *BMC Anesthesiol* 2021; 21(1):114. PMID: 33845790. Full Text

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BACKGROUND: Enhanced recovery protocols optimize pain control via multimodal approaches that include transversus abdominis plane (TAP) block. The aim of this study was to evaluate the effect of preoperative vs. postoperative plain 0.25 % bupivacaine TAP block on postoperative opioid use after colorectal surgery. METHODS: A retrospective cohort study comparing postoperative opioid use in patients who received preoperative (n = 240) vs. postoperative (n = 22) plain 0.25 % bupivacaine TAP blocks. The study was conducted in a single tertiary care institution and included patients who underwent colorectal resections between August 2018 and January 2020. The primary outcome of the study was postoperative opioid use. Secondary outcomes included operative details, length of stay, reoperation, and readmission rates. RESULTS: Patients who received postoperative plain 0.25 % bupivacaine TAP blocks were less likely to require postoperative patient-controlled analgesia (PCA) (59.1 % vs. 83.3 %; p = 0.012) and opioid medications on discharge (6.4 % vs. 16.9 %; p = 0.004) relative to patients who received preoperative TAP. When needed, a significantly smaller amount of opioid was prescribed to the postoperative group (84.5 vs. 32.0 mg, p = 0.047). No significant differences were noted in the duration of postoperative PCA use, amount of oral opioid use, and length of stay. CONCLUSIONS: Plain 0.25 % bupivacaine TAP block administered postoperatively was associated with significantly lower need for postoperative PCA and discharge opioid medications. The overall hospital length of stay was not affected by the timing of TAP block. Because of the limited sample size in this study, conclusions cannot be generalized, and more research will be required.

Surgery

Ivanics T, **Zimnicki K**, **Ahmad H**, **Saab I**, Liu V, **Tepper D**, and **Siddiqui A**. Fat grafting: A novel technique for difficult ostomy management. *Surgery* 2021; Epub ahead of print. PMID: 33820652. Full Text

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Surgery

Schwartz T. Just Say No: The Case Against Opioid-Based Postoperative Pain Management Regimens Following Breast Surgery. *Ann Surg Oncol* 2021; Epub ahead of print. PMID: 33813672. Full Text

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Surgery

Luker J, Tajran J, Marquette L, Tepper D, **Carlin A**, Darian V, and **Siddiqui A**. Long-Term Weight Loss with Body Contour Surgery After Roux-en-Y Gastric Bypass. *Obes Surg* 2021; Epub ahead of print. PMID: 33851305. Full Text

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BACKGROUND: Bariatric surgery is accepted as an evidence-based treatment for morbid obesity. Many patients seek out body contour surgery afterwards to correct acquired deformities. This study seeks to better define the impact of body contour surgery on long-term weight loss. METHODS: This study is a single-center retrospective review of 78 patients who underwent body contouring surgery post-Roux-en-Y gastric bypass compared with 221 matched control patients who underwent Roux-en-Y gastric bypass only. Data was collected for patients at least 7 years post-Roux-en-Y gastric bypass. RESULTS: Patients who underwent both bariatric surgery and body contour surgery maintained mean long-term weight loss of 58 kg. The matched control group mean weight loss over the same time interval was 42 kg. The difference was statistically and clinically significant ($p = 0.005$). Change in body mass index, percent total weight loss, and percent excess body mass index loss were all statistically significant between the 2 groups. CONCLUSION: Patients who underwent body contour surgery better maintained long-term weight reduction in comparison to those who only had gastric bypass. Further understanding of the etiology of this association is important for patients contemplating body contouring surgery.

Surgery

Joseph MS, **Tinney F**, Naik A, Parasuraman R, **Samaniego-Picota M**, and Bhave NM. Right Ventricular Dysfunction and Adverse Outcomes after Renal Transplantation. *Cardiorenal Med* 2021; 11(2):109-118. PMID: 33853060. Full Text

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INTRODUCTION: Pulmonary hypertension is common among patients with end-stage renal disease, although data regarding the impact of right ventricular (RV) failure on postoperative outcomes remain limited. We hypothesized that echocardiographic findings of RV dilation and dysfunction are associated with adverse clinical outcomes after renal transplant. METHODS: A retrospective review of adult renal transplant recipients at a single institution from January 2008 to June 2010 was conducted. Patients with transthoracic echocardiograms (TTEs) within 1 year leading up to transplant were included. The primary end point was a composite of delayed graft function, graft failure, and all-cause mortality. RESULTS: Eighty patients were included. Mean follow-up time was 9.4 ± 0.8 years. Eight patients (100%) with qualitative RV dysfunction met the primary end point, while 39/65 patients (60.0%) without RV dysfunction met the end point ($p = 0.026$). Qualitative RV dilation was associated with a significantly shorter time to all-cause graft failure ($p = 0.03$) and death ($p = 0.048$). RV systolic pressure was not measurable in 45/80 patients (56%) and was not associated with outcomes in the remaining patients. CONCLUSION: RV dilation and dysfunction are associated with adverse outcomes after renal transplant. TTE assessment of RV size and function should be a standard part of the pre-kidney transplant cardiovascular risk assessment.

Urology

Nocera L, Collà Ruvolo C, Stolzenbach LF, Deuker M, Tian Z, Gandaglia G, Fossati N, **Abdollah F**, Suardi N, Mirone V, Graefen M, Chun FK, Saad F, Montorsi F, Briganti A, and Karakiewicz PI. Improving the stratification of intermediate risk prostate cancer. *Minerva Urol Nephrol* 2021; Epub ahead of print. PMID: 33887893. Request Article

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BACKGROUND: Intermediate risk prostate cancer (IR PCa) may exhibit a wide array of phenotypes, from favorable to unfavorable. NCCN criteria help distinguishing between favorable versus unfavorable subgroups. We studied and attempted to improve this classification. METHODS: Within the SEER database 2010-2016, we identified 19,193 IR PCa patients treated with radical prostatectomy. A multivariable logistic regression model predicting unfavorable IR PCa was developed and externally validated, in addition to a head-to-head comparison with NCCN IR PCa stratification. RESULTS: Model development (development cohort n=13,436: 3,585 unfavorable versus 9,851 favorable) rested on age, PSA, clinical T stage, biopsy Gleason Grade Group (GGG) and percentage of positive cores. All were independent predictors of unfavorable IR PCa. In external validation cohort (n=5,757: 1,652 unfavorable versus 4,105 favorable), NCCN stratification was 61.8% accurate in discriminating between favorable versus unfavorable, compared to 67.6% for nomogram, which exhibited excellent calibration, less pronounced departures from ideal prediction and greater net-benefit in decision curve analyses (DCA) than NCCN stratification. The optimal nomogram cutoff misclassified 312 of 1976 patients (15.8%) versus 598 of 2877 (20.8%) for NCCN stratification. Of NCCN misclassified patients, 90.0% harbored pT3-4 stages versus 84.6% of nomogram. CONCLUSIONS: The newly developed, externally validated nomogram discriminates better between favorable versus unfavorable IR PCa, according to overall accuracy, calibration, DCA, and actual numbers and stage distribution of misclassified patients.

Urology
Rogers CG. Point/Counterpoint of Controversial Topics in Robotic Surgery Editorial Comment. *J Endourol* 2021; Epub ahead of print. PMID: 33913740. Full Text

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Urology
Dalela D, and **Abdollah F**. Reply to Letter to the Editor Re: Generalizability of prostate-specific antigen (PSA) screening trials in a "real world" setting: a nationwide survey analysis. *Urology* 2021; Epub ahead of print. PMID: 33823172. Full Text

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Urology

Katims AB, Say R, Derweesh I, Uzzo R, Minervini A, Wu Z, **Abdollah F**, Sundaram C, Ferro M, Rha K, Mottrie A, Rosiello G, Simone G, Eun DD, Reese A, Kidd LC, Porter J, Bhattu AS, Gonzalgo ML, Margulis V, **Marcus J**, **Danno A**, Meagher M, Tellini R, Mari A, Veccia A, Ghoreifi A, Autorino R, Djaladat H, and Mehrazin R. Risk Factors for Intravesical Recurrence After Minimally Invasive Nephroureterctomy for Upper Tract Urothelial Cancer (Robuust Collaboration). *J Urol* 2021; Epub ahead of print. PMID: 33881931. Full Text

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PURPOSE: Intravesical recurrence (IVR) after radical nephroureterectomy (RNU) for upper tract urothelial carcinoma (UTUC) has an incidence of approximately 20-50%. Studies to date have been composed of mixed treatment cohorts - open, laparoscopic, and robotic. The objective of this study is to assess clinicopathologic risk factors for intravesical recurrence after RNU for UTUC in a completely minimally invasive cohort. MATERIALS AND METHODS: We performed a multicenter, retrospective analysis of 485 patients with UTUC without prior or concurrent bladder cancer who underwent robotic or laparoscopic RNU. Patients were selected from an international cohort of 17 institutions across the United States, Europe, and Asia. Univariate and multiple Cox regression models were used to identify risk factors for bladder recurrence. RESULTS: A total of 485 (389 robotic, 89 laparoscopic) patients were included in analysis. Overall, 110 (22.7%) of patients developed IVR. The average time to recurrence was 15.2 months (SD 15.5 months). Hypertension was a significant risk factor on multiple regression [HR 1.99, CI 1.06; 3.71, p=0.030]. Diagnostic ureteroscopic biopsy incurred a 50% higher chance of developing IVR [HR 1.49, CI 1.00; 2.20, p=0.048]. Treatment specific risk factors included positive surgical margins [HR 3.36, CI 1.36; 8.33, p=0.009] and transurethral resection for bladder cuff management [HR 2.73, CI 1.10; 6.76, p=0.031]. CONCLUSIONS: IVR after minimally RNU for UTUC is a relatively common event. Risk factors include a ureteroscopic biopsy, transurethral resection of the bladder cuff, and positive surgical margins. When possible, avoidance of transurethral resection of the bladder cuff and alternative strategies for obtaining biopsy tissue sample should be considered.

Urology

Fedrigon D, Faris A, **Kachroo N**, Jain R, Elia M, Wilkins L, Li J, De S, Noble M, Monga M, and Sivalingam S. SKOPE - Study of Ketorolac vs Opioid for Pain after Endoscopy: A Double-Blinded Randomized Control Trial in Patients Undergoing Ureteroscopy. *J Urol* 2021; Epub ahead of print. PMID: 33819072. Full Text

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University of Rochester- Department of Urology.
University of Washington- Department of Surgery.
Johns Hopkins- Brady Urological Institute.
Cleveland Clinic- Department of Quantitative Health Sciences.
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PURPOSE: Pain is the leading cause for unplanned emergency department visits and readmissions after ureteroscopy (URS), making post-operative analgesic stewardship a priority given the current opioid epidemic. We conducted a double-blinded, randomized controlled trial (RCT), with non-inferiority design, comparing nonsteroidal anti-inflammatory drugs (NSAIDs) to opiates for postoperative pain control in patients undergoing URS for urolithiasis. MATERIALS AND METHODS: Patients were randomized and blinded to either oxycodone (5mg) or ketorolac (10mg), taken as needed, with 3 non-blinded oxycodone rescue pills for breakthrough pain. Primary study outcome was visual analog scale pain score on post-operative days 1-5. Secondary outcomes included medication utilization, side effects, and Ureteral Stent Symptoms Questionnaire (USSQ) scores. RESULTS: Eighty-one patients were included (43 oxycodone, 38 ketorolac). The two groups had comparable patient, stone, and perioperative characteristics. No differences were found in post-operative pain scores, study medication or rescue pill usage, or side effects. Higher maximum pain scores on days 1-5 ($p<0.05$) and higher USSQ score (28.1 vs 21.7, $p=0.045$) correlated with analgesic usage, irrespective of treatment group. Patients receiving ketorolac reported significantly fewer days confined to bed (1.3±1.3 vs 2.3±2.6, $p=0.02$). There was no difference in unscheduled post-operative physician encounters. CONCLUSIONS: This is the first double-blinded RCT comparing NSAIDs and opiates post-URS and demonstrates non-inferiority of NSAIDs in pain control with similar efficacy, safety profile, physician contact and notably, earlier convalescence compared to the opioid group. This provides strong evidence against routine opioid use post-URS, justifying continued investigation into reducing post-operative opiate prescriptions.

Conference Abstracts

Cardiology/Cardiovascular Research

Genovese L, Yin M, **Michaels A**, Singh R, Tang D, Indaram M, Kanwar M, **Cowger J**, Drakos S, and Shah P. Multicenter Study of Favorable Patient Characteristics Associated with Cardiac Reverse Remodeling in Left Ventricular Assist Device Patients. *J Heart Lung Transplant* 2021; 40(4):S176.

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Purpose: This study analyzed a multicenter cohort of patients who underwent left ventricular assist device (LVAD) implantation to distinguish favorable characteristics that increase the likelihood for cardiac reverse remodeling and myocardial recovery. Methods: This was a multicenter study at 4 LVAD implanting sites in the U.S. Baseline patient characteristics, including demographics, medical history and echocardiographic parameters were reviewed. Echocardiographic parameters of LV structure and function were obtained pre-implant and at 1, 3, 6, and 12 months of LVAD support. Responders to LVAD therapy had echocardiographic evidence of reverse cardiac remodeling and achieved an LVEF ≥ 40% and LV ventricular internal diastolic diameter (LVIDd) ≤ 6.0cm. Univariate and multivariate analyses were performed to determine the odds ratio of achieving responder status. Results: The study retrospectively reviewed 311 chronic HF patients receiving LVAD support. The average patient age was 55.6 ± 12.9 years, 17.7% were female, 53% had an ischemic cardiomyopathy, and the average duration of HF was 3.4 ± 3.0 years pre-implant. In the cohort, 9.32% of patients achieved responder status. Univariate analysis of baseline characteristics was performed to identify predictors of responder status at final echocardiographic time point. Female sex and age ≤ 65 years had improved odds of myocardial recovery (OR 2.31, 95%CI: 1.0 to 5.4, $p=0.05$ and 2.26, 95%CI: 1.03 to 4.98, $p=0.04$). Other significant predictors of cardiac reverse remodeling are presented in the figure. In a multivariate analysis, female sex, age ≤ 65 years and an LVIDd ≤ 7.3cm were each individually associated with a 2-fold increase in the odds of

cardiac reverse remodeling. Conclusion: In a contemporary, multicenter study of LVAD patients, we identified a combination of baseline clinical and echocardiographic characteristics associated with significant cardiac reverse remodeling during LVAD support.

Cardiology/Cardiovascular Research
Kyriakopoulos CP, Taleb I, Koliopoulou AG, Ijaz N, **Demertzis Z**, **Peruri A**, Dranow E, Wever-Pinzon O, Yin MY, Shah KS, Kemeyou L, Richins TJ, Tang DG, **Nemeh HW**, Stehlik J, Selzman CH, Alharethi R, Caine WT, Kfoury AG, Fang JC, **Cowger JA**, Shah P, and Drakos SG. Predicting Right Ventricular Failure Following Left Ventricular Assist Device Support: A Derivation-Validation Multicenter Risk Score. *J Heart Lung Transplant* 2021; 40(4):S98.

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Purpose: Despite several models predicting right ventricular failure (RVF) after durable left ventricular assist device (LVAD) support, poor performance when externally validated has limited their widespread use. We sought to derive a predictive model for RVF after LVAD implantation, and ascertain its performance in an independent cohort. Methods: End-stage heart failure (HF) patients requiring continuous-flow LVAD were prospectively enrolled at one US program (n=477, derivation cohort), with two other US medical centers forming the validation cohort (n=321). The primary outcome was RVF incidence, defined as the need for right ventricular assist device or inotropes for >14 days. Multivariable logistic regression in the derivation set yielded a RVF predictive model, which was subsequently applied to the validation cohort, and a risk score was ultimately developed. Results: Derivation cohort included patients less likely to be African-Americans (7% vs 37%; p<0.001), Hispanics (7% vs 30%; p<0.001), have a remote history of hypertension (49% vs 60%; p=0.002) or be bridged with short-term MCS (8% vs 16%; p=0.001), compared to the validation set. RVF incidence was 16% in the derivation and 36% in the validation cohort (p<0.001). Multivariable analysis identified 7 variables (Figure) as predictive of RVF, with the model achieving a C statistic of 0.734 (95% CI=0.674-0.794) in the derivation and 0.709 (95% CI=0.651-0.767) in the heterogeneous validation cohort. Patients were stratified into 3 RVF risk groups (all comparisons; p<0.001) (Figure). Conclusion: We propose a novel scoring system to predict post-LVAD RVF, achieving high discriminative performance in distinct, heterogeneous LVAD cohorts.

Cardiology/Cardiovascular Research
Ravichandran AK, **Cowger JA**, Feller ED, Mahr C, Hiesinger W, Klein L, Jacoski MV, Lampert B, and Moazami N. An Analysis of Driveline Infections with Left Ventricular Assist Devices Utilizing Carbothane versus Pellethane Driveline Sheaths. *J Heart Lung Transplant* 2021; 40(4):S434-S435.

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Purpose: Strategies underlying the use of Left ventricular assist devices (LVAD) for patients with end-stage heart failure include its use as bridge to transplant (BTT) or as destination therapies (DT). Survival outcomes of patients undergoing these LVAD implant strategies were evaluated and compared. Methods: A retrospective analysis of single center database heart transplant patients that received LVADs from Nov. 2009 to Sep. 2020 (n=137). Patients were placed into the following cohorts based on the implant strategy: 1) BTT (n=31), 2) DT (n=106). Demographics were compared between groups for significance. Kaplan Meier curves were calculated and compared via log rank tests, and Cox Regression Analysis was performed. P-values <0.05 was considered significant. Results: Demographics between the groups were: diagnosis (p=0.257), CPB time (p=0.957), XC time (p=0.763), ischemic time (p=0.478), warm ischemic time (p=0.332), age (p=0.323), race (p=0.067), length of stay (p=0.355) and PRA (p=0.701). Of 137

patients that received LVADs used for BTT or DT prior to heart transplant, the BTT group had better survival outcomes than DT (p=0.0467). Median survival time for DT group was 2554 days, and median survival time for BTT group was 3030 days. The type of LVADs used between the two groups were significantly different (p=0.0009), therefore cox regression was run to control for statistically significant variables, with device showing no significant effect on survival. In cox regression BTT had a protective effect over DT with a hazard ratio of 1.439, p=0.0364. Conclusion: Implant strategies for LVAD as BTT or DT show a difference in survival outcomes for end-stage heart failure patients, however both had reasonable outcomes. This paper supports the current literature in that LVADs are viable for use in patients of all types, with slightly better effects in BTT patients.

Cardiology/Cardiovascular Research
So CY, Kang G, and **Eng M**. Chase the Leak - A Case of Valve-in-Ring with Mitral PVL Closure. *J Am Coll Cardiol* 2021; 77(14):S247-S248.

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Cardiology/Cardiovascular Research
Tedford RJ, Potapov E, **Cowger JA**, Hayward C, Rich JD, Kusmierczyk M, Jacoski MV, Lavine K, and Moazami N. An Analysis of Post-Implant Severe Right Heart Failure in Real-World Use of the HeartWare (TM) HVAD (TM) System in Destination Therapy. *J Heart Lung Transplant* 2021; 40(4):S435-S435.

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Purpose: Patients with the HeartWare HVAD require careful medical management in order to maintain an INR within therapeutic range (2-3) and prevent thrombotic events. We compared the incidence of epistaxis in patients with the HVAD and HeartMate 3 using propensity score matching (PSM). Methods: Ninety-eight patients implanted with a left ventricular assist device (LVAD) from 2015-2020 were included in this study. Patients were matched on the basis of baseline characteristics, including age, gender, body mass index (BMI), indication, etiology, concomitant procedures, and the right ventricular assist device (RVAD) usage. Results: To our knowledge, this is the first study to perform a PSM comparison of epistaxis events in patients with the HVAD and HeartMate 3. After matching, there were no significant differences in any of the baseline characteristics between groups (P >0.05 for all). Patients with the HVAD were more likely to suffer from epistaxis than HeartMate 3 patients (43% vs 18%, P = 0.027), an absolute risk increase of 25% (95% CI 5.7-44.3%) and a number needed to harm of 4 patients (95% CI 2.3-17.6). In both the univariate and multivariate analyses, HVAD usage was significantly associated with epistaxis (P <0.05). Independent predictors of epistaxis were found to be HVAD usage (OR 3.39, 95% CI 1.13-11.15, P = 0.034) and out of range INR at discharge (OR 7.16, 95% CI 2.46-23.09, P <0.001). Out of range INR was also associated with a significantly longer length of stay (P = 0.01). Between patients with the HVAD and those with the HeartMate 3, there were no significant differences in length of stay, survival, and whether INR at discharge was in therapeutic range (P >0.05 for all). Conclusion: Patients with the HVAD may be at a greater risk for developing epistaxis than those with the HeartMate 3. However, other outcomes such as length of stay and survival are comparable. Prospective, multi-center studies should be done to accurately assess the impact of device type on clinical outcomes following LVAD implantation.

Cardiology/Cardiovascular Research
Yin M, **Michaels A**, Genovese L, Indaram M, Shah K, Singh R, Caine W, Nemeh H, Alharethi R, Tang D, Selzman C, Kanwar M, **Cowger J**, Shah P, and Drakos SG. Comparison of Cardiac Reverse Remodeling between Older and Newer Generation Continuous-Flow LVAD. *J Heart Lung Transplant* 2021; 40(4):S82.

M. Yin, Cardiology, University of Utah School of Medicine, Salt Lake City, UT, United States

Purpose: The purpose of our study is to compare the left ventricular (LV) functional and structural changes following mechanical circulatory support (MCS) between continuous-flow left ventricular assist devices (CF-LVADs) that provide mechanical unloading characterized by specific bioengineering differences. Methods: The study enrolled 311 chronic HF patients undergoing MCS with HVAD (HW, hybrid levitation centrifugal pump, n=95), HeartMate 3 (HM3, full magnetic levitation centrifugal pump, n=140), and HeartMate II (HM2, axial flow pump, n=76) at four sites across the US. Echocardiographic parameters of LV structure and function were obtained pre-implant and at 1, 3, 6, and 12 months of CF-LVAD support. Results: There were no significant differences in baseline characteristics between groups. At 3 months post-LVAD support the LV ejection fraction (LVEF) was higher (p=0.03, Figure 1A) and left ventricular end diastolic diameter (LVEDD) was lower (p=0.04, Figure 1B) in HMII patients, but there were no significant difference in LVEF and LVEDD between devices at 6 or 12 months. The proportion of patients achieving “cardiac reverse remodeling responder” status (defined as improvement of LVEF to ≥40% and LVEDD <6.0cm) was 9.32%, and comparable between the CF-LVADs. Conclusion: The newest generation full magnetically levitated CF-LVAD results in similar cardiac reverse remodeling as older generation CF-LVADs. These findings suggest that the fully magnetically levitated device technology could provide an adequate platform to further study and promote reverse cardiac remodeling clinically.

Cardiology/Cardiovascular Research

Zweck E, Thayer KL, Helgestad OK, Kanwar M, Ayouty M, Garan A, Hernandez-Montfort J, Mahr C, Wencker D, Sinha S, Vorovich E, Abraham J, **O'Neill W**, Li S, Hickey GW, Jossiasen J, Hassager C, Jensen LO, Holmvang L, Schmidt H, Ravn HB, Moeller JE, Burkhoff D, and Kapur NK. Compatibility of Novel Cardiogenic Shock Phenotypes from the Cardiogenic Shock Working Group (CSWG) with the SCAI Staging System. *J Heart Lung Transplant* 2021; 40(4):S128.

Purpose: Cardiogenic shock (CS) is a heterogeneous syndrome that represents an acute and fulminant form of heart failure (HF). We (1) employed machine learning (ML) to identify distinct CS phenotypes which could help define treatment algorithms based on individual risk and (2) tested the correlation of the SCAI staging system. Methods: We included data from 1957 CS patients from 2 cohorts: CSWG Registry, further grouped for myocardial infarction (CSWG-MI, n=408) and acute on chronic HF (CSWG-HF, n=480); and the Danish Retroshock Registry containing MI patients (DRR, n=1069). Independent consensus k means clustering derived phenotypes at admission in the CSWG-MI cohort that were then validated in the CSWG-HF and DRR cohorts. Patients were also categorized by the most severe SCAI stage reached during the hospitalization. Results: The ML algorithms revealed 3 distinct clusters that we designated: ‘non-congested (I)’, ‘cardio-renal (II)’ and ‘cardio-metabolic (III)’. In-hospital mortality was 21% vs 29% vs 10%, 42% vs 46% vs 32%, and 55% vs 57% vs 54% among the CSWG-MI vs DDR vs CSWG-HF for Clusters I, II and III, respectively. Despite baseline differences among the overall cohorts, clusters presented similarly across the 3 cohorts. The risk of escalating to stage D or E shock was lowest in Cluster I and highest in Cluster III for both CS-MI and CS-HF patients. Within each phenotype, the SCAI staging (C-E) further stratified mortality (fig). Conclusion: Using ML, we derived and externally validated 3 distinct CS phenotypes. SCAI stages and CSWG CS phenotypes identify patients at risk for in-hospital mortality.

Dermatology

Su JC, Spelman LJ, Eichenfield LF, **Stein Gold LF**, Cha A, Graham D, Takiya L, Werth JL, Zang C, and Vlahos B. Crisaborole ointment, 2%, in patients 3 months of age and older with mild-to-moderate atopic dermatitis (AD). *Australas J Dermatol* 2021; 62(SUPPL 1):123-124.

J.C. Su, Murdoch Children's Research Institute, Royal Children's Hospital, University of Melbourne, Melbourne, VIC, Australia

Introduction: Crisaborole is a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild-to-moderate AD. AD-301 (NCT02118766) and AD-302 (NCT02118792) were pivotal phase 3 studies of

crisaborole in patients aged ≥ 2 years. CrisADe CARE 1 was a single-arm, openlabel phase 4 study (NCT03356977) of crisaborole in patients aged 3 to < 24 months. Methods: Patients aged 3 to < 24 months (CARE 1) or ≥ 2 years (AD-301/AD-302) with mild-to-moderate AD received twice-daily crisaborole (or vehicle in AD-301/AD-302) for 28 days. Safety was the primary endpoint in CARE 1. ISGA success (clear [0]/almost clear [1] with a ≥ 2-grade improvement from baseline) at day 29 was an exploratory endpoint in CARE 1 and the primary endpoint in AD-301/ AD-302. Results: CARE 1 included 137 infants, all treated with crisaborole (mean age, 13.6 months [SD, 6.42]). In AD-301/ AD-302, 1016 patients were treated with crisaborole (12.3 years [12.16]). Treatment-emergent AEs were reported for 88 (64.2%) patients in CARE 1 and 297 (29.3%) patients in AD-301/AD-302; 98.8% in CARE 1 and 94.3% in AD-301/AD-302 were mild/moderate. Rates of treatment-related application site pain (3.6%) and application site discomfort (2.9%) in CARE 1 were consistent with the rate of application site pain for crisaborole-treated patients in AD-301/AD-302 (4.4%). In CARE 1, 30.2% and 47.3% of patients achieved ISGA success and ISGA clear/ almost clear at day 29, respectively, consistent with observations for crisaborole-treated patients in AD-301/AD-302 (32.1% and 51.7%). Conclusions: Based on these studies, crisaborole was well tolerated and effective in patients with mild-to-moderate AD, 3 months of age and older.

Hematology-Oncology

Riely GJ, Ou SHI, **Rybkin I**, Spira A, Papadopoulos K, Sabari JK, Johnson M, Heist RS, Bazhenova L, Barve M, Pacheco JM, Velastegui K, Cilliers C, Olson P, Christensen JG, Kheoh T, Chao RC, and Janne PA. KRYSTAL-1: Activity and preliminary pharmacodynamic (PD) analysis of adagrasib (MRTX849) in patients (Pts) with advanced non-small cell lung cancer (NSCLC) harboring KRASG12C mutation. *J Thorac Oncol* 2021; 16(4):S751-S752.

[Riely, G. J.] Weill Cornell Med Coll, Mem Sloan Kettering Canc Ctr, Thorac Oncol Serv, Div Solid Tumor,Dept Med, New York, NY USA. [Ou, S-H. I.] Univ Calif Irvine, Orange, CA 92668 USA. [Rybkin, I.] Henry Ford Hosp, Henry Ford Canc Inst, Detroit, MI 48202 USA. [Spira, A.] Virginia Canc Specialist, Res Inst, Fairfax, VA USA. [Papadopoulos, K.] South Texas Accelerated Res Therapeut START, Clin Res Dept, San Antonio, TX USA. [Sabari, J. K.] New York Univ Langone Hlth, Perlmutter Canc Ctr, New York, NY USA. [Johnson, M.] Tennessee Oncol, Sarah Cannon Res Inst, Lung Canc Res, Nashville, TN USA. [Heist, R. S.] Massachusetts Gen Hosp, Boston, MA 02114 USA. [Bazhenova, L.] UC San Diego Hlth, Moores Canc Ctr, Med, La Jolla, CA USA. [Barve, M.] Mary Crowley Canc Res, Dallas, TX USA. [Pacheco, J. M.] Univ Colorado Anschutz Med Campus, Dept Med, Div Med Oncol, Aurora, CO USA. [Velastegui, K.; Cilliers, C.; Olson, P.; Christensen, J. G.; Kheoh, T.; Chao, R. C.] Mirati Therapeut Inc, San Diego, CA USA. [Janne, P. A.] Dana Farber Canc Inst, Lowe Ctr Thorac Oncol, Boston, MA 02115 USA.

Background: KRAS, the most frequently mutated oncogene in cancer, is a key mediator of the RAS/MAPK signaling cascade that promotes cellular growth and proliferation. KRASG12C mutations occur in approximately 14% of NSCLC (adenocarcinoma). Adagrasib, an investigational agent, is a potent, covalent inhibitor of KRASG12C that irreversibly and selectively binds to KRASG12C, locking it in its inactive state and was optimized for favorable PK properties, including oral bioavailability, long half-life (~24 h), and extensive tissue distribution. Methods: KRYSTAL-1 (NCT03785249) is a multi-cohort phase I/II study evaluating adagrasib in pts with advanced or metastatic solid tumors, including NSCLC, harboring a KRASG12C mutation previously treated with chemotherapy and an anti-PD-(L)1. Exploratory endpoints include correlative analysis of co-occurring genetic alterations in tumor tissue at baseline and evaluation of the modulation of PD markers, including transcriptomics, in pretreatment and on-study biopsies. Results: As of 30 August 2020, 79 pts with pretreated NSCLC were treated with adagrasib 600 mg BID (phase I/Ib and phase II). Most commonly reported (>20%) TRAEs included: nausea (54%), diarrhea (48%), vomiting (34%), fatigue (28%), and increased ALT (23%). Among the 51 pts evaluable for clinical activity, 45% (23/51) had a partial response (PR) and 26 pts had stable disease (SD). In a subpopulation of pts with STK11-comutations, ORR was 64% (9/14). Preliminary PD and mechanistic biomarker analyses on pre- and posttreatment tumor NSCLC biopsies (n = 3) demonstrate own regulation of KRAS/MAPK pathway genes including DUSP6 and SPRY4. In pts with tumors harboring STK11-comutations, there was minimal expression of immune transcripts (eg, CD4 and CD8) at baseline and these transcripts were increased after treatment with adagrasib suggesting a potential immune response

to therapy.Conclusions: Adagrasib is tolerable and has demonstrated clinical activity in pts with previously treated KRASG12C-mutant NSCLC. Additional PD and mechanistic data will be presented.
Clinical trial identification: NCT03785249.

Infectious Diseases

Heldman MR, Kates OS, Multani A, Steinbrink JM, Lewis AV, Alexander BD, Beaird OE, Sehgal S, Mishkin AD, La Hoz RM, Blumberg EA, Nelson J, Safa K, Kotton CN, Hemmersbach-Miller M, **Chaudhry ZS**, Saharia K, Morillas JA, Rakita RM, Sait AS, Meloni F, Wilkens H, Camargo P, Tanna SD, Tomic R, Ison MG, Lease ED, Fisher CE, and Limaye AP. A Multicenter Prospective Registry Study of Lung Transplant Recipients Hospitalized with COVID-19. *J Heart Lung Transplant* 2021; 40(4):S141.

M.R. Heldman, Department of Medicine, Division of Allergy and Infectious Diseases, University of Washington, Seattle, WA, United States

Purpose: Outcomes of lung transplant recipients (LTR) hospitalized for COVID-19 and comparisons to non-lung solid organ transplant recipients (SOTR) are incompletely described. Methods: Using a multicenter prospective registry of SOTR, we examined 28-day outcomes (mortality [primary outcome], intensive care unit (ICU) admission, mechanical ventilation, and bacterial pneumonia) among both LTR and non-lung SOTR hospitalized with laboratory-confirmed COVID-19 diagnosed between March 1, 2020 and September 21, 2020. Data were analyzed using Stata (StataCorp, College Station, TX); chi-square tests were used to compare categorical variables and multivariable logistic regression was used to assess risk factors for mortality. Results: The cohort included 72 LTR and 392 non-lung SOTR (Table 1). Overall, 28-day mortality trended higher in LTR vs. non-lung SOTR (27.8% vs. 19.9%, P=0.136). Other 28-day outcomes were similar between LTR and non-lung SOTR: ICU admission (45.8% vs. 39.1%, P=0.28), mechanical ventilation (32.9% vs. 31.1%, P=0.78), and bacterial pneumonia (15.3% vs. 8.2%, P=0.063). Congestive heart failure, diabetes, age >65 years, and obesity (BMI >= 30) were independently associated with mortality in non-lung SOTR, but not in LTR (Table 2). Conclusion: In this large prospective cohort comparing lung and non-lung SOTR hospitalized for COVID-19, there were high but not significantly different rates of short-term morbidity and mortality. Baseline comorbidities appeared to drive mortality in non-lung SOTR but not LTR. Further studies are needed to identify risk factors for mortality among LTR.

Internal Medicine

Kyriakopoulos CP, Taleb I, Koliopoulou AG, Ijaz N, **Demertzis Z**, **Peruri A**, Dranow E, Wever-Pinzon O, Yin MY, Shah KS, Kemeyou L, Richins TJ, Tang DG, **Nemeh HW**, Stehlik J, Selzman CH, Alharethi R, Caine WT, Kfoury AG, Fang JC, **Cowger JA**, Shah P, and Drakos SG. Predicting Right Ventricular Failure Following Left Ventricular Assist Device Support: A Derivation-Validation Multicenter Risk Score. *J Heart Lung Transplant* 2021; 40(4):S98.

C.P. Kyriakopoulos, U.T.A.H. Cardiac Transplant Program (University of Utah Health & School of Medicine, Intermountain Medical Center, George E. Wahlen VA Medical Center), Salt Lake City, UT, United States

Purpose: Despite several models predicting right ventricular failure (RVF) after durable left ventricular assist device (LVAD) support, poor performance when externally validated has limited their widespread use. We sought to derive a predictive model for RVF after LVAD implantation, and ascertain its performance in an independent cohort. Methods: End-stage heart failure (HF) patients requiring continuous-flow LVAD were prospectively enrolled at one US program (n=477, derivation cohort), with two other US medical centers forming the validation cohort (n=321). The primary outcome was RVF incidence, defined as the need for right ventricular assist device or inotropes for >14 days. Multivariable logistic regression in the derivation set yielded a RVF predictive model, which was subsequently applied to the validation cohort, and a risk score was ultimately developed. Results: Derivation cohort included patients less likely to be African-Americans (7% vs 37%; p<0.001), Hispanics (7% vs 30%; p<0.001), have a remote history of hypertension (49% vs 60%; p=0.002) or be bridged with short-term MCS (8% vs 16%; p=0.001), compared to the validation set. RVF incidence was 16% in the derivation and 36% in the validation cohort (p<0.001). Multivariable analysis identified 7 variables (Figure) as predictive of RVF, with

the model achieving a C statistic of 0.734 (95% CI=0.674-0.794) in the derivation and 0.709 (95% CI=0.651-0.767) in the heterogeneous validation cohort. Patients were stratified into 3 RVF risk groups (all comparisons; p<0.001) (Figure). Conclusion: We propose a novel scoring system to predict post-LVAD RVF, achieving high discriminative performance in distinct, heterogeneous LVAD cohorts.

Nephrology

Lambers Heerspink H, Toto RD, Jongs N, Vart P, Chertow GM, Hou FF, McMurray JJV, Pecoits-Filho R, Correa-Rotter R, Rossing P, Sjöström CD, Stefánsson BV, **Umanath K**, Langkilde AM, and Wheeler DC. POS-832 DAPAGLIFLOZIN IN IgA NEPHROPATHY: FINDINGS FROM THE DAPA-CKD TRIAL. *Kidney Int Rep* 2021; 6(4):S362.

Introduction: IgA nephropathy (IgAN) is the most common primary glomerulonephritis globally. Despite the use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers, up to 40% of patients with IgAN are at risk of progressing to end-stage kidney disease (ESKD). Additional therapies to slow kidney function decline are highly desired. The DAPA-CKD trial demonstrated that the sodium glucose co-transporter 2 inhibitor dapagliflozin significantly reduced the risk of kidney failure and prolonged survival in participants with chronic kidney disease with and without type 2 diabetes. The DAPA-CKD population included patients with IgAN. We determined the long-term efficacy and safety of dapagliflozin on major kidney and cardiovascular outcomes in these patients. Methods: Patients with an estimated glomerular filtration rate (eGFR) of 25-75 ml/min/1.73m2 and urinary albumin-to-creatinine ratio (UACR) 200-5000 mg/g, were randomized to dapagliflozin (10 mg once daily) or placebo. The primary endpoint was a composite of sustained decline in eGFR ≥50%, ESKD, or kidney or cardiovascular death and was analyzed by Cox proportional hazard regression. This subanalysis was conducted in patients with an IgAN diagnosis. Results: Of the 270 participants with IgAN (93% confirmed by a previous kidney biopsy), 137 were assigned to dapagliflozin and 133 to placebo. Their mean (SD) age was 51.2 (13.1) years, eGFR was 43.8 (12.2) ml/min/1.73m2 and median UACR was 900 (25th to 75th Percentile 540-1515) mg/g. Median follow-up was 2.4 years. The primary outcome occurred in 6 patients (4.4%) in the dapagliflozin group and 20 patients (15%) in the placebo group (hazard ratio, 0.29; 95% confidence interval, 0.12-0.73). An abstract including secondary outcomes, eGFR trajectories and effects on UACR and blood pressure will be submitted by 10 February 2021, and we plan to present these results at the World Congress of Nephrology, 2021. Conclusions: Of the 270 participants with IgAN (93% confirmed by a previous kidney biopsy), 137 were assigned to dapagliflozin and 133 to placebo. Their mean (SD) age was 51.2 (13.1) years, eGFR was 43.8 (12.2) ml/min/1.73m2 and median UACR was 900 (25th to 75th Percentile 540-1515) mg/g. Median follow-up was 2.4 years. The primary outcome occurred in 6 patients (4%) in the dapagliflozin group and 20 patients (15%) in the placebo group (hazard ratio, 0.29; 95% confidence interval [CI], 0.12-0.73). Mean annual rates of eGFR decline with dapagliflozin and placebo were −3.5 and −4.7 mL/min/1.73m2/year (difference 1.2 [95%CI, −0.12-2.51] mL/min/1.73m2). Dapagliflozin reduced UACR by 26% (95%CI, 14-37) relative to placebo. Adverse events leading to study drug discontinuation were similar with dapagliflozin and placebo; there were fewer serious adverse events with dapagliflozin. Conflict of Interest: This study was funded by AstraZeneca. Dr. Heerspink reports grants and honoraria (paid to his employer) from AstraZeneca, Janssen, Abbvie and Boehringer Ingelheim, and honoraria (paid to his employer) from Merck, Gilead, Mitsubishi Tanabe, Mundipharma, Retrophin, Bayer, Chinook, Novo Nordisk and CSL Pharma.

Pharmacy

To L. A program evaluation of the hospital elder life program in a community teaching hospital. *J Am Geriatr Soc* 2021; 69(SUPPL 1):S40.

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BACKGROUND/OBJECTIVES The growing population of older adults and the numerous negative outcomes associated with delirium challenges health systems to provide specialized older adult care. One intervention that has been shown to have positive effects on older adults is the Hospital Elder Life Program (HELP) which utilizes volunteers to help prevent delirium and immobility. This project sought to answer the following questions: What was the effect of HELP volunteers on clinical outcomes (rate of patient falls, use of patient sitters and lengths of stay) and what was the associated financial impact?

METHODS This project was a retrospective program outcomes evaluation. SETTING/PARTICIPANTS Charts of patients that were 70 years and older admitted to the Neurology/Stroke Unit, at community-based teaching hospital in Metro- Detroit Michigan between February 2017 and May 2018 were reviewed. MEASURES The time frame includes 8 months pre-implementation of HELP volunteers and 8 months post-implementation. To analyze the patient population and compare the homogeneity of both groups before and after implementation, the Chi-square test was used for gender, race, ethnicity, and language, and T-test was used for age. Descriptive statistics was used to describe fall rates. The Wilcoxon rank test was used to analyze length of stay and sitter hours. A study site statistician conducted the analysis of data using Statistical Analysis System. The financial services department assisted in obtaining information regarding the financial impact of falls, patient sitters, and LOS. RESULTS A total of 1670 patients were included in the review. Falls decreased from 15 during the pre-implementation period to 9 falls post implementation. Average length of stay decreased from 4.1 days to 3.9 days (p= 0.027). Total patient sitter hours decreased from 4,210.10 hours to 3,742.70 hours, for a difference of 475.40 hours (p= 0.80). The estimated cost of a fall, with or without injury, while hospitalized was unable to be obtained from the financial department. In the post-implementation study period, HELP volunteers on one nursing unit showed minimum cost savings of $48,053.05 through the reduction of LOS and use of patient sitters. CONCLUSION The results of this project are consistent with literature, concluding that volunteer visits from the HELP positively impacts patient outcomes and reduces financial costs and substantiates the need to sustain and expand the current program.

Surgery

Kyriakopoulos CP, Taleb I, Koliopoulou AG, Ijaz N, **Demertzis Z**, **Peruri A**, Dranow E, Wever-Pinzon O, Yin MY, Shah KS, Kemeyou L, Richins TJ, Tang DG, **Nemeh HW**, Stehlik J, Selzman CH, Alharethi R, Caine WT, Kfoury AG, Fang JC, **Cowger JA**, Shah P, and Drakos SG. Predicting Right Ventricular Failure Following Left Ventricular Assist Device Support: A Derivation-Validation Multicenter Risk Score. *J Heart Lung Transplant* 2021; 40(4):S98.

C.P. Kyriakopoulos, U.T.A.H. Cardiac Transplant Program (University of Utah Health & School of Medicine, Intermountain Medical Center, George E. Wahlen VA Medical Center), Salt Lake City, UT, United States

Purpose: Despite several models predicting right ventricular failure (RVF) after durable left ventricular assist device (LVAD) support, poor performance when externally validated has limited their widespread use. We sought to derive a predictive model for RVF after LVAD implantation, and ascertain its performance in an independent cohort. Methods: End-stage heart failure (HF) patients requiring continuous-flow LVAD were prospectively enrolled at one US program (n=477, derivation cohort), with two other US medical centers forming the validation cohort (n=321). The primary outcome was RVF incidence, defined as the need for right ventricular assist device or inotropes for >14 days. Multivariable logistic regression in the derivation set yielded a RVF predictive model, which was subsequently applied to the validation cohort, and a risk score was ultimately developed. Results: Derivation cohort included patients less likely to be African-Americans (7% vs 37%; p<0.001), Hispanics (7% vs 30%; p<0.001), have a remote history of hypertension (49% vs 60%; p=0.002) or be bridged with short-term MCS (8% vs 16%; p=0.001), compared to the validation set. RVF incidence was 16% in the derivation and 36% in the validation cohort (p<0.001). Multivariable analysis identified 7 variables (Figure) as predictive of RVF, with the model achieving a C statistic of 0.734 (95% CI=0.674-0.794) in the derivation and 0.709 (95% CI=0.651-0.767) in the heterogeneous validation cohort. Patients were stratified into 3 RVF risk groups (all comparisons; p<0.001) (Figure). Conclusion: We propose a novel scoring system to predict post-LVAD RVF, achieving high discriminative performance in distinct, heterogeneous LVAD cohorts.

HFHS Publications on COVID-19

Cardiology/Cardiovascular Research
Valdez-Lowe C, **Parikh S**, and **Kenel KL**. Running a cardiology consult service during a pandemic: Experiences from the front lines. *J Am Assoc Nurse Pract* 2021; Epub ahead of print. PMID: 33927158. Full Text

Dermatology
Boothby-Shoemaker W, **Lim HW**, **Kohli I**, and **Ozog DM**. Changes in Google search for "sunburn" during the COVID-19 pandemic. *Photodermatol Photoimmunol Photomed* 2021; Epub ahead of print. PMID: 33830570. Full Text

Dermatology
McMahon DE, Amerson E, Rosenbach M, Lipoff JB, Moustafa D, Tyagi A, Desai SR, French LE, **Lim HW**, Thiers BH, Hruza GJ, Blumenthal KG, Fox LP, and Freeman EE. Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: A registry-based study of 414 cases. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 33838206. Full Text

Diagnostic Radiology
Zintsmaster MP, and **Myers DT**. Patients avoided important care during the early weeks of the coronavirus pandemic: diverticulitis patients were more likely to present with an abscess on CT. *Emerg Radiol* 2021; 28(2):279-282. PMID: 32979139. Full Text

Emergency Medicine
Mikhjian G, **Elghoroury A**, **Cronovich K**, **Brody K**, and Jarski R. Using Quantitative D-Dimer to Determine the Need for Pulmonary CT Angiography in COVID-19 Patients. *Spartan Med Res J* 2021; 6(1):18652. PMID: 33870000. Full Text

Infectious Diseases
Heldman MR, Kates OS, Multani A, Steinbrink JM, Lewis AV, Alexander BD, Beaird OE, Sehgal S, Mishkin AD, La Hoz RM, Blumberg EA, Nelson J, Safa K, Kotton CN, Hemmersbach-Miller M, **Chaudhry ZS**, Saharia K, Morillas JA, Rakita RM, Sait AS, Meloni F, Wilkens H, Camargo P, Tanna SD, Tomic R, Ison MG, Lease ED, Fisher CE, and Limaye AP. A Multicenter Prospective Registry Study of Lung Transplant Recipients Hospitalized with COVID-19. *J Heart Lung Transplant* 2021; 40(4):S141.