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HENRY FORD HEALTH

Henry Ford Health Publication List – April 2022

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 personnel. Searches were conducted in PubMed, Embase, and Web of Science during the month, and then imported into EndNote for formatting. There are 123 unique citations listed this month, with 7 articles and 2 conference abstracts on COVID-19.

Articles are listed first, followed by conference abstracts, books and book chapters, and a bibliography of publications on COVID-19. Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health authors.

Click the "Full Text" link to view the articles to which Sladen Library provides access. If the full-text of the article is not available, you may request it through ILLiad by clicking on "Request Article," or calling us at (313) 916-2550. If you would like to be added to the monthly email distribution list to automatically receive a PDF of this bibliography, or you have any questions or comments, please contact smoore31@hfhs.org. If your published work has been missed, please use this form to notify us for inclusion on next month's list. All articles and abstracts listed here are deposited into Scholarly Commons, the Henry Ford Health institutional repository.

Articles

Conference Abstracts

Articles

Anesthesiology

Sanders J, and Morrissey C. Pro: Virtual Fellowship Interviews are Here to Stay. *J Cardiothorac Vasc Anesth* 2022; 36(4):1207-1208. PMID: 34906384. Full Text

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Anesthesiology

Schuijt MTU, Hol L, Nijbroek SG, **Ahuja S**, van Meenen D, Mazzinari G, **Hemmes S**, Bluth T, Ball L, Gama-de Abreu M, Pelosi P, Schultz MJ, and Serpa Neto A. Associations of dynamic driving pressure and mechanical power with postoperative pulmonary complications-posthoc analysis of two randomised clinical trials in open abdominal surgery. *EClinicalMedicine* 2022; 47:101397. PMID: 35480074. Full Text

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Department of Anaesthesiology and Critical Care Medicine, Pulmonary Engineering Group, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany.
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Department of Intensive Care and Resuscitation, Cleveland Clinic, Cleveland, Ohio, The United States of America.
Department of Outcomes Research, Anaesthesiology Institute, Cleveland Clinic, Cleveland, Ohio, The United States of America.
Mahidol Oxford Tropical Medicine Research Unit (MORU), Mahidol University, Bangkok, Thailand.
Nuffield Department of Medicine, University of Oxford, Oxford, The United Kingdom.
Department of Medical Affairs, Hamilton Medical AG, Bonaduz, Switzerland.
Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), Monash University, Melbourne, Australia.
Department of Critical Care, Melbourne Medical School, University of Melbourne, Austin Hospital, Melbourne, Australia.
Department of Critical Care Medicine, Hospital Israelita Albert Einstein, São Paulo, Brazil.
Cardio-Pulmonary Department, Pulmonary Division, Faculdade de Medicina, Instituto do Coração, Hospital das Clinicas HCFMUSP, Universidade de Sao Paulo, Sao Paulo, Brazil.

BACKGROUND: While an association of the intraoperative driving pressure with postoperative pulmonary complications has been described before, it is uncertain whether the intraoperative mechanical power is associated with postoperative pulmonary complications. METHODS: Posthoc analysis of two international, multicentre randomised clinical trials (ISRCTN70332574 and NCT02148692) conducted between 2011-2013 and 2014-2018, in patients undergoing open abdominal surgery comparing the effect of two different positive end-expiratory pressure (PEEP) levels on postoperative pulmonary complications. Time-weighted average dynamic driving pressure and mechanical power were calculated for individual patients. A multivariable logistic regression model adjusted for confounders was used to assess the independent associations of driving pressure and mechanical power with the occurrence of a composite of postoperative pulmonary complications, the primary endpoint of this posthoc analysis. FINDINGS: In 1191 patients included, postoperative pulmonary complications occurrence was 35.9%. Median time-weighted average driving pressure and mechanical power were 14·0 [11·0-17·0] cmH(2)O, and 7·6 [5·1-10·0] J/min, respectively. While driving pressure was not independently associated with postoperative pulmonary complications (odds ratio, 1·06 [95% CI 0·88-1·28]; p=0.534), the mechanical power had an independent association with the occurrence of postoperative pulmonary complications (odds ratio, 1·28

[95% CI 1·05-1·57]; p=0.016). These findings were independent of body mass index or the level of PEEP used, i.e., independent of the randomisation arm. INTERPRETATION: In this merged cohort of surgery patients, higher intraoperative mechanical power was independently associated with postoperative pulmonary complications. Mechanical power could serve as a summary ventilatory biomarker for the risk for postoperative pulmonary complications in these patients, but our findings need confirmation in other, preferably prospective studies. FUNDING: The two original studies were supported by unrestricted grants from the European Society of Anaesthesiology and the Amsterdam University Medical Centers, Location AMC. For this current analysis, no additional funding was requested. The funding sources had neither a role in the design, collection of data, statistical analysis, interpretation of data, writing of the report, nor in the decision to submit the paper for publication.

Anesthesiology

Vijayanarayanan A, **Wlosinski L**, **El-Bashir J**, **Galusca D**, **Nagai S**, **Yoshida A**, **Abouljoud MS**, and **Otrock ZK**. Lack of alloimmunization to the D antigen in D-negative orthotopic liver transplant recipients receiving D-positive red blood cells perioperatively. *Vox Sang* 2022; Epub ahead of print. PMID: 35393659. Full Text

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BACKGROUND AND OBJECTIVES: D-negative patients undergoing orthotopic liver transplantation (OLT) might require a large number of red blood cell (RBC) units, which can impact the inventory of D-negative blood. The blood bank might need to supply these patients with D-positive RBCs because of inventory constraints. This study evaluates the prevalence of anti-D formation in D-negative OLT patients who received D-positive RBCs perioperatively, as this will assist in successful patient blood management. MATERIALS AND METHODS: This was a retrospective study performed at a single academic medical centre. Electronic medical records for all 1052 consecutive patients who underwent OLT from January 2007 through December 2017 were reviewed. D-negative patients who were transfused perioperatively with D-positive RBCs and had antibody screening at least 30 days after transfusion were included. RESULTS: Of a total of 155 D-negative patients, 23 (14.8%) received D-positive RBCs perioperatively. Seventeen patients were included in the study. The median age was 54 years (range 36-67 years); 13 (76.5%) were male. The median number of D-positive RBC units transfused perioperatively was 7 (range 1-66 units). There was no evidence of D alloimmunization in any patient after a median serologic follow-up of 49.5 months (range 31 days to 127.7 months). The average number of antibody screening post OLT was 7.29. CONCLUSION: Our study showed that transfusion of D-positive RBCs in D-negative OLT recipients is a safe and acceptable practice in the setting of immunosuppression. This practice allows the conservation of D-negative RBC inventory.

Behavioral Health Services/Psychiatry/Neuropsychology

Cassidy-Bushrow AE, **Sitarik AR**, **Johnson CC**, **Johnson-Hooper TM**, **Kassem Z**, **Levin AM**, Lynch SV, Ownby DR, **Phillips JM**, Yong GJM, **Wegienka G**, and **Straughen JK**. Early-life gut microbiota and attention deficit hyperactivity disorder in preadolescents. *Pediatr Res* 2022; Epub ahead of print. PMID: 35440767. Request Article

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BACKGROUND: Gut microbiota maturation coincides with nervous system development. Cross-sectional data suggest gut microbiota of individuals with and without attention deficit hyperactivity disorder (ADHD) differs. We hypothesized that infant gut microbiota composition is associated with later ADHD development in our on-going birth cohort study, WHEALS. METHODS: Gut microbiota was profiled using 16S ribosomal RNA and the internal transcribed spacer region 2 (ITS2) sequencing in stool samples from 1 month and 6 months of age. ADHD was defined by parent-reported or medical record doctor diagnosis at age 10. RESULTS: A total of 314 children had gut microbiota and ADHD data; 59 (18.8%) had ADHD. After covariate adjustment, bacterial phylogenetic diversity ($p = 0.017$) and bacterial composition (unweighted UniFrac $p = 0.006$, $R(2) = 0.9\%$) at age 6 months were associated with development of ADHD. At 1 month of age, 18 bacterial and 3 fungal OTUs were associated with ADHD development. At 6 months of age, 51 bacterial OTUs were associated with ADHD; 14 of the order Lactobacillales. Three fungal OTUs at 6 months of age were associated with ADHD development. CONCLUSIONS: Infant gut microbiota is associated with ADHD development in pre-adolescents. Further studies replicating these findings and evaluating potential mechanisms of the association are needed. IMPACT: Cross-sectional studies suggest that the gut microbiota of individuals with and without ADHD differs. We found evidence that the bacterial gut microbiota of infants at 1 month and 6 months of age is associated with ADHD at age 10 years. We also found novel evidence that the fungal gut microbiota in infancy (ages 1 month and 6 months) is associated with ADHD at age 10 years. This study addresses a gap in the literature in providing longitudinal evidence for an association of the infant gut microbiota with later ADHD development.

Behavioral Health Services/Psychiatry/Neuropsychology
Sablaban IM, and **Gautam M**. Kratom & Stimulant Co-Addiction: A Case Series and Brief Review. *J Addict Dis* 2022;1-4. Epub ahead of print. PMID: 35441584. Request Article

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Kratom (Mitragyna speciosa) is an easily accessible dietary supplement gaining notoriety in medicine for its use as a surrogate form of self-driven opioid use disorder treatment, albeit one with a lack of evidence and significant risks. Both misuse and withdrawal from kratom have been appreciated in the literature and addressed in a fashion analogous to that of opioids. Because of this, it has largely been studied through the looking glass of its properties of agonizing μ-opioid and likely α(2)-adrenergic receptors. While an important area of study, the correlation with kratom and stimulant use, reflected in the National Survey on Drug Use and Health, is one that often gets neglected clinically. In our manuscript we present three unique cases, demonstrative of the overlap kratom misuse may have with stimulant use disorders in distinct settings. We provide a discussion and review of this correlation in light of kratom use increasing in the United States.

Cardiology/Cardiovascular Research
Chiang M, **Gonzalez PE**, **Villablanca PA**, **O'Neill BP**, **Lee J**, **Frisoli T**, **Wang DD**, **Eng MH**, and **O'Neill WW**. Aorto-Left Ventricular Fistula From Aortic Pseudoaneurysm After TAVR: Transcatheter Treatment With Multimodality Imaging. *JACC Cardiovasc Interv* 2022; Epub ahead of print. PMID: 35430171. Full Text

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Cardiology/Cardiovascular Research
Cusin CN, **Clark PA**, **Lauderbach CW, Jr.**, and **Wyman J**. Reducing length of stay for patients undergoing transcatheter aortic valve replacement using a prescreening approach. *J Am Assoc Nurse Pract* 2022; Epub ahead of print. PMID: 35472192. Full Text

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BACKGROUND: As transcatheter aortic valve replacement (TAVR) becomes a preferred treatment option for patients with aortic valve stenosis, and demand for TAVR increases, it is imperative that length of stay (LOS) is reduced while maintaining safety and effectiveness. LOCAL PROBLEM: As TAVR procedures have become less invasive and more streamlined, current protocols have not been updated to reflect today's postprocedure requirements. METHODS: The next-day discharge (NDD) protocol was established using available literature. A convenience sample was evaluated for NDD protocol inclusion during aortic multidisciplinary team conference using predetermined inclusion and exclusion criteria. Length of stay for NDD protocol participants was compared with LOS from a retrospective convenience sample of patients undergoing TAVR in the time frame mirroring NDD protocol initiation of the year prior. INTERVENTIONS: Patients meeting inclusion criteria were enrolled in the NDD protocol with a goal of discharge to home on postprocedural day 1 by 2:00 p.m. The NDD protocol included preprocedure expectation setting, prescheduled same-day postprocedure imaging, and discharge priority on postprocedure day 1. RESULTS: There is a significant difference in LOS between the NDD eligible retrospective and prospective groups. The prospective group has a significantly lower LOS than the retrospective group (M = 1.6 vs 2.1, respectively; p = .0454). CONCLUSIONS: An NDD protocol can help reduce LOS after TAVR in appropriately selected patients. Further protocol revision will be required to optimize LOS outcomes.

Cardiology/Cardiovascular Research

Dalia T, Chan WC, Sauer AJ, Ranka S, Goyal A, Mastoris I, Pothuru S, Abicht T, Danter M, Vidic A, Gupta K, Tedford RJ, **Cowger J**, Fang JC, and Shah Z. Outcomes in Patients with Chronic Kidney Disease and End Stage Renal Disease and Durable Left Ventricular Assist Device: Insights from United States Renal Data System Database. *J Card Fail* 2022; Epub ahead of print. PMID: 35470059. Full Text

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BACKGROUND: There is paucity of data regarding durable LVAD outcomes in patients with chronic kidney disease (CKD) stage 3-5 and CKD stage 5 on dialysis (ESRD: end stage renal disease). METHODS: We conducted a retrospective study of Medicare beneficiaries with ESRD and 5% sample of CKD with LVAD (2006 to 2018) to determine one-year outcomes utilizing the United States Renal Data System (USRDS) database. The LVAD implantation, comorbidities and outcomes were identified using appropriate ICD-9 and ICD-10 codes. RESULTS: We identified 496 CKD and 95 ESRD patients who underwent LVAD implantation. The ESRD patients were younger (59 vs 66 years; p <0.001), had more Blacks (40% vs 24.6%; p=0.009), compared to the CKD group. One-year mortality (49.5% vs 30.9%; p <0.001) and index mortality (27.4% vs 16.7%; p=0.014) was higher in ESRD. Subgroup analysis showed significantly higher mortality in ESRD vs CKD 3 (49.5% vs 30.2%, adjusted p=0.009), but no significant difference in mortality between stage 3 vs 4/5 (30.2% vs 30.8%; adjusted p=0.941). There was no significant difference in secondary outcomes (bleeding, stroke, and sepsis/infection) during follow-up between two groups. CONCLUSIONS: Patients with ESRD undergoing LVAD implantation had significantly higher index and 1-year mortality compared to CKD patients.

Cardiology/Cardiovascular Research

Devgun J, De Potter T, Fabbricatore D, and **Wang DD**. Pre-cath Laboratory Planning for Left Atrial Appendage Occlusion - Optional or Essential? *Interv Cardiol Clin* 2022; 11(2):143-152. PMID: 35361459. Full Text

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In the wake of rapid advancement in cardiovascular procedural technologies, physician-led preprocedural planning utilizing multi-modality imaging training is increasingly recognized as invaluable for procedural accuracy. Left atrial appendage occlusion (LAAO) is one such procedure in which complications such as device leak, cardiac injury, and device embolization can be decreased substantially with incorporation of physician driven imaging and digital tools. We discuss the benefits of cardiac CT and 3D printing in preprocedural planning for the Heart Team, as well as novel applications by physicians of intraprocedural 3D angiography and dynamic fusion imaging. Furthermore, incorporation of computational modeling and artificial intelligence (AI) may yield promise. For optimal patient-centric procedural success, we advocate for standardized preprocedural imaging planning by physicians within the Heart Team as an essential part of LAAO.

Cardiology/Cardiovascular Research
Gomez JMD, **Zimmerman AC**, du Fay de Lavallaz J, Wagner J, Tung L, Bouroukas A, Nguyen TTP, Canzolino J, Goldberg A, Santos Volgman A, Suboc T, and Rao AK. Echocardiographic predictors of mortality and morbidity in COVID-19 disease using focused cardiovascular ultrasound. *Int J Cardiol Heart Vasc* 2022; 39:100982. PMID: 35233442. Full Text

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BACKGROUND: Focused transthoracic echocardiography (fTTE) has emerged as a critical diagnostic tool during the COVID-19 pandemic, allowing for efficient cardiac imaging while minimizing staff exposure. The utility of fTTE in predicting clinical outcomes in COVID-19 remains under investigation. METHODS: We conducted a retrospective study of 2,266 hospitalized patients at Rush University Medical Center with COVID-19 infection between March and November 2020 who received a fTTE. fTTE data were analyzed for association with primary adverse outcomes (60-day mortality) and with secondary adverse outcomes (need for renal replacement therapy, need for invasive ventilation, shock, and venous thromboembolism). RESULTS: Of the 427 hospitalized patients who had a fTTE performed (mean 62 years, 43% female), 109 (26%) had died by 60 days. Among patients with an available fTTE measurement, right ventricular (RV) dilation was noted in 34% (106/309), 43% (166/386) had RV dysfunction, and 17% (72/421) had left ventricular (LV) dysfunction. In multivariable models accounting for fTTE data, RV dilation was significantly associated with 60-day mortality (OR 1.93 [CI 1.13-3.3], p = 0.016). LV dysfunction was not significantly associated with 60-day mortality (OR 0.95 [CI: 0.51-1.78], p = 0.87). CONCLUSIONS: Abnormalities in RV echocardiographic parameters are adverse prognosticators in COVID-19 disease. Patients with RV dilation experienced double the risk for 60-day mortality due to COVID-19. To our knowledge, this is the largest study to date that highlights the adverse prognostic implications of RV dilation as determined through fTTE in hospitalized COVID-19 patients.

Cardiology/Cardiovascular Research
Granger BB, Kaltenbach LA, Fonarow GC, Allen LA, **Lanfear DE**, Albert NM, Al-Khalidi HR, Butler J, Cooper LB, DeWald T, Felker GM, Heidenreich P, Kottam A, Lewis EF, Piña IL, Yancy CW, Granger CB, Hernandez AF, and DeVore AD. Health System-Level Performance in Prescribing Guideline-Directed

Medical Therapy for Patients with HFrEF: Results from the CONNECT-HF Trial. *J Card Fail* 2022; Epub ahead of print. PMID: 35462033. Full Text

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BACKGROUND: Health system-level interventions to improve use of guideline-directed medical therapy (GDMT) often fail in the acute care setting. We sought to identify factors associated with high performance in adoption of GDMT among health systems in CONNECT-HF. METHODS AND RESULTS: Site-level composite quality scores were calculated at discharge and last follow-up. Site performance was defined as the average change in score from baseline to last follow-up and analyzed by performance tertile using a mixed-effects model with baseline performance as a fixed effect and site as a random effect. Among 150 randomized sites, mean 12-month improvement in GDMT was 1.8% (-26.4% to 60.0%). Achievement of ≥50% target dose for angiotensin-converting enzymes/angiotensin receptor blockers/angiotensin receptor-neprilysin inhibitors and beta blockers at 12 months was modest, even at the highest performing sites (median 29.6% [23%, 41%] and 41.2% [29%, 50%]). Sites achieving higher GDMT scores had care teams that included social workers and pharmacists and patients able to afford medications and access medication lists in the electronic health record. CONCLUSIONS: Substantial gaps in site-level use of GDMT were found even among highest performing sites. Failure of hospital-level interventions to improve quality metrics suggests that a team-based approach to care and improved patient access to medications are needed for post-discharge success.

Cardiology/Cardiovascular Research

Jehangir Q, Lee Y, **Latack K**, **Poisson L**, **Wang DD**, **Song S**, Apala DR, Patel K, Halabi AR, Krishnamoorthy G, and Sule AA. Incidence, Mortality, and Imaging Outcomes of Atrial Arrhythmias in COVID-19. *Am J Cardiol* 2022; Epub ahead of print. PMID: 35382929. Full Text

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Atrial arrhythmias (AAs) are common in hospitalized patients with COVID-19; however, it remains uncertain if AAs are a poor prognostic factor in SARS-CoV-2 infection. In this retrospective cohort study from 2014 to 2021, we report in-hospital mortality in patients with new-onset AA and history of AA. The incidence of new-onset congestive heart failure (CHF), hospital length of stay and readmission rate, intensive care unit admission, arterial and venous thromboembolism, and imaging outcomes were also analyzed. We further compared the clinical outcomes with a propensity-matched influenza cohort. Generalized linear regression was performed to identify the association of AA with mortality and other

outcomes, relative to those without an AA diagnosis. Predictors of new-onset AA were also modeled. A total of 6,927 patients with COVID-19 were included (626 with new-onset AA, 779 with history of AA). We found that history of AA (adjusted relative risk [aRR] 1.38, confidence interval [CI], 1.11 to 1.71, p = 0.003) and new-onset AA (aRR 2.02, 95% CI 1.68 to 2.43, p <0.001) were independent predictors of in-hospital mortality. The incidence of new-onset CHF was 6.3% in history of AA (odds ratio 1.91, 95% CI 1.30 to 2.79, p <0.001) and 11.3% in new-onset AA (odds ratio 4.01, 95% CI 3.00 to 5.35, p <0.001). New-onset AA was shown to be associated with worse clinical outcomes within the propensity-matched COVID-19 and influenza cohorts. The risk of new-onset AA was higher in patients with COVID-19 than influenza (aRR 2.02, 95% CI 1.76 to 2.32, p <0.0001), but mortality associated with new-onset AA was higher in influenza (aRR 12.58, 95% CI 4.27 to 37.06, p <0.0001) than COVID-19 (aRR 1.86, 95% CI 1.55 to 2.22, p <0.0001). In a subset of the patients with COVID-19 for which echocardiographic data were captured, abnormalities were common, including valvular abnormalities (40.9%), right ventricular dilation (29.6%), and elevated pulmonary artery systolic pressure (16.5%); although there was no evidence of a difference in incidence among the 3 groups. In conclusion, new-onset AAs are associated with poor clinical outcomes in patients with COVID-19.

Cardiology/Cardiovascular Research
Jehangir Q, Lee Y, Latack K, **Poisson L**, **Wang DD**, **Song S**, Apala DR, Patel K, Halabi AR, Krishnamoorthy G, and Sule AA. Data of atrial arrhythmias in hospitalized COVID-19 and influenza patients. *Data Brief* 2022; 42:108177. PMID: 35449710. Full Text

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Atrial arrhythmias (AA) are common in hospitalized COVID-19 patients with limited data on their association with COVID-19 infection, clinical and imaging outcomes. In the related research article using retrospective research data from one quaternary care and five community hospitals, patients aged 18 years and above with positive SARS-CoV-2 polymerase chain reaction test were included. 6927 patients met the inclusion criteria. The data in this article provides demographics, home medications, in-hospital events and COVID-19 treatments, multivariable generalized linear regression regression models using a log link with a Poisson distribution (multi-parameter regression [MPR]) to determine predictors of new-onset AA and mortality in COVID-19 patients, computerized tomography chest scan findings, echocardiographic findings, and International Classification of Diseases-Tenth Revision codes. The clinical outcomes were compared to a propensity-matched cohort of influenza patients. For influenza, data is reported on baseline demographics, comorbid conditions, and in-hospital events. Generalized linear regression models were built for COVID-19 patients using demographic characteristics, comorbid conditions, and presenting labs which were significantly different between the groups, and hypoxia in the emergency room. Statistical analysis was performed using R programming language (version 4, ggplot2 package). Multivariable generalized linear regression model showed that, relative to normal sinus rhythm, history of AA (adjusted relative risk [RR]: 1.38; 95% CI: 1.11-1.71; p = 0.003) and newly-detected AA (adjusted RR: 2.02 95% CI: 1.68-2.43; p < 0.001) were independently associated with higher in-hospital mortality. Age in increments of 10 years, male sex, White race, prior history of coronary artery disease, congestive heart failure, end-stage renal disease, presenting leukocytosis, hypermagnesemia, and hypomagnesemia were found to be independent predictors of new-onset AA in the MPR model. The dataset reported is related to the research article entitled "Incidence, Mortality, and Imaging Outcomes of Atrial Arrhythmias in COVID-19" [Jehangir et al. Incidence, Mortality, and Imaging Outcomes of Atrial Arrhythmias in COVID-19, American Journal of Cardiology] [1].

Cardiology/Cardiovascular Research
Maqsood MH, Khalil M, Maraey A, Elzanaty AM, Louka B, Elbadawi A, Ong K, **Megaly M**, and Garcia S. Temporal Trends and Outcomes of Same-Day Discharge After Left Atrial Appendage Occlusion: Insight

from National Readmission Database. *Am J Cardiol* 2022; Epub ahead of print. PMID: 35431051. Full Text

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Cardiology/Cardiovascular Research

Megaly M, **Basir MB**, Brilakis E, and **Alaswad K**. Extra-stent subintimal plaque modification; a novel technique to overcome resistant stent underexpansion. *Cardiovasc Revasc Med* 2022; Epub ahead of print. PMID: 35410847. Full Text

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Cardiology/Cardiovascular Research

Megaly M, Sedhom R, Hakam L, and Garcia S. The MANTA vascular closure device: Requiring attention from beginning to end, reply. *Cardiovasc Revasc Med* 2022; Epub ahead of print. PMID: 35469758. Full Text

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Cardiology/Cardiovascular Research

Molina EJ, **Cowger J**, Lee S, Horstmanshof D, Cleveland JC, Jr., Goldstein DJ, Mehra MR, Uriel N, Salerno CT, Bourque K, Chuang J, and Naka Y. Outcomes in Smaller Body Size Adults after HeartMate 3 Left Ventricular Assist Device Implantation. *Ann Thorac Surg* 2022; Epub ahead of print. PMID: 35452663. Full Text

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BACKGROUND: Outcomes in patients with smaller body size following HeartMate 3 Left Ventricular Assist Device (HM3) implantation are not well characterized. We sought to evaluate outcomes in smaller vs. larger BSA patients in the MOMENTUM 3 pivotal trial and its Continued Access Protocol cohort. METHODS: The analysis cohort included 1015 HM3 patients divided into 2 groups: BSA≤1.70 m(2) (small patients, n=82) and BSA>1.70 m(2) (large patients, n=933). The composite primary endpoint was survival at 2-years free of disabling stroke or reoperation to replace or remove a malfunctioning device. Adverse events were compared between groups. RESULTS: Smaller patients were more frequently women (56.1% vs. 17.7%, P<.001), had lower prevalence of diabetes (28.1% vs. 43.9%, P=.005) and hypertension (51.2% vs. 71.9%, P<.001), larger median indexed LVEDD (normalized by BSA, 40 vs. 33 mm/m(2), P<.001), and lower median serum creatinine (1.1 vs. 1.3 mg/dl, P<.001). The proportion of patients achieving the composite endpoint at 2-years was 77% in both groups (adjusted HR = 1.14 [95% confidence interval: 0.68-1.91], P=.62). Two-year adverse event rates were also similar between groups except for sepsis (6.1% vs. 14.9%, P=.029) and cardiac arrhythmias (24.4% vs. 35.3%, P=.005), which were higher in the larger patients. CONCLUSIONS: Outcomes following HM3 implantation were comparable between small and large patients. Smaller body size should not be used to deny HM3 implantation in patients who are otherwise suitable durable MCS candidates.

Cardiology/Cardiovascular Research
Mshelbwala FS, and **Ananthasubramaniam K**. All that glitters is not sarcoidosis: Importance of systematic review of (18)F-FDG-PET data and integration of clinical information. *J Nucl Cardiol* 2022; Epub ahead of print. PMID: 35411429. Request Article

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Cardiology/Cardiovascular Research
Sedhom R, **Megaly M**, Saad M, Elbadawi A, Witzke CF, Garcia S, Latib A, and Gafoor SA. Transcatheter edge-to-edge repair of the tricuspid valve: The US experience. *Catheter Cardiovasc Interv* 2022; Epub ahead of print. PMID: 35362665. Full Text

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OBJECTIVES: To examine the trends in utilization and outcomes of tricuspid valve (TV) transcatheter edge-to-edge repair (TEER). BACKGROUND: Surgery for isolated tricuspid regurgitation is associated with high morbidity and mortality and is rarely performed. TV TEER is an attractive alternative. METHODS: The Nationwide Readmissions Database was queried using the International Classification of Diseases, 10th Revision, procedure code for TV TEER for years 2016-2019. The main outcomes were trends in utilization and in-hospital all-cause mortality. RESULTS: We identified 918 hospitalizations for TV TEER. There was an uptrend in its utilization from 13 cases in the first quarter of 2016 to 122 cases in the last quarter of 2019 (p trend < 0.001). Concomitant mitral valve (MV) TEER was performed in 42.1% of admissions. The overall in-hospital mortality was 2.1%. Surgical TV replacement was needed in 1.1% of admissions; none of them died during the index hospitalization. Unplanned rehospitalizations were

common at 30 days (15.7%); 38.2% of those were due to heart failure. There was no difference in in-hospital mortality between isolated TV TEER and combined MV and TV TEER (1.7% vs. 2.6%, p = 0.359). However, admissions receiving combined procedure had lower length of stay and urgent readmission rate. CONCLUSION: The current study showed that there was an increase in the utilization of TV TEER over 2016-2019 in the United States. TV TEER was associated with low rates of in-hospital mortality; however, the rate of urgent readmission remains high, mainly due to heart failure.

Cardiology/Cardiovascular Research

Shea MG, Headley S, Mullin EM, **Brawner CA**, Schilling P, and Pack QR. Comparison of Ratings of Perceived Exertion and Target Heart Rate-Based Exercise Prescription in Cardiac Rehabilitation: A RANDOMIZED CONTROLLED PILOT STUDY. *J Cardiopulm Rehabil Prev* 2022; Epub ahead of print. PMID: 35383680. Full Text

Division of Cardiovascular Medicine (Drs Shea and Pack and Mr Schilling), Institute for Healthcare Delivery and Population Science (Drs Headley and Pack), and Department of Medicine (Dr Pack), University of Massachusetts Medical School-Baystate, Springfield; Springfield College Department of Exercise Science and Athletic Training, Springfield, Massachusetts (Drs Shea, Headley, and Mullin); Mayo Clinic Arizona, Scottsdale (Dr Shea); and Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan (Dr Brawner).

PURPOSE: Although ratings of perceived exertion (RPE) are widely used to guide exercise intensity in cardiac rehabilitation (CR), it is unclear whether target heart rate ranges (THRRs) can be implemented in CR programs that predominantly use RPE and what impact this has on changes in exercise capacity. METHODS: We conducted a three-group pilot randomized control trial (#NCT03925493) comparing RPE of 3-4 on the 10-point modified Borg scale, 60-80% of heart rate reserve (HRR) with heart rate (HR) monitored by telemetry, or 60-80% of HRR with a personal HR monitor (HRM) for high-fidelity adherence to THRR. Primary outcomes were protocol fidelity and feasibility. Secondary outcomes included exercise HR, RPE, and changes in functional exercise capacity. RESULTS: Of 48 participants randomized, four patients dropped out, 20 stopped prematurely (COVID-19 pandemic), and 24 completed the protocol. Adherence to THRR was high regardless of HRM, and patients attended a median (IQR) of 33 (23, 36) sessions with no difference between groups. After randomization, HR increased by 1 ± 6, 6 ± 5, and 10 ± 9 bpm (P = .02); RPE (average score 3.0 ± 0.05) was unchanged, and functional exercise capacity increased by 1.0 ± 1.0, 1.9 ± 1.5, 2.0 ± 1.3 workload METs (effect size between groups, $\eta p2 = 0.11$, P = .20) for the RPE, THRR, and THRR + HRM groups, respectively. CONCLUSIONS: We successfully implemented THRR in an all-RPE CR program without needing an HRM. Patients randomized to THRR had higher exercise HR but similar RPE ratings. The THRR may be preferable to RPE in CR populations for cardiorespiratory fitness gains, but this needs confirmation in an adequately powered trial.

Cardiology/Cardiovascular Research

Simsek B, Kostantinis S, Karacsonyi J, **Alaswad K**, Karmpaliotis D, Masoumi A, Jaffer FA, Doshi D, Khatri J, Poommipanit P, Gorgulu S, Rafeh NA, Goktekin O, Krestyaninov O, Davies R, ElGuindy A, Jefferson BK, Patel TN, Patel M, Chandwaney RH, Mastrodemos OC, Rangan BV, and Brilakis ES. Prevalence and outcomes of balloon undilatable chronic total occlusions: Insights from the PROGRESS-CTO. *Int J Cardiol* 2022; Epub ahead of print. PMID: 35483480. Full Text

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BACKGROUND: The prevalence, treatment, and outcomes of balloon undilatable lesions encountered in chronic total occlusion (CTO) percutaneous coronary intervention (PCI) have received limited study. METHODS: We examined the clinical characteristics and procedural outcomes of balloon undilatable lesions in the Prospective Global Registry for the Study of CTO Intervention (PROGRESS-CTO). RESULTS: Of 6535 CTO PCIs performed between 2012 and 2022, 558 (8.5%) lesions were balloon undilatable. In this subset, patients were older (mean age 67 ± 10 vs. 64 ± 10, $p < 0.001$) and had higher prevalence of comorbidities: diabetes mellitus (54% vs. 40%, $p < 0.001$), prior PCI (71% vs. 59%, $p < 0.001$), prior myocardial infarction (52% vs. 45%, $p = 0.003$), and prior coronary artery bypass graft surgery (44% vs. 25%, $p < 0.001$). The CTO lesion length was estimated to be 34 ± 23 mm, mean J-CTO score was 2.9 ± 1.1 and mean PROGRESS-CTO score was 1.4 ± 1.0. A cutting balloon was used in 27%, a scoring balloon in 15%, laser in 14%, rotational atherectomy in 28%, orbital atherectomy in 10%, intravascular lithotripsy in 1% and other modalities/approaches in 5%. Balloon undilatable lesions had lower technical success (90.9% vs. 93.8%, $p = 0.007$) and higher incidence of major adverse cardiovascular events (MACE, composite of in-hospital death, acute myocardial infarction, stroke, re-PCI, emergency CABG, pericardiocentesis) (5.0% versus 1.3%, $p < 0.001$). CONCLUSION: Approximately 1 in 12 CTO (8.5%) lesions are balloon undilatable. Treatment of balloon undilatable lesions is associated with lower technical success and higher in-hospital MACE.

Cardiology/Cardiovascular Research

Spertus JA, Birmingham MC, Nassif M, Damaraju CV, Abbate A, Butler J, **Lanfear DE**, Lingvay I, Kosiborod MN, and Januzzi JL. The SGLT2 inhibitor canagliflozin in heart failure: the CHIEF-HF remote, patient-centered randomized trial. *Nat Med* 2022; 28(4):809-813. PMID: 35228753. Full Text

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Large traditional clinical trials suggest that sodium-glucose co-transporter 2 inhibitors improve symptoms in patients with heart failure and reduced ejection fraction (HFrEF) and in patients with heart failure and preserved ejection fraction (HFpEF). In the midst of the Coronavirus Disease 2019 pandemic, we sought to confirm these benefits in a new type of trial that was patient centered and conducted in a completely remote fashion. In the CHIEF-HF trial (NCT04252287), 476 participants with HF, regardless of EF or diabetes status, were randomized to 100 mg of canagliflozin or placebo. Enrollment was stopped early due to shifting sponsor priorities, without unblinding. The primary outcome was change in the Kansas City Cardiomyopathy Questionnaire Total Symptom Score (KCCQ TSS) at 12 weeks. The 12-week change in KCCQ TSS was 4.3 points (95% confidence interval, 0.8-7.8; $P = 0.016$) higher with canagliflozin than with placebo, meeting the primary endpoint. Similar effects were observed in participants with HFpEF and in those with HFrEF and in participants with and without diabetes, demonstrating that canagliflozin significantly improves symptom burden in HF, regardless of EF or diabetes status. This randomized,

double-blind trial, conducted without in-person interactions between doctor and patient, can serve as a model for future all-virtual clinical trials.

Center for Health Policy and Health Services Research
Joseph CLM, **Tang A**, Chesla DW, Epstein MM, Pawloski PA, Stevens AB, Waring SC, **Ahmedani BK**, **Johnson CC**, and **Peltz-Rauchman CD**. Demographic differences in willingness to share electronic health records in the All of Us Research Program. *J Am Med Inform Assoc* 2022; Epub ahead of print. PMID: 35472083. Full Text

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OBJECTIVE: Participant willingness to share electronic health record (EHR) information is central to success of the National Institutes of Health All of Us Research Program (AoURP). We describe the demographic characteristics of participants who decline access to their EHR data. MATERIALS AND METHODS: We included participants enrolling in AoURP between June 6, 2017 and December 31, 2019 through the Trans-American Consortium for the Health Care Systems Research Network (TACH). TACH is a consortium of health care systems spanning 6 states, and an AoURP research partner. RESULTS: We analyzed data for 25 852 participants (89.3% of those enrolled). Mean age = 52.0 years (SD 16.8), with 66.5% White, 18.7% Black/African American, 7.7% Hispanic, 32.5% female, and 76% with >a high school diploma. Overall, 2.3% of participants declined to share access to their EHR data (range across TACH sites = 1.3% to 3.5%). Younger age, female sex, and education >high school were significantly associated with decline to share EHR data, odds ratio (95% confidence interval) = 1.26 (1.19-1.33), 1.74 (1.42-2.14), and 2.44 (1.86-3.21), respectively. Results were similar when several sensitivity analyses were performed. DISCUSSION: AoURP seeks a dataset reflecting our nation's diversity in all aspects of participation. Those under-represented in biomedical research may be reluctant to share access to their EHR data. CONCLUSION: In our data, race and ethnicity were not independently related to participant decision to decline access to their EHR information. Results suggest that the value of the AoURP dataset is unlikely to be constrained by the size or the racial/ethnic composition of this subgroup.

Dermatology
Ezekwe N, **Maghfour J**, and **Kohli I**. Visible Light and The Skin. *Photochem Photobiol* 2022; Epub ahead of print. PMID: 35429353. Full Text

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Visible light (VL, 400-700 nm) was previously regarded as non-significant with minimal to no photobiologic effects on the skin. Recent studies have demonstrated that in dark-skinned individuals (skin phototypes IV-VI), VL can induce more intense and longer lasting pigmentation compared to ultraviolet A1 (UVA1, 340-400 nm). Additionally, long wavelength UVA1 (370-400 nm) has been shown to potentiate these effects of VL. The combination of VL and UVA1 (VL+UVA1, 370-700nm) was also able to induce erythema in light-skinned individuals (skin phototypes I-III), which is a novel finding since the erythemogenic spectrum of sunlight has primarily been attributed to ultraviolet B (UVB, 290-320 nm) and short wavelength UVA2 (320-340 nm) only. Although biologic effects of VL+UVA1 have been established, there are no guidelines in any country to test for photoprotection against this waveband. This invited

perspective aims to present the evolution of knowledge of photobiologic effects of VL, associated phototesting methodologies, and current position on VL photoprotection.

Dermatology
Guan LL, **Lim HW**, and **Mohammad TF**. Recognizing photoallergy, phototoxicity, and immune-mediated photodermatoses. *J Allergy Clin Immunol* 2022; 149(4):1206-1209. PMID: 35396082. Full Text

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Dermatology
Lyons A, **Narla S**, **Kohli I**, **Zubair R**, **Jacobsen G**, **Ceresnie M**, **Parks-Miller A**, and **Hamzavi I**. Safety and Efficacy of Intense Pulsed Light With Radiofrequency in United States Hidradenitis Suppurativa Patients. *J Drugs Dermatol* 2022; 21(4):430-432. PMID: 35389583. Full Text

The combination of intense pulsed light and radiofrequency has been described in German populations to be a noninvasive therapy option for patients with hidradenitis suppurativa, demonstrating significant improvements in the quality of life and reduction in number of inflammatory lesions. OBJECTIVE: To evaluate the efficacy and safety of combination intense pulsed light and radiofrequency therapy in patients with hidradenitis suppurativa in the United States. METHODS: A prospective split body was conducted in the United States on patients with bilateral hidradenitis suppurativa. Subjects received 3 passes of intense pulsed light and radiofrequency per treatment session to a single involved body region on a randomized side of the body at least 2 weeks apart over 9 to 10 treatment sessions. RESULTS: When measured from baseline to final visit, the overall mean difference in Dermatology Life Quality Index was found to be statistically significant (-2.8, P=0.043, n = 9). Patients reported mild discomfort during therapy and no adverse events occurred during or after treatment sessions. CONCLUSIONS: Although statistically significant, the mean difference in Dermatology Life Quality Index in treated patients found in this study did not reach the minimal clinically important difference for inflammatory skin disease. J Drugs Dermatol. 2022;21(4):430-432. .doi:10.36849/JDD.6562.

Dermatology
Lyons AB, **Ozog DM**, **Lim HW**, **Viola K**, **Tang A**, and **Jones LR**. The Detroit Keloid Scale: A Validated Tool for Rating Keloids. *Facial Plast Surg Aesthet Med* 2022; Epub ahead of print. PMID: 35394356. Full Text

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Background: Comparing keloid treatment modalities and assessing response to treatments may be predicted by a better classification system. Objectives: To develop and validate the Detroit Keloid Scale (DKS), a standardized method of keloid assessment. Methods: Forty-seven physicians were polled to develop the DKS. The scale was validated in 52 patients against the Vancouver Scar Scale (VSS), Patient and Observer Scar Assessment Scale (POSAS), and Dermatology Life Quality Index (DLQI). Results: The inter-rater reliability was "substantial" for observer DKS and only "moderate" for VSS and observer POSAS (intraclass correlation coefficient were 0.80, 0.60, and 0.47, respectively). Pearson's correlation indicated "moderate" association between observer DKS with observer POSAS ($\rho = 0.56$, $p < 0.001$) and "substantial" relationship between observer DKS and VSS ($\rho = 0.63$, $p < 0.001$). Pearson's correlation indicated "moderate" association between patient portion of DKS and patient portion of POSAS and patient portion of the DKS and DLQI (0.61 and 0.60, respectively, $p < 0.05$). DKS total score consistently showed significant "substantial" relationship with POSAS total score ($\rho = 0.65$, $p < 0.001$). Conclusions: The DKS offers a validated keloid-specific outcome measure for comparing keloid treatments.

Dermatology

Picardo M, **Huggins RH**, Jones H, Marino R, Ogunsola M, and Seneschal J. The Humanistic Burden of Vitiligo: A Systematic Literature Review of Quality-of-Life Outcomes. *J Eur Acad Dermatol Venereol* 2022; Epub ahead of print. PMID: 35366355. Full Text

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Despite historical mischaracterization as a cosmetic condition, patients with the autoimmune disorder vitiligo experience substantial quality-of-life (QoL) burden. This systematic literature review of peer-reviewed observational and interventional studies describes comprehensive evidence for humanistic burden in patients with vitiligo. PubMed, EMBASE, Scopus, and the Cochrane databases were searched through February 10, 2021, to qualitatively assess QoL in vitiligo. Two independent reviewers assessed articles for inclusion and extracted data for qualitative synthesis. A total of 130 included studies were published between 1996 and 2021. Geographic regions with the most studies were Europe (32.3%) and the Middle East (26.9%). Dermatology-specific instruments, including the Dermatology Life Quality Index (DLQI; 80 studies) and its variants for children (CDLQI; 10 studies) and families (FDLQI; 4 studies), as well as Skindex instruments (Skindex-29, 15 studies; Skindex-16, 4 studies), were most commonly used to measure humanistic burden. Vitiligo-specific instruments, including the Vitiligo-specific QoL (VitiQoL; 11 studies) instrument and 22-item Vitiligo Impact Scale (VIS-22; 4 studies), were administered in fewer studies. Among studies that reported total scores for the overall population, a majority revealed moderate or worse effects of vitiligo on patient QoL (DLQI, 35/54 studies; Skindex, 8/8 studies; VitiQoL, 6/6 studies; VIS-22, 3/3 studies). Vitiligo also had a significant impact on the QoL of families and caregivers; 4/4 studies reporting FDLQI scores indicated moderate or worse effects on QoL. In general, treatment significantly ($P<0.05$) improved QoL, but there were no trends for types or duration of treatment. Among studies that reported factors significantly ($P\leq0.05$) associated with reduced QoL, female sex and visible lesions and/or lesions in sensitive areas were most common. In summary, vitiligo has clinically meaningful effects on the QoL of patients, highlighting that greater attention should be dedicated to QoL decrement awareness and improvement in patients with vitiligo.

Dermatology

Prasad S, McMahon DE, Tyagi A, Ali R, Singh R, Rosenbach M, **Lim HW**, Fox LP, Blumenthal K, Hruza GJ, French LE, and Freeman EE. Cutaneous Reactions Following Booster Dose Administration of COVID-19 mRNA Vaccine: a first look from the AAD/ILDS Registry. *JAAD Int* 2022; Epub ahead of print. PMID: 35498758. Full Text

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Dermatology

Sattler SS, Magro CM, Shapiro L, Merves JF, Levy R, **Veenstra J**, and **Patel P**. Gastrointestinal Kohlmeier-Degos disease: a narrative review. *Orphanet J Rare Dis* 2022; 17(1):172. PMID: 35443671. Full Text

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INTRODUCTION: Kohlmeier-Degos (K-D) disease is a rare obliterative vasculopathy that can present as a benign cutaneous form or with potentially malignant systemic involvement. The gastrointestinal tract is most frequently involved in systemic disease and mortality is often related to bowel perforations. Herein, we provide information to providers and patients regarding gastrointestinal K-D symptomology, pathology, treatment, and diagnosis, with a focus on the importance of timely diagnostic laparoscopy. We present three new cases of gastrointestinal K-D to highlight varying disease presentations and outcomes. BODY: Based on reviewed reports, perforation is preceded by at least one gastrointestinal symptom: abdominal pain/cramping, anorexia/weight loss, vomiting, diarrhea, nausea, gastrointestinal bleeding, obstipation, constipation, and abdominal fullness. Perforation most commonly occurs in the small intestine and often results in sepsis and death. Although underutilized, laparoscopy is the most sensitive and specific diagnostic technique, demonstrating serosal porcelain plaques similar to those on the skin and characteristic for K-D. The combination of eculizumab and treprostinil is presently the most effective treatment option for gastrointestinal K-D. The pathology of gastrointestinal K-D is characterized by an obliterative intimal arteriopathy eventuating in occlusive acellular deposits of mucin and collagen along with an extravascular pauci-cellular sclerosing process resembling scleroderma confined to the subserosal fat. C5b-9 and interferon-alpha are both expressed in all caliber of vessels in the affected intestine. While C5b-9 blockade does not prevent the intimal expansion, enhanced type I interferon signaling is likely a key determinant to intimal expansion by, causing an influx of monocytes which transdifferentiate into procollagen-producing myofibroblast-like cells. CONCLUSION: Prompt laparoscopic evaluation is necessary in any K-D patient with an abdominal symptom to facilitate diagnosis and treatment initiation, as well as to hopefully decrease mortality. Those with gastrointestinal K-D should start on eculizumab as soon as possible, as onset of action is immediate.

Emergency Medicine

Bruen C, Al-Saadi M, Michelson EA, Tanios M, Mendoza-Ayala R, **Miller J**, Zhang J, Stauderman K, Hebbar S, and Hou PC. Auxora vs. placebo for the treatment of patients with severe COVID-19 pneumonia: a randomized-controlled clinical trial. *Crit Care* 2022; 26(1):101. PMID: 35395943. Full Text

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BACKGROUND: Calcium release-activated calcium (CRAC) channel inhibitors block proinflammatory cytokine release, preserve endothelial integrity and may effectively treat patients with severe COVID-19 pneumonia. METHODS: CARDEA was a phase 2, randomized, double-blind, placebo-controlled trial evaluating the addition of Auxora, a CRAC channel inhibitor, to corticosteroids and standard of care in adults with severe COVID-19 pneumonia. Eligible patients were adults with ≥ 1 symptom consistent with COVID-19 infection, a diagnosis of COVID-19 confirmed by laboratory testing using polymerase chain reaction or other assay, and pneumonia documented by chest imaging. Patients were also required to be receiving oxygen therapy using either a high flow or low flow nasal cannula at the time of enrolment and have at the time of enrollment a baseline imputed PaO(2)/FiO(2) ratio > 75 and ≤ 300. The PaO(2)/FiO(2) was imputed from a SpO(2)/FiO(2) determine by pulse oximetry using a non-linear equation. Patients could not be receiving either non-invasive or invasive mechanical ventilation at the time of enrolment. The primary endpoint was time to recovery through Day 60, with secondary endpoints of all-cause mortality at Day 60 and Day 30. Due to declining rates of COVID-19 hospitalizations and utilization of standard of care medications prohibited by regulatory guidance, the trial was stopped early. RESULTS: The pre-specified efficacy set consisted of the 261 patients with a baseline imputed PaO(2)/FiO(2)≤ 200 with 130 and 131 in the Auxora and placebo groups, respectively. Time to recovery was 7 vs. 10 days (P = 0.0979) for patients who received Auxora vs. placebo, respectively. The all-cause mortality rate at Day 60 was 13.8% with Auxora vs. 20.6% with placebo (P = 0.1449); Day 30 all-cause mortality was 7.7% and 17.6%, respectively (P = 0.0165). Similar trends were noted in all randomized patients, patients on high flow nasal cannula at baseline or those with a baseline imputed PaO(2)/FiO(2) ≤ 100. Serious adverse events (SAEs) were less frequent in patients treated with Auxora vs. placebo and occurred in 34 patients (24.1%) receiving Auxora and 49 (35.0%) receiving placebo (P = 0.0616). The most common SAEs were respiratory failure, acute respiratory distress syndrome, and pneumonia. CONCLUSIONS: Auxora was safe and well tolerated with strong signals in both time to recovery and all-cause mortality through Day 60 in patients with severe COVID-19 pneumonia. Further studies of Auxora in patients with severe COVID-19 pneumonia are warranted. Trial registration NCT04345614.

Emergency Medicine

Eswaran V, Chang AM, Wilkerson RG, O'Laughlin KN, Chinnock B, Eucker SA, Baumann BM, Anaya N, Miller DG, Haggins AN, Torres JR, Anderson ES, Lim SC, **Caldwell MT**, Raja AS, and Rodriguez RM. Facemasks: Perceptions and use in an ED population during COVID-19. *PLoS One* 2022; 17(4):e0266148. PMID: 35417505. Full Text

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STUDY OBJECTIVE: Facemask use is associated with reduced transmission of SARS-CoV-2. Most surveys assessing perceptions and practices of mask use miss the most vulnerable racial, ethnic, and socio-economic populations. These same populations have suffered disproportionate impacts from the pandemic. The purpose of this study was to assess beliefs, access, and practices of mask wearing across 15 urban emergency department (ED) populations. METHODS: This was a secondary analysis of a cross-sectional study of ED patients from December 2020 to March 2021 at 15 geographically diverse, safety net EDs across the US. The primary outcome was frequency of mask use outside the home and around others. Other outcome measures included having enough masks and difficulty obtaining them. RESULTS: Of 2,575 patients approached, 2,301 (89%) agreed to participate; nine had missing data pertaining to the primary outcome, leaving 2,292 included in the final analysis. A total of 79% of respondents reported wearing masks "all of the time" and 96% reported wearing masks over half the time. Subjects with PCPs were more likely to report wearing masks over half the time compared to those without PCPs (97% vs 92%). Individuals experiencing homelessness were less likely to wear a mask over half the time compared to those who were housed (81% vs 96%). CONCLUSIONS: Study participants reported high rates of facemask use. Respondents who did not have PCPs and those who were homeless were less likely to report wearing a mask over half the time and more likely to report barriers in obtaining masks. The ED may serve a critical role in education regarding, and provision of, masks for vulnerable populations.

Emergency Medicine

Etu EE, Monplaisir L, Aguwa C, Arslanturk S, Masoud S, Markevych I, and **Miller J**. Identifying indicators influencing emergency department performance during a medical surge: A consensus-based modified fuzzy Delphi approach. *PLoS One* 2022; 17(4):e0265101. PMID: 35446857. Full Text

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During a medical surge, resource scarcity and other factors influence the performance of the healthcare systems. To enhance their performance, hospitals need to identify the critical indicators that affect their operations for better decision-making. This study aims to model a pertinent set of indicators for improving emergency departments' (ED) performance during a medical surge. The framework comprises a three-stage process to survey, evaluate, and rank such indicators in a systematic approach. The first stage consists of a survey based on the literature and interviews to extract quality indicators that impact the EDs' performance. The second stage consists of forming a panel of medical professionals to complete the survey questionnaire and applying our proposed consensus-based modified fuzzy Delphi method, which integrates text mining to address the fuzziness and obtain the sentiment scores in expert responses. The final stage ranks the indicators based on their stability and convergence. Here, twenty-nine potential indicators are extracted in the first stage, categorized into five healthcare performance factors, are reduced to twenty consentaneous indicators monitoring ED's efficacy. The Mann-Whitney test confirmed the stability of the group opinions ($p < 0.05$). The agreement percentage indicates that ED beds (77.8%), nurse staffing per patient seen (77.3%), and length of stay (75.0%) are among the most significant indicators affecting the ED's performance when responding to a surge. This research proposes a framework that helps hospital administrators determine essential indicators to monitor, manage, and improve the performance of EDs systematically during a surge event.

Emergency Medicine

Ko ER, Henao R, Frankey K, Petzold EA, Isner PD, **Jaehne AK**, **Allen N**, **Gardner-Gray J**, **Hurst G**, **Pflaum-Carlson J**, **Jayaprakash N**, **Rivers EP**, Wang H, Ugalde I, Amanullah S, Mercurio L, Chun TH, May L, Hickey RW, Lazarus JE, Gunaratne SH, Pallin DJ, Jambaulikar G, Huckins DS, Ampofo K, Jhaveri R, Jiang Y, Komarow L, Evans SR, Ginsburg GS, Tillekeratne LG, McClain MT, Burke TW, Woods CW, and Tsalik EL. Prospective Validation of a Rapid Host Gene Expression Test to Discriminate Bacterial From Viral Respiratory Infection. *JAMA Netw Open* 2022; 5(4):e227299. PMID: 35420659. Full Text

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Department of Pediatrics, University of North Carolina at Chapel Hill.
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IMPORTANCE: Bacterial and viral causes of acute respiratory illness (ARI) are difficult to clinically distinguish, resulting in the inappropriate use of antibacterial therapy. The use of a host gene expression-based test that is able to discriminate bacterial from viral infection in less than 1 hour may improve care and antimicrobial stewardship. OBJECTIVE: To validate the host response bacterial/viral (HR-B/V) test and assess its ability to accurately differentiate bacterial from viral infection among patients with ARI. DESIGN, SETTING, AND PARTICIPANTS: This prospective multicenter diagnostic study enrolled 755 children and adults with febrile ARI of 7 or fewer days' duration from 10 US emergency departments. Participants were enrolled from October 3, 2014, to September 1, 2019, followed by additional enrollment of patients with COVID-19 from March 20 to December 3, 2020. Clinical adjudication of enrolled participants identified 616 individuals as having bacterial or viral infection. The primary analysis cohort included 334 participants with high-confidence reference adjudications (based on adjudicator concordance and the presence of an identified pathogen confirmed by microbiological testing). A secondary analysis of the entire cohort of 616 participants included cases with low-confidence reference

adjudications (based on adjudicator discordance or the absence of an identified pathogen in microbiological testing). Thirty-three participants with COVID-19 were included post hoc. INTERVENTIONS: The HR-B/V test quantified the expression of 45 host messenger RNAs in approximately 45 minutes to derive a probability of bacterial infection. MAIN OUTCOMES AND MEASURES: Performance characteristics for the HR-B/V test compared with clinical adjudication were reported as either bacterial or viral infection or categorized into 4 likelihood groups (viral very likely [probability score <0.19], viral likely [probability score of 0.19-0.40], bacterial likely [probability score of 0.41-0.73], and bacterial very likely [probability score >0.73]) and compared with procalcitonin measurement. RESULTS: Among 755 enrolled participants, the median age was 26 years (IQR, 16-52 years); 360 participants (47.7%) were female, and 395 (52.3%) were male. A total of 13 participants (1.7%) were American Indian, 13 (1.7%) were Asian, 368 (48.7%) were Black, 131 (17.4%) were Hispanic, 3 (0.4%) were Native Hawaiian or Pacific Islander, 297 (39.3%) were White, and 60 (7.9%) were of unspecified race and/or ethnicity. In the primary analysis involving 334 participants, the HR-B/V test had sensitivity of 89.8% (95% CI, 77.8%-96.2%), specificity of 82.1% (95% CI, 77.4%-86.6%), and a negative predictive value (NPV) of 97.9% (95% CI, 95.3%-99.1%) for bacterial infection. In comparison, the sensitivity of procalcitonin measurement was 28.6% (95% CI, 16.2%-40.9%; P < .001), the specificity was 87.0% (95% CI, 82.7%-90.7%; P = .006), and the NPV was 87.6% (95% CI, 85.5%-89.5%; P < .001). When stratified into likelihood groups, the HR-B/V test had an NPV of 98.9% (95% CI, 96.1%-100%) for bacterial infection in the viral very likely group and a positive predictive value of 63.4% (95% CI, 47.2%-77.9%) for bacterial infection in the bacterial very likely group. The HR-B/V test correctly identified 30 of 33 participants (90.9%) with acute COVID-19 as having a viral infection. CONCLUSIONS AND RELEVANCE: In this study, the HR-B/V test accurately discriminated bacterial from viral infection among patients with febrile ARI and was superior to procalcitonin measurement. The findings suggest that an accurate point-of-need host response test with high NPV may offer an opportunity to improve antibiotic stewardship and patient outcomes.

Global Health Initiative

Green L, McHale T, Mishori R, **Kaljee L**, and Akter Chowdhury S. "Most of the cases are very similar.": Documenting and corroborating conflict-related sexual violence affecting Rohingya refugees. *BMC Public Health* 2022; 22(1):700. PMID: 35397528. Full Text

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BACKGROUND: In August 2017, a large population of Rohingya from northern Rakhine state in Myanmar fled to Bangladesh due to "clearance operations" by the Myanmar security forces characterized by widespread and systematic violence, including extensive conflict-related sexual violence (CRSV). This study sought to document the patterns of injuries and conditions experienced by the Rohingya, with a specific focus on sexual violence. METHODS: Qualitative interviews were conducted with 26 health care professionals who cared for Rohingya refugees after their arrival in Bangladesh between November 2019 and August 2020. RESULTS: Health care workers universally reported hearing accounts and seeing evidence of sexual and gender-based violence committed against Rohingya people of all genders by the Myanmar military and security forces. They observed physical and psychological consequences of such acts against the Rohingya while patients were seeking care. Health care workers shared that patients faced pressure not to disclose their experiences of CRSV, likely resulted in an underreporting of the prevalence of sexual violence. Forced witnessing of sexual violence and observed increases in pregnancy and birth rates as a result of rape are two less-reported issues that emerged from these data. CONCLUSIONS: Healthcare workers corroborated previous reports that the Rohingya experienced CRSV at the hands of the Myanmar military and security forces. Survivors often revealed their experiences of sexual violence while seeking care for a variety of physical and psychological conditions. Stigma, cultural pressure, and trauma created barriers to disclosing experiences of sexual violence and likely resulted in an underreporting of the prevalence of sexual violence. The findings of this research emphasize the importance of offering universal and comprehensive trauma-informed services to all refugees with the

presumption of high rates of trauma in this population and many survivors who may never identify themselves as such.

Hematology-Oncology

Farooq MZ, Aqeel SB, Lingamaneni P, **Pichardo RC**, Jawed A, Khalid S, Banskota SU, Fu P, and Mangla A. Association of Immune Checkpoint Inhibitors With Neurologic Adverse Events: A Systematic Review and Meta-analysis. *JAMA Netw Open* 2022; 5(4):e227722. PMID: 35438755. Full Text

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IMPORTANCE: Neurologic adverse events (NAEs) due to immune checkpoint inhibitors (ICIs) can be fatal but are underexplored. OBJECTIVE: To compare NAEs reported in randomized clinical trials (RCTs) of US Food and Drug Administration-approved ICIs with other forms of chemotherapy and placebo. DATA SOURCES: Bibliographic databases (Embase, Ovid, MEDLINE, and Scopus data) and trial registries (ClinicalTrials.gov) were searched from inception through March 1, 2020. STUDY SELECTION: Phase II/III RCTs evaluating the use of ICIs were eligible for inclusion. Unpublished trials were excluded from the analysis. DATA EXTRACTION AND SYNTHESIS: Two investigators independently performed screening of trials using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline. NAEs were recorded for each arm. Data were pooled using a random-effects model. MAIN OUTCOMES AND MEASURES: The risk of NAEs with ICI use compared with any drug regimen, cytotoxic chemotherapy, and placebo. RESULTS: A total 39 trials including 23 705 patients were analyzed (16 135 [68.0%] men, 7866 [33.1%] White). The overall risk of a NAE was lower in the ICI group (risk ratio [RR], 0.59; 95% CI, 0.45-0.77) and in the subgroup of RCTs comparing ICI use with chemotherapy (RR, 0.22; 95% CI, 0.13-0.39). In the subgroup of RCTs comparing ICI with placebo, the overall risk of NAE was significantly higher in the ICI group (RR, 1.57; 95% CI, 1.30-1.89). Peripheral neuropathy (RR, 0.30; 95% CI, 0.17-0.51) and dysgeusia (RR, 0.41; 95% CI, 0.27-0.63) were significantly lower in the ICI group. Headache was more common with the use of ICIs (RR, 1.32; 95% CI, 1.10-1.59). In the subgroup analysis of RCTs comparing ICI use with chemotherapy, peripheral neuropathy (RR, 0.09; 95% CI, 0.05-0.17), dysgeusia (RR, 0.42; 95% CI, 0.21-0.85), and paresthesia (RR, 0.29; 95% CI, 0.13-0.67) were significantly lower in the ICI group. RCTs comparing ICIs with placebo showed a higher risk of headache with ICI use (RR, 1.63; 95%, CI, 1.32-2.02). CONCLUSIONS AND RELEVANCE: Results of this meta-analysis suggest that the overall risk of NAEs, peripheral neuropathy, and dysgeusia is lower with the use of ICI. When compared with chemotherapy, the overall risk of NAE, peripheral neuropathy, paresthesia, and dysgeusia was lower with ICI use; however, when compared with placebo, the risk of NAEs is higher with the use of ICI.

Hematology-Oncology

Hinton T, Karnak D, Tang M, Jiang R, Luo Y, Boonstra P, Sun Y, Nancarrow DJ, **Sandford E**, Ray P, Maurino C, Matuszak M, Schipper MJ, Green MD, **Yanik GA**, **Tewari M**, Naqa IE, Schonewolf CA, Haken RT, Jolly S, Lawrence TS, and Ray D. Improved prediction of radiation pneumonitis by combining biological and radiobiological parameters using a data-driven Bayesian network analysis. *Transl Oncol* 2022; 21:101428. PMID: 35460942. Full Text

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Grade 2 and higher radiation pneumonitis (RP2) is a potentially fatal toxicity that limits efficacy of radiation therapy (RT). We wished to identify a combined biomarker signature of circulating miRNAs and cytokines which, along with radiobiological and clinical parameters, may better predict a targetable RP2 pathway. In a prospective clinical trial of response-adapted RT for patients (n = 39) with locally advanced non-small cell lung cancer, we analyzed patients' plasma, collected pre- and during RT, for microRNAs (miRNAs) and cytokines using array and multiplex enzyme linked immunosorbent assay (ELISA), respectively. Interactions between candidate biomarkers, radiobiological, and clinical parameters were analyzed using data-driven Bayesian network (DD-BN) analysis. We identified alterations in specific miRNAs (miR-532, -99b and -495, let-7c, -451 and -139-3p) correlating with lung toxicity. High levels of soluble tumor necrosis factor alpha receptor 1 (sTNFR1) were detected in a majority of lung cancer patients. However, among RP patients, within 2 weeks of RT initiation, we noted a trend of temporary decline in sTNFR1 (a physiological scavenger of TNFα) and ADAM17 (a shedding protease that cleaves both membrane-bound TNFα and TNFR1) levels. Cytokine signature identified activation of inflammatory pathway. Using DD-BN we combined miRNA and cytokine data along with generalized equivalent uniform dose (gEUD) to identify pathways with better accuracy of predicting RP2 as compared to either miRNA or cytokines alone. This signature suggests that activation of the TNFα-NFκB inflammatory pathway plays a key role in RP which could be specifically ameliorated by etanercept rather than current therapy of non-specific leukotoxic corticosteroids.

Hematology-Oncology
Schwartz T. Personal Systemic Therapy Decision-Making has Officially Arrived for Node-Positive Breast Cancer. *Ann Surg Oncol* 2022; Epub ahead of print. PMID: 35430658. Full Text

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Hospital Medicine
Song M, Haymart B, Kong X, Ali M, **Kaatz S**, Kozlowski J, **Krol G**, Schaefer J, Froehlich JB, and Barnes GD. Association of adding antiplatelet therapy to warfarin for management of venous thromboembolism with bleeding and other adverse events. *Vasc Med* 2022; Epub ahead of print. PMID: 35400235. Full Text

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Hypertension and Vascular Research
Monu SR, **Wang H**, **Potter DL**, **Liao TD**, and **Ortiz PA**. Decreased tubuloglomerular feedback response in high-fat diet-induced obesity. *Am J Physiol Renal Physiol* 2022; 322(4):F429-f436. PMID: 35224993. Full Text

Division of Hypertension and Vascular Research, Department of Internal Medicine, grid.413103.4Henry Ford Hospital, Detroit, Michigan.

Obesity increases the risk of renal damage, but the mechanisms are not clear. Normally, kidneys autoregulate to keep the glomerular capillary pressure (P(GC)), renal blood flow, and glomerular filtration rate in a steady state. However, in obesity, higher P(GC), renal blood flow, and glomerular filtration rate are noted. Together, these may lead to glomerular damage. P(GC) is controlled mainly by afferent arteriole resistance, which, in turn, is regulated by tubuloglomerular feedback (TGF), a vasoconstrictor mechanism. High fat-induced obesity causes renal damage, and this may be related to increased P(GC). However, there are no studies as to whether high-fat diet (HFD)-induced obesity affects TGF. We hypothesized that TGF would be attenuated in obesity caused by HFD feeding (60% fat) in Sprague-Dawley rats. Sprague-Dawley rats fed a normal-fat diet (NFD; 12% fat) served as the control. We studied 4 and 16 wk of HFD feeding using in vivo renal micropuncture of individual rat nephrons. We did not observe significant differences in body weight, TGF response, and mean arterial pressure at 4 wk of HFD feeding, but after 16 wk of HFD, rats were heavier and hypertensive. The maximal TGF response was smaller in HFD-fed rats than in NFD-fed rats, indicating an attenuation of TGF in HFD-induced obesity. Baseline P(GC) was higher in HFD-fed rats than in NFD-fed rats and was associated with higher glomerulosclerosis. We conclude that attenuated TGF and higher P(GC) along with hypertension in HFD-fed obese Sprague-Dawley rats could explain the higher propensity of glomerular damage observed in obesity.NEW & NOTEWORTHY Reduced tubuloglomerular feedback, higher glomerular capillary pressure, and hypertension in combination may explain the higher glomerular damage observed in high-fat diet-induced obesity.

Infectious Diseases

Kheil MH, Jain D, Jomaa J, Askar B, Alcodray Y, Wahbi S, Brikho S, Kadouh A, Harajli D, Jawad ZN, Fehmi Z, Elhage M, Tawil T, Fehmi O, Alzouhayli SJ, Ujayli D, Suleiman N, Kazziha O, Saleh R, Abada E, **Shallal A**, Kim S, Kumar VA, **Zervos M**, Cote ML, and Ali-Fehmi R. COVID-19 Vaccine Hesitancy among Arab Americans. *Vaccines (Basel)* 2022; 10(4). PMID: 35455359. Full Text

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(1) Background: Coronavirus disease-2019 (COVID-19) vaccines have a significant impact on reducing morbidity and mortality from infection. However, vaccine hesitancy remains an obstacle in combating the pandemic. The Arab American (AA) population is understudied; thus, we aimed to explore COVID-19 attitudes within this community. (2) Methods: This was a cross-sectional study. An anonymous online survey was distributed to members of different AA associations and to the community through the snowball method. (3) Results: A total of 1746 participants completed the survey. A total of 92% of respondents reported having received at least one dose of a COVID-19 vaccine. A total of 73% reported willingness to receive a booster, and 72% plan to give their children the vaccine. On multivariate analysis, respondents were more likely to be vaccine-hesitant if they were hesitant about receiving any vaccine in general. They were less likely to be vaccine-hesitant if they were immigrants, over the age of 40, up to

date on their general vaccination and if they believed that COVID-19 vaccines are safe and effective in preventing an infection. The belief that all vaccines are effective at preventing diseases was also associated with lower hesitancy. (4) Conclusions: This sample of AAs have higher vaccination rates and are more willing to vaccinate their children against COVID-19 when compared to the rest of the population. However, a reemergence of hesitancy might be arising towards the boosters.

Internal Medicine

Shamaa TM, **Shamaa O**, **Crombez C**, **Konel JM**, **Kitajima T**, **Shimada S**, **Ivanics T**, **Mohamed A**, **Collins K**, **Nagai S**, **Yoshida A**, **Abouljoud M**, and **Rizzari M**. The use of normothermic liver preservation in combined liver and lung transplantation: A single-center experience. *Am J Transplant* 2022; Epub ahead of print. PMID: 35384271. Full Text

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Combined liver and lung transplantation (CLLT) is indicated in patients with both end-stage liver and lung disease. Ex-situ normothermic machine perfusion (NMP) has been previously used for extended normothermic lung preservation in CLLT. We aim to describe our single-center experience using ex-situ NMP for extended normothermic liver preservation in CLLT. Four CLLTs were performed from 2019 to 2020 with the lung transplanted first for all patients. Median ex-situ pump time for the liver was 413 min (IQR 400-424). Over a median follow-up of 15 months (IQR 14-19), all patients were alive and doing well. Normothermic extended liver preservation is a safe method to allow prolonged cold ischemia using normothermic perfusion of the liver during CLLT.

Internal Medicine

Song M, Haymart B, Kong X, Ali M, **Kaatz S**, Kozlowski J, **Krol G**, Schaefer J, Froehlich JB, and Barnes GD. Association of adding antiplatelet therapy to warfarin for management of venous thromboembolism with bleeding and other adverse events. *Vasc Med* 2022; Epub ahead of print. PMID: 35400235. Full Text

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Internal Medicine

Soreide KK, **Solomon O**, **Farhat NM**, **Kolander S**, **Gottschall T**, **George DL**, **Szandzik EG**, **Kalus JS**, and **Thomas E**. Pharmacist hypertension management using an electronic health record-based approach. *Am J Manag Care* 2022; 28(4):e121-e125. PMID: 35420749. Full Text

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OBJECTIVES: To evaluate the impact of the chronic medication optimization pharmacist (CMOP) program on blood pressure (BP) control and time to goal compared with usual care in the ambulatory care setting. STUDY DESIGN: This was a retrospective cohort study that included patients from June 2018 to June 2020 who were seen in an ambulatory care clinic for hypertension management. METHODS: Patients aged 18 to 80 years were divided into 2 cohorts based on hypertension management by usual care or the CMOP program. Patients were enrolled in the CMOP program either by referral or identification via a data analytics tool. The primary outcome assessed the proportion of patients within BP goal (< 140/90 mm Hg) at 3 months. Secondary outcomes assessed the proportion of patients within goal at 6 months, time and number of visits to goal, and adherence (CMOP cohort only). RESULTS: The primary end point demonstrated a greater proportion of patients within goal in the CMOP cohort compared with usual care (69.4% vs 42.3%; P < .001). The CMOP cohort also displayed a greater

proportion of patients achieving goal within 6 months (75.7% vs 60.4%; P = .014) and faster time to goal (42.99 vs 63.12 days; P = .002), but more visits (1.67 vs 1.18; P = .001). Lastly, adherence improved from 50.4% to 72.1% in the patients with a documented adherence assessment in the pharmacist group (P = .03). CONCLUSIONS: The pharmacist intervention improved BP control in a primarily African American patient population compared with usual care. Future studies should assess the sustainability of this intervention.

Nephrology
Kant S, **Soman S**, Choi MJ, Jaar BG, and Adey DB. Management of Hospitalized Kidney Transplant Recipients for Hospitalists and Internists. *Am J Med* 2022; Epub ahead of print. PMID: 35472384. Full Text

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The number of kidney transplant recipients have grown incrementally over the years. These patients have a high comorbidity index and require special attention to immunosuppression management. In addition, this population has an increased risk for cardiovascular events, electrolyte abnormalities, allograft dysfunction and infectious complications. . It is vital for hospitalists and internists to understand the risks and nuances in the care of this increasingly prevalent but also high-risk population.

Nephrology
Lamerato L, James G, van Haalen H, Hedman K, Sloand JA, **Tang A**, Wittbrodt ET, and **Yee J**. Epidemiology and outcomes in patients with anemia of CKD not on dialysis from a large US healthcare system database: a retrospective observational study. *BMC Nephrol* 2022; 23(1):166. PMID: 35490226. Full Text

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BACKGROUND: Optimal management of anemia of chronic kidney disease (CKD) remains controversial. This retrospective study aimed to describe the epidemiology and selected clinical outcomes of anemia in patients with CKD in the US. METHODS: Data were extracted from Henry Ford Health System databases. Adults with stages 3a-5 CKD not on dialysis (estimated glomerular filtration

rate < 60 mL/min/1.73m(2)) between January 1, 2013 and December 31, 2017 were identified. Patients on renal replacement therapy or with active cancer or bleeding were excluded. Patients were followed for ≥12 months until December 31, 2018. Outcomes included incidence rates per 100 person-years (PY) of anemia (hemoglobin < 10 g/dL), renal and major adverse cardiovascular events, and of bleeding and hospitalization outcomes. Adjusted Cox proportional hazards models identified factors associated with outcomes after 1 and 5 years. RESULTS: Among the study cohort (N = 50,701), prevalence of anemia at baseline was 23.0%. Treatments used by these patients included erythropoiesis-stimulating agents (4.1%), iron replacement (24.2%), and red blood cell transfusions (11.0%). Anemia incidence rates per 100 PY in patients without baseline anemia were 7.4 and 9.7 after 1 and 5 years, respectively. Baseline anemia was associated with increased risk of renal and major cardiovascular events, hospitalizations (all-cause and for bleeding), and transfusion requirements. Increasing CKD stage was associated with increased risk of incident anemia, renal and major adverse cardiovascular events, and hospitalizations. CONCLUSIONS: Anemia was a prevalent condition associated with adverse renal, cardiovascular, and bleeding/hospitalization outcomes in US patients with CKD. Anemia treatment was infrequent.

Neurology

Siokas V, Aloizou AM, Liampas I, Bakirtzis C, Nasios G, Paterakis K, Sgantzos M, Bogdanos DP, Spandidos DA, Tsatsakis A, **Mitsias PD**, and Dardiotis E. Lack of an association between SCFD1 rs10139154 polymorphism and amyotrophic lateral sclerosis. *Mol Med Rep* 2022; 25(4). PMID: 35234271. Full Text

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Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease. Through a genome-wide association study (GWAS), the Sec1 family domain-containing protein 1 (SCFD1) rs10139154 variant at 14q12 has emerged as a risk factor gene for ALS. Moreover, it has been reported to influence the age at onset (AAO) of patients with ALS. The aim of the present study was to assess the association of the SCFD1 rs10139154 polymorphism with the risk of developing ALS. For this purpose, 155 patients with sporadic ALS and 155 healthy controls were genotyped for the SCFD1 rs10139154. The effect of the SCFD1 rs10139154 polymorphism was then examined on the following parameters: i) The risk of developing ALS; ii) the AAO of ALS; iii) the site of ALS onset (patients with bulbar onset ALS vs. healthy controls; and patients with limb onset ALS vs. healthy controls); and iv) the AAO of ALS onset with subgroup analyses based on the site of onset (bulbar and limb, crude and adjusted for sex). The analysis of all the outcomes was performed assuming five genetic models. Crude and adjusted analyses were applied. The threshold for statistical significance was set at 0.05. The results revealed no association between SCFD1 rs10139154 and any of the examined phenotypes in any of the models examined. On the whole, based on the findings of the present study, SCFD1 rs10139154 does not appear to play a determining role in the risk of developing ALS.

Neurosurgery

Air EL. Remove Gender Pay Disparity Excuses. *Health Aff (Millwood)* 2022; 41(4):608. PMID: 35377758. Full Text

Henry Ford Health System Detroit, Michigan.

Neurosurgery
Kalkanis SN. Presidential Address to the 2021 Annual Meeting of the Congress of Neurological Surgeons. *Neurosurgery* 2022; 68:1-5. PMID: Not assigned. Full Text

Neurosurgery
Robin AM, **Pawloski JA**, **Snyder JM**, **Walbert T**, **Rogers L**, **Mikkelsen T**, **Noushmehr H**, **Lee I**, **Rock J**, **Kalkanis SN**, and **Rosenblum ML**. Neurosurgery's Impact on Neuro-Oncology-"Can We Do Better?"-Lessons Learned Over 50 Years. *Neurosurgery* 2022; 68:17-26. PMID: Not assigned. Full Text

Neurosurgery
Walsh LE, Polacek LC, Panageas K, Reiner A, **Walbert T**, Thomas AA, Buthorn J, Sigler A, Prigerson HG, Applebaum AJ, and Diamond EL. Coping with glioblastoma: prognostic communication and prognostic understanding among patients with recurrent glioblastoma, caregivers, and oncologists. *J Neurooncol* 2022; Epub ahead of print. PMID: 35437688. Full Text

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PURPOSE: Glioblastoma (GBM) is a devastating neuro-oncologic disease with invariably poor prognosis. Despite this, research shows patients have unrealistic perceptions of their prognosis, which may relate in part to communication patterns between patients, caregivers and oncologists. The purpose of this study was to examine communication processes and goals among patients, caregivers, and oncologists to elucidate drivers of prognostic understanding (PU) in the context of recurrent GBM. METHODS: This was a prospective, multi-center study enrolling adult patients with GBM, caregivers, and oncologists, who independently reported the content of a specific discussion involving the disclosure of GBM recurrence. Communication processes and goals were characterized for each participant, and concordance between all dyads and patient-caregiver-oncologist triads were calculated. RESULTS: Seventeen patient, caregiver, and oncologist triads were analyzed. At the individual level, three (17.6%) patients and 8 (47.1%) caregivers reported having discussed prognosis during the clinical encounter, as compared to ten oncologists (58.8%). Seven patients (41.2%) and 5 caregivers (29.4%), versus thirteen oncologists (76.5%) reported ever discussing prognosis or life expectancy at previous appointments. Generally, patient-caregiver concordance (i.e., both answered the same) regarding communication goals and processes was low. Triads showed limited concordant responses in discussing curability (n = 5), prognosis (n = 4), end-of-life treatment goals (n = 4), and ever discussing prognosis (n = 3). CONCLUSION: Patients, caregivers and oncologists had discordant views regarding communication processes and prognostic goals, even when recalling a single discussion. This study highlights the importance of clear and frequent communication about prognosis, and the need for further research on communication and PU in the neuro-oncology setting.

Ophthalmology and Eye Care Services
Humenny JA. Ophthalmic Photographers' Society Exhibit, July 2021. *J Cataract Refract Surg* 2022; 48(4):507. PMID: 35435178. Full Text

Henry Ford Health System, Detroit, Michigan.

Orthopedics/Bone and Joint Center

Abed V, **Koolmees DS**, **Elhage K**, **Hessburg L**, and **Makhni EC**. Institution Origin and Medical School Rank Impact the Citation Frequency and Publication Rate in Orthopaedic Sports Medicine Journals. *Arthrosc Sports Med Rehabil* 2022; 4(2):e295-e300. PMID: 35494303. Full Text

Henry Ford Health System, Detroit, Michigan, U.S.A.

PURPOSE: To examine the trends between various categories of institutions with their respective published orthopaedic sports medicine content and to determine the publication output and citation rate from the 25 highest-ranked medical schools compared with lower-ranked institutions. METHODS: Publications between 2015 and 2019 from the American Journal of Sports Medicine, Journal of Bone and Joint Surgery, Journal of Shoulder and Elbow Surgery, Clinical Orthopaedics and Related Research, and Arthroscopy were categorized into university/university affiliated hospitals, non-university affiliated teaching hospitals, public/semi-government research institutes, nonprofit research institutes, private sector institutions, government institutions, and other institutions. Citation rates were collected from PubMed for the first and corresponding author. Similarly, corresponding authors were stratified by U.S. News and World Report 2021 medical school research rankings. RESULTS: Of the 12,152 publications identified, 5,044 publications met the inclusion criteria. Nonprofit research institutions garnered the greatest number of citations on average (6.44 based on first author, SD 8.83, n = 214; 6.62 based on corresponding author, SD 9.65, n = 208; P < .001), while university/university-affiliated hospitals produced the majority of published articles (77.0% based on first author, 76.8% based on corresponding author), but had lower average citation rates (4.48 based on first author, SD 6.67, n = 3,886; 4.44 based on corresponding author, SD 6.55, n = 3,873; P < .001). Furthermore, of 1953 medical school publications, the top 25 accounted for 53.1% of publications; however, there was no statistical difference between their citation rates and those of lower rankings (P = 0.47). CONCLUSIONS: Publications are cited at different rates, depending on their institution of origin. In addition, high-ranking medical schools produce a disproportionately greater output of publications than lower-ranking schools, but there is no statistically significant difference in citation rates on an individual publication basis. CLINICAL RELEVANCE: Knowing how an institution's ranking influences publication and citation rates can help us understand bias in the scientific literature.

Orthopedics/Bone and Joint Center

Boyan BD, Berger MB, **Nelson FR**, Donahue HJ, and Schwartz Z. The Biological Basis for Surface-dependent Regulation of Osteogenesis and Implant Osseointegration. *J Am Acad Orthop Surg* 2022; Epub ahead of print. PMID: 35383608. Full Text

From the Department of Biomedical Engineering, Virginia Commonwealth University, Richmond, VA (Boyan, Berger, Donahue, and Schwartz), the Wallace B. Coulter Department at Biomedical Engineering, Georgia Institute of Technology, Atlanta, GA (Boyan), the Department of Orthopaedics, Henry Ford Hospital, School of Medicine, Wayne State University, Detroit, MI (Nelson), and the Department of Periodontics, University of Texas Health Science Center at San Antonio, San Antonio, TX (Schwartz).

Bone marrow stromal cells are regulated by the chemical and physical features of a biomaterial surface. When grown on titanium (Ti) and Ti alloy surfaces, such as titanium-aluminum-vanadium, with specific topographies that mimic the microscale, mesoscale, and nanoscale features of an osteoclast resorption pit, they undergo a rapid change in cell shape to assume a columnar morphology typical of a secretory osteoblast. These cells exhibit markers associated with an osteoblast phenotype, including osteocalcin and osteopontin, and they secrete factors associated with osteogenesis, including bone morphogenetic protein 2, vascular endothelial growth factor, and neurotrophic semaphorins. The pathway involves a shift in integrin expression from α5β1 to α2β1 and signaling by Wnt5a rather than Wnt3a. Conditioned media from these cultures can stimulate vasculogenesis by human endothelial cells and osteoblastic differentiation of marrow stromal cells not grown on the biomimetic substrate, suggesting that the surface could promote osteogenesis in vivo through similar mechanisms. In vivo studies using a variety of animal models confirm that implants with biomimetic surfaces result in improved osseointegration compared with Ti implants with smooth surfaces, as do meta-analyses comparing clinical performance of implant surface topographies.

Orthopedics/Bone and Joint Center

Castle JP, Cotter DL, **Jildeh TR**, **Abbas MJ**, **Gaudiani MA**, Ghali A, Bridges C, and **Moutzouros V**. Reduced Career Longevity but Return to Baseline Performance After Arthroscopic Shoulder Labral Repair in National Hockey League Players. *Arthrosc Sports Med Rehabil* 2022; 4(2):e599-e605. PMID: 35494311. Full Text

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PURPOSE: To investigate the impact of arthroscopic shoulder labral repair without shoulder instability on career longevity, game use, and performance in National Hockey League (NHL) athletes. METHODS: A retrospective review of all NHL players who underwent arthroscopic shoulder labral repair from 2004 to 2020 was performed. A 2:1 matched control group was used for comparison. Controls were matched by age, body mass index, position, and experience prior to the index year. Demographic characteristics, game use, and performance metrics were collected for all athletes. Statistical analysis examined game use and performance both at 1-year and 3-year follow-up compared with one season before injury. RESULTS: Twenty-nine players who underwent arthroscopic shoulder labral surgery returned to play (100%) and were matched with 55 control players. The operative cohort experienced shorter careers compared with controls (4.4 ± 3.1 vs 6.0 ± 3.6 seasons, P < .05). After one season, injured players experienced significant reductions in goals per 60 (0.6 ± 0.4 vs 0.8 ± 0.5, P = .013), points per 60 (1.5 ± 0.9 vs 2.0 ± 0.9, P = .001), and shooting percentage, (8.5 ± 5.8 vs 10.5 ± 5.2, P = .02) compared with the year prior. The reduction in goals (0.6 ± 0.4 vs 0.8 ± 0.5, P = .01) and shooting % (8.5 ± 4.7 vs 10.5 ± 5.2, P = .04) persisted at 3 years. Compared with controls, the surgical group experienced significant reductions at one season postindex in percentage of goals, assists, points per 60, and shooting percentage. Only the reduction in goals per 60 persisted at 3 seasons postindex. CONCLUSIONS: Following return to play after arthroscopic shoulder labral repair, NHL players demonstrated reduced career longevity compared with healthy controls. Players exhibited significant reductions in game use and performance at one season after injury but returned closer to baseline after 3 seasons. LEVEL OF EVIDENCE: Level III; retrospective case control.

Orthopedics/Bone and Joint Center

Castle JP, **Khalil LS**, **Abbas MJ**, **DeBolle S**, Tandron M, **Cross AG**, Rodriguez GA, and Okoroha KR. Maximum subjective outcome improvement is reported by 3 Months following arthroscopic partial meniscectomy: A systematic review. *J Orthop* 2022; 31:78-85. PMID: 35496357. Full Text

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PURPOSE: To review patient outcomes in the literature following arthroscopic partial meniscectomy (APM) in order to identify when patients report reaching subjective maximal improvement postoperatively. METHODS: A systematic review of the literature from January 2004 to August 2019 was conducted using PRISMA guidelines to identify articles evaluating patient-reported outcome measures (PROMs) up to a minimum of 6 months after APM in patients >18 years old. Studies were excluded if additional interventions were performed such as repairs, ligamentous reconstruction or repair, cartilaginous manipulation, or revision surgery. PROMs were pooled between studies at preoperative, 3 months, 6 months, 1 year, and 2 year time points. Weighted averages were used within a mixed model method in order to account for the differences in sample size and variance among studies. Significant improvements in PROMs at various time intervals were statistically analyzed using minimal clinically important difference. RESULTS: A total of 12 studies including 1663 patients who underwent APM were selected for the review. The pooled cohort consisted of 1033 (62%) males and 630 (38%) females. Significant improvements were demonstrated from preoperative scores to 3 months postoperatively in Knee Injury and Osteoarthritis Outcome Score subcategories, Lysholm, and visual analog scale scores while no

differences were found for Tegner and International Knee Documentation Committee scores. Although statistically significant improvement in PROMs remained at all postoperative time points compared to preoperative scores, no significant differences were observed after 3 months postoperatively. CONCLUSIONS: Patients undergoing APM had significant mean changes in legacy PROMs by 3 months postoperatively that exceeded given minimal clinically important difference values, without further clinically important improvement reported up to 2 years postoperatively. STUDY DESIGN: Level III, systematic review.

Orthopedics/Bone and Joint Center
Jildeh TR, **Abbas MJ**, Hasan L, **Moutzouros V**, and Okoroha KR. Multimodal Nonopioid Pain Protocol Provides Better or Equivalent Pain Control Compared to Opioid Analgesia Following Arthroscopic Rotator Cuff Surgery: A Prospective Randomized Controlled Trial. *Arthroscopy* 2022; 38(4):1077-1085. PMID: 34838987. Full Text

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PURPOSE: To evaluate the efficacy of a multimodal nonopioid analgesic protocol in controlling postoperative pain compared to opioids following a primary arthroscopic rotator cuff repair. METHODS: Seventy consecutive patients undergoing a primary rotator cuff repair were assessed for eligibility. An observer-blinded prospective randomized controlled trial was designed in accordance with the Consolidated Standards of Reporting Trials 2010 (CONSORT) statement. The two arms of the study included a multimodal nonopioid pain regimen for the experimental group, and a standard of care narcotics for the control group. The primary outcome was visual analog scale (VAS) pain scores for the first 10 postoperative days. Secondary outcomes included PROMIS-PI (Patient-Reported Outcomes Measurement Information System-Pain Interference) scale, patient satisfaction, and adverse drug events. RESULTS: Thirty patients declined to participate or were excluded, and 40 patients were included in the final analysis. A total of 23 patients were in the traditional group, and 17 patients were in the nonopioid group. Control patients on opioid pain management reported a significantly higher VAS pain score on postoperative day 1 (opioid: 5.7 ± 2, nonopioid: 3.7 ± 2.2; P = .011) and postoperative day 4 (opioid: 4.4 ± 2.7, nonopioid: 2.4 ± 2.2; P = .023). No significant difference was seen on any other postoperative day. When mixed measured models were used to control for confounding factors, the nonopioid group demonstrated significantly lower VAS and PROMIS-PI scores (P < .01) at every time point. Patients in the traditional analgesia group reported significantly more days with constipation (P = .003) and days with upset stomach (P = .020) than those in the nonopioid group. CONCUSSION: The present study found that a multimodal nonopioid pain protocol provided equivalent or better pain control compared to traditional opioid analgesics in patients undergoing primary arthroscopic rotator cuff repair. Minimal side effects were noted with some improvement in the multimodal nonopioid pain cohort. All patients reported satisfaction with their pain management. LEVEL OF EVIDENCE: Level I, prospective randomized controlled trial.

Orthopedics/Bone and Joint Center
Kadado A, **Akioyamen NO**, **Garfinkel R**, **Nahm N**, and **Zeni F**. Staged Correction of Severe Recurrent Clubfoot Deformity With Dislocation of the Chopart Joint Using a Hexapod External Fixator and Unconventional Arthrodesis. *J Am Acad Orthop Surg Glob Res Rev* 2022; 6(4). PMID: 35389910. Full Text

From the Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, MI.

Despite success of the Ponseti method, a subset of patients with clubfeet experience residual deformity. Surgical release after unsuccessful serial casting can lead to residual clubfoot deformities, including a flat-top talus. We present a case of a 17-year-old boy with a dysmorphic ankle and a complete dorsal dislocation of the Chopart joint. Because of pain with activities and functional limitations, the patient

underwent a staged correction of the dislocation. The deformity was corrected through a staged approach using a Taylor Spatial Frame, navicular excision, talocuneiform arthrodesis, and calcaneocuboid arthrodesis. One year postoperatively, the patient is pain free with notable functional gains.

Orthopedics/Bone and Joint Center
Meta F, **Khalil LS**, **Ziedas AC**, **Gulledge CM**, **Muh SJ**, **Moutzouros V**, and **Makhni EC**. Preoperative Opioid Use is Associated with Inferior Patient-Reported Outcomes Measurement Information System Scores Following Rotator Cuff Repair. *Arthroscopy* 2022; Epub ahead of print. PMID: 35398483. Full Text

Henry Ford Hospital, Department of Orthopedic Surgery, 2799 W. Grand Blvd, Detroit, MI 48202. Wayne State University School of Medicine, 540 E. Canfield St, Detroit, MI 48201.

PURPOSE: To determine the influence of preoperative opioid use on Patient-Reported Outcomes Measurement Information System (PROMIS) scores pre- and post-operatively in patients undergoing arthroscopic rotator cuff repair (RCR). METHODS: A retrospective review of all RCR patients aged >18 years old was performed. PROMIS pain interference ("PROMIS PI"), upper extremity function ("PROMIS UE") and depression ("PROMIS D") scores, were reviewed. These measures were collected at preoperative, 6-month, and 1-year postoperative time points. A Prescription Drug Monitoring Program was queried to track opioid prescriptions. Patients were categorized as chronic users, acute users and non-users based on prescriptions filled. Comparison of means were carried out using ANOVA and least squares means. Effect sizes and 95% confidence intervals were calculated. RESULTS: 184 RCR patients were included. Preoperatively, non-users (n=92) had superior PROMIS UE (30.6 vs 28.9 vs 26.1; p<0.05) and PI scores (61.5 vs 64.9 vs 65.3; p<0.001) compared to acute users (n=65) and chronic users (n=27), respectively. 6 months postoperatively, non-users demonstrated significantly higher PROMIS UE (41.7 vs 35.6 vs. 33.5; p<0.001), lower PROMIS D (41.6 vs 45.8 vs 51.1; p<0.001), and lower PROMIS PI scores (50.7 vs 56.3 vs 58.1; p<0.01) when compared to acute and chronic users, respectively. Non-users had lower PROMIS PI (47.9 vs 54.3 vs 57.4; p<0.0001) and PROMIS D (41.6 vs 48.3 vs 49.2; p=0.0002) scores compared to acute and chronic users at 1-year postoperatively. Non-users experienced a significantly greater magnitude of improvement in PROMIS D 6 months postoperatively compared to chronic opioid users (-5.9 vs 0.0; p < 0.01). CONCLUSIONS: Patients undergoing RCR demonstrated superior PROMIS scores pre- and post-operatively if they did not utilize opioids within 3 months prior to surgery. LEVEL OF EVIDENCE: III, retrospective comparative trial.

Orthopedics/Bone and Joint Center
Nelson FR. Spinal-Pelvic-Femoral Relationships Change After Total Hip Arthroplasty: A Clear Path Forward: Commentary on an article by Moritz M. Innmann, MD, et al.: "Spinopelvic Characteristics Normalize 1 Year After Total Hip Arthroplasty. A Prospective, Longitudinal, Case-Controlled Study". *J Bone Joint Surg Am* 2022; 104(8):e32. PMID: 35442249. Full Text

Division of Orthopaedic Surgery, The Henry Ford Health System, Detroit, Michigan.

Orthopedics/Bone and Joint Center
Oravec D, **Kim W**, **Flynn MJ**, and **Yeni YN**. The relationship of whole human vertebral body creep to bone density and texture via clinically available imaging modalities. *J Biomech* 2022; 135:111021. PMID: 35245836. Full Text

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Creep deformation of human vertebrae accumulates under physiological levels of load and is understood to contribute to the progression toward clinically observable vertebral fracture. However, little information is available in terms of clinically measurable predictors of creep behavior in human vertebrae. In this study, creep tests were performed on 22 human cadaveric T12 vertebrae (13 male, 9 female; age 41-90). Areal and volumetric bone density parameters were measured from the same specimens using dual x-ray

absorptiometry and high resolution computed tomography. Image textural analyses (which probe the organization of image intensities within the cancellous bone in low resolution clinical imaging) were performed using digital tomosynthesis (DTS) images. Multiple regression models were constructed to examine the relationship between creep properties and bone density and DTS image textural parameters. For the standard clinical imaging configuration, models including DTS derived image textural parameters alone were generally more explanatory (adjusted R(2): 0.14-0.68) than those with bone density parameters forced in the models (adjusted R(2): 0.17-0.61). Metrics of textural heterogeneity and anisotropy presented as the most explanatory imaging markers for creep deformation and recovery from creep. These metrics of image texture may help provide, independent from bone mass, important clinically measurable indicators of the time dependent deformation of human vertebrae.

Orthopedics/Bone and Joint Center
Singleton IM, **Garfinkel RJ**, Malone JB, Temkit MH, and Belthur MV. Perceived Physician Empathy in Pediatric Orthopedics: A Cross-Sectional Study. *J Patient Exp* 2022; 9. PMID: 35450088. Full Text

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Empathy is the cornerstone of the patient-physician relationship and is consistently ranked by patients as one of the most important factors in the quality of their care. In this paper we examine the degree to which perceived physician empathy is associated with the characteristics of the caregiver (parent or legal guardian) and physician in pediatric orthopedic surgery. This was a cross-sectional survey study of 200 English-speaking caregivers of pediatric patients at a large children's hospital. The Consultation and Relational Empathy (CARE) Measure was used to measure perceived physician empathy. Only if the caregiver felt carefully listened to by the physician (p-value < 0.001), and if the physician showed respect for what the caregiver had to say (p-value = 0.007) were statistically significant and positively associated with perceived physician empathy. The most significant determinant of perceived physician empathy is whether the caregiver felt listened to during the encounter. Other factors such as caregiver demographics, health literacy, self-rated mental health, wait time, and time spent with the physician do not significantly affect perceived physician empathy.

Otolaryngology – Head and Neck Surgery
DiPonio A, Sargent E, and **McClain K**. Sudden Onset and Unremitting Vertigo in a Middle-aged Woman. *JAMA Otolaryngol Head Neck Surg* 2022; Epub ahead of print. PMID: 35446367. Full Text

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Otolaryngology – Head and Neck Surgery
Lyons AB, **Ozog DM**, **Lim HW**, **Viola K**, **Tang A**, and **Jones LR**. The Detroit Keloid Scale: A Validated Tool for Rating Keloids. *Facial Plast Surg Aesthet Med* 2022; Epub ahead of print. PMID: 35394356. Full Text

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Background: Comparing keloid treatment modalities and assessing response to treatments may be predicted by a better classification system. Objectives: To develop and validate the Detroit Keloid Scale

(DKS), a standardized method of keloid assessment. Methods: Forty-seven physicians were polled to develop the DKS. The scale was validated in 52 patients against the Vancouver Scar Scale (VSS), Patient and Observer Scar Assessment Scale (POSAS), and Dermatology Life Quality Index (DLQI). Results: The inter-rater reliability was "substantial" for observer DKS and only "moderate" for VSS and observer POSAS (intraclass correlation coefficient were 0.80, 0.60, and 0.47, respectively). Pearson's correlation indicated "moderate" association between observer DKS with observer POSAS ($\rho = 0.56$, $p < 0.001$) and "substantial" relationship between observer DKS and VSS ($\rho = 0.63$, $p < 0.001$). Pearson's correlation indicated "moderate" association between patient portion of DKS and patient portion of POSAS and patient portion of the DKS and DLQI (0.61 and 0.60, respectively, $p < 0.05$). DKS total score consistently showed significant "substantial" relationship with POSAS total score ($\rho = 0.65$, $p < 0.001$). Conclusions: The DKS offers a validated keloid-specific outcome measure for comparing keloid treatments.

Otolaryngology – Head and Neck Surgery

Slijepcevic AA, Young G, Shinn J, Cannady SB, Hanasono M, Old M, **Grewal JS**, **Ghanem T**, Ducic Y, Curry JM, and Wax MK. Success and Outcomes Following a Second Salvage Attempt for Free Flap Compromise in Patients Undergoing Head and Neck Reconstruction. *JAMA Otolaryngol Head Neck Surg* 2022; Epub ahead of print. PMID: 35476871. Full Text

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Department of Otolaryngology-Head & Neck Surgery, College of Medicine, The Ohio State University, Columbus.
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IMPORTANCE: Incidence of perioperative free flap compromise is low, with successful salvage in up to 70%. When the flap is compromised a second time, the value of intervening is unknown. OBJECTIVE: To assess the outcomes of a second revascularization attempt for compromised free flaps. DESIGN, SETTING, AND PARTICIPANTS: This multicenter retrospective medical record review included patients undergoing head and neck reconstruction with free flaps at 6 US medical centers from January 1, 2000, through December 30, 2020. Patients were 18 years or older with a history of head and neck defects from cancer, osteoradionecrosis, or other wounds. Of 3510 flaps identified, 79 were successfully salvaged once, became compromised a second time, and underwent attempted salvage. MAIN OUTCOME AND MEASURE: Flaps with a history of initial compromise and successful revascularization demonstrating second episodes of compromise followed by second salvage attempts. RESULTS: A total of 79 patients (mean age, 64 years; 61 [77%] men) were included in the analysis. Of the 79 flaps undergoing second salvage attempts, 24 (30%) survived while 55 (70%) demonstrated necrosis. Arterial or venous thrombectomy was performed in 17 of the 24 (71%) flaps that survived and 23 of the 55 (42%) flaps demonstrating necrosis (odds ratio, 3.38; 95% CI, 1.21-9.47). When venous compromise was encountered, changing the anastomotic vein was associated with decreased survival compared with not changing the vein (29 of 55 [53%] flaps vs 10 of 24 [42%] flaps); vein revision to an alternative branch was completed in 1 of the 24 (4%) flaps that survived and 19 of the 55 (35%) flaps with necrosis (odds ratio, 0.08; 95% CI, 0.00-0.60). Factors that were not associated with flap survival following second salvage attempts included flap type, cause of flap failure, postoperative complications, patient comorbidities, and heparin administration after second salvage. CONCLUSIONS AND RELEVANCE: In this cohort study, second salvage was successful in 30% of free flaps. Flaps that underwent arterial or venous thrombectomy demonstrated better survival, while vein revision to neighboring branch veins was associated with worse flap outcomes.

Otolaryngology – Head and Neck Surgery

Ward MC, Koyfman SA, Bakst RL, Margalit DN, Beadle BM, Beitler JJ, **Chang SS**, Cooper JS, Galloway TJ, Ridge JA, Robbins JR, Sacco AG, Tsai CJ, Yom SS, and Siddiqui F. Retreatment of Recurrent or Second Primary Head and Neck Cancer After Prior Radiation: Executive Summary of the American Radium Society® (ARS) Appropriate Use Criteria (AUC): Expert Panel on Radiation Oncology - Head and Neck Cancer. *Int J Radiat Oncol Biol Phys* 2022; Epub ahead of print. PMID: 35398456. Full Text

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Dana-Farber/Brigham & Women's Cancer Center, Harvard Medical School, Boston, MA.
Stanford University School of Medicine, Palo Alto, CA.
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Fox Chase Cancer Center, Philadelphia, PA.
University of Arizona College of Medicine Tucson, Tucson, AZ.
University of California San Diego Moores Cancer Center, La Jolla, CA.
Memorial Sloan Kettering Cancer Center, New York, NY.
University of California San Francisco, San Francisco, CA.

BACKGROUND: Re-treatment of recurrent or second primary head and neck cancers occurring in a previously irradiated field is complex. Few guidelines exist to support practice. METHODS: We performed an updated literature search of peer-reviewed journals in a systematic fashion. Search terms, key questions, and associated clinical case variants were formed by panel consensus. The literature search informed the committee during a blinded vote on the appropriateness of treatment options via the modified Delphi method. RESULTS: The final number of citations retained for review was 274. These informed five key questions, which focused on patient selection, adjuvant re-irradiation, definitive re-irradiation, stereotactic body radiation (SBRT), and re-irradiation to treat non-squamous cancer. Results of the consensus voting are presented along with discussion of the most current evidence. CONCLUSIONS: This provides updated evidence-based recommendations and guidelines for the re-treatment of recurrent or second primary cancer of the head and neck.

Pathology and Laboratory Medicine

Hayes T, Cunningham M, and Trepanier A. Investigating factors that influence genetic counselors' decisions to refer patients to mental health providers. *J Genet Couns* 2022; Epub ahead of print. PMID: 35460529. Full Text

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Genetic counselors (GC) serve patients who are often in distress at the time of their consultation. GC competency includes providing short-term, client-centered counseling, while using community resources, such as mental health providers (MHPs), for psychosocial support. The purpose of this study was to assess the mental health referral practices of GCs; specifically, the rate of referrals, factors influencing a GC's decision to refer, and barriers to referrals. GCs working in direct patient care for at least one year were recruited to take a novel 27 question survey created based on the results of a previous qualitative study. A link to the web-based survey was distributed through the National Society of Genetic Counselors Student Research Program and American Board of Genetic Counselors by email. A total of 144 individuals opened the survey for an estimated response rate of 3%. A majority of respondents (54.3%) reported they assess a patient's need for a mental health referral at least half of the time. The mean number of referrals made in the past 12 months was 5.13. After post-hoc analyses, there were no differences in referral rates between specialties. Common referral indications included patient history of

mental illness, distress about having a genetic condition, and limited social support. Common barriers to referral were financial or insurance related, patient receptiveness, and the patient not perceiving a benefit. GCs felt that providing psychosocial support is within their scope of practice, but that MHPs are better equipped to manage long-term needs and those related to a mental health condition. This study provides insight into how GCs decide when they can manage patient distress, circumstances that prompt a referral to MHPs, and barriers. Recognizing common referral indications and barriers may lead to better strategies for connecting patients with such services.

Pathology and Laboratory Medicine

Vijayanarayanan A, **Wlosinski L**, **El-Bashir J**, **Galusca D**, **Nagai S**, **Yoshida A**, **Abouljoud MS**, and **Otrock ZK**. Lack of alloimmunization to the D antigen in D-negative orthotopic liver transplant recipients receiving D-positive red blood cells perioperatively. *Vox Sang* 2022; Epub ahead of print. PMID: 35393659. Full Text

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BACKGROUND AND OBJECTIVES: D-negative patients undergoing orthotopic liver transplantation (OLT) might require a large number of red blood cell (RBC) units, which can impact the inventory of D-negative blood. The blood bank might need to supply these patients with D-positive RBCs because of inventory constraints. This study evaluates the prevalence of anti-D formation in D-negative OLT patients who received D-positive RBCs perioperatively, as this will assist in successful patient blood management. MATERIALS AND METHODS: This was a retrospective study performed at a single academic medical centre. Electronic medical records for all 1052 consecutive patients who underwent OLT from January 2007 through December 2017 were reviewed. D-negative patients who were transfused perioperatively with D-positive RBCs and had antibody screening at least 30 days after transfusion were included. RESULTS: Of a total of 155 D-negative patients, 23 (14.8%) received D-positive RBCs perioperatively. Seventeen patients were included in the study. The median age was 54 years (range 36-67 years); 13 (76.5%) were male. The median number of D-positive RBC units transfused perioperatively was 7 (range 1-66 units). There was no evidence of D alloimmunization in any patient after a median serologic follow-up of 49.5 months (range 31 days to 127.7 months). The average number of antibody screening post OLT was 7.29. CONCLUSION: Our study showed that transfusion of D-positive RBCs in D-negative OLT recipients is a safe and acceptable practice in the setting of immunosuppression. This practice allows the conservation of D-negative RBC inventory.

Pediatrics

Cassidy-Bushrow AE, **Sitarik AR**, **Johnson CC**, **Johnson-Hooper TM**, **Kassem Z**, **Levin AM**, Lynch SV, Ownby DR, **Phillips JM**, Yong GJM, **Wegienka G**, and **Straughen JK**. Early-life gut microbiota and attention deficit hyperactivity disorder in preadolescents. *Pediatr Res* 2022; Epub ahead of print. PMID: 35440767. Request Article

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BACKGROUND: Gut microbiota maturation coincides with nervous system development. Cross-sectional data suggest gut microbiota of individuals with and without attention deficit hyperactivity disorder (ADHD) differs. We hypothesized that infant gut microbiota composition is associated with later ADHD development in our on-going birth cohort study, WHEALS. METHODS: Gut microbiota was profiled using 16S ribosomal RNA and the internal transcribed spacer region 2 (ITS2) sequencing in stool samples from 1 month and 6 months of age. ADHD was defined by parent-reported or medical record doctor diagnosis at age 10. RESULTS: A total of 314 children had gut microbiota and ADHD data; 59 (18.8%) had ADHD. After covariate adjustment, bacterial phylogenetic diversity ($p = 0.017$) and bacterial composition (unweighted UniFrac $p = 0.006$, $R(2) = 0.9\%$) at age 6 months were associated with development of ADHD. At 1 month of age, 18 bacterial and 3 fungal OTUs were associated with ADHD development. At 6 months of age, 51 bacterial OTUs were associated with ADHD; 14 of the order Lactobacillales. Three fungal OTUs at 6 months of age were associated with ADHD development. CONCLUSIONS: Infant gut microbiota is associated with ADHD development in pre-adolescents. Further studies replicating these findings and evaluating potential mechanisms of the association are needed. IMPACT: Cross-sectional studies suggest that the gut microbiota of individuals with and without ADHD differs. We found evidence that the bacterial gut microbiota of infants at 1 month and 6 months of age is associated with ADHD at age 10 years. We also found novel evidence that the fungal gut microbiota in infancy (ages 1 month and 6 months) is associated with ADHD at age 10 years. This study addresses a gap in the literature in providing longitudinal evidence for an association of the infant gut microbiota with later ADHD development.

Pediatrics

Ko ER, Henao R, Frankey K, Petzold EA, Isner PD, **Jaehne AK**, **Allen N**, **Gardner-Gray J**, **Hurst G**, **Pflaum-Carlson J**, **Jayaprakash N**, **Rivers EP**, Wang H, Ugalde I, Amanullah S, Mercurio L, Chun TH, May L, Hickey RW, Lazarus JE, Gunaratne SH, Pallin DJ, Jambaulikar G, Huckins DS, Ampofo K, Jhaveri R, Jiang Y, Komarow L, Evans SR, Ginsburg GS, Tillekeratne LG, McClain MT, Burke TW, Woods CW, and Tsalik EL. Prospective Validation of a Rapid Host Gene Expression Test to Discriminate Bacterial From Viral Respiratory Infection. *JAMA Netw Open* 2022; 5(4):e227299. PMID: 35420659. Full Text

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Emergency Medicine Service, Durham Veterans Affairs Health Care System, Durham, North Carolina.

IMPORTANCE: Bacterial and viral causes of acute respiratory illness (ARI) are difficult to clinically distinguish, resulting in the inappropriate use of antibacterial therapy. The use of a host gene expression-based test that is able to discriminate bacterial from viral infection in less than 1 hour may improve care and antimicrobial stewardship. OBJECTIVE: To validate the host response bacterial/viral (HR-B/V) test and assess its ability to accurately differentiate bacterial from viral infection among patients with ARI. DESIGN, SETTING, AND PARTICIPANTS: This prospective multicenter diagnostic study enrolled 755 children and adults with febrile ARI of 7 or fewer days' duration from 10 US emergency departments. Participants were enrolled from October 3, 2014, to September 1, 2019, followed by additional enrollment of patients with COVID-19 from March 20 to December 3, 2020. Clinical adjudication of enrolled participants identified 616 individuals as having bacterial or viral infection. The primary analysis cohort included 334 participants with high-confidence reference adjudications (based on adjudicator concordance and the presence of an identified pathogen confirmed by microbiological testing). A secondary analysis of the entire cohort of 616 participants included cases with low-confidence reference adjudications (based on adjudicator discordance or the absence of an identified pathogen in microbiological testing). Thirty-three participants with COVID-19 were included post hoc. INTERVENTIONS: The HR-B/V test quantified the expression of 45 host messenger RNAs in approximately 45 minutes to derive a probability of bacterial infection. MAIN OUTCOMES AND MEASURES: Performance characteristics for the HR-B/V test compared with clinical adjudication were reported as either bacterial or viral infection or categorized into 4 likelihood groups (viral very likely [probability score <0.19], viral likely [probability score of 0.19-0.40], bacterial likely [probability score of 0.41-0.73], and bacterial very likely [probability score >0.73]) and compared with procalcitonin measurement. RESULTS: Among 755 enrolled participants, the median age was 26 years (IQR, 16-52 years); 360 participants (47.7%) were female, and 395 (52.3%) were male. A total of 13 participants (1.7%) were American Indian, 13 (1.7%) were Asian, 368 (48.7%) were Black, 131 (17.4%) were Hispanic, 3 (0.4%) were Native Hawaiian or Pacific Islander, 297 (39.3%) were White, and 60 (7.9%) were of unspecified race and/or ethnicity. In the primary analysis involving 334 participants, the HR-B/V test had sensitivity of 89.8% (95% CI, 77.8%-96.2%), specificity of 82.1% (95% CI, 77.4%-86.6%), and a negative predictive value (NPV) of 97.9% (95% CI, 95.3%-99.1%) for bacterial infection. In comparison, the sensitivity of procalcitonin measurement was 28.6% (95% CI, 16.2%-40.9%; P < .001), the specificity was 87.0% (95% CI, 82.7%-90.7%; P = .006), and the NPV was 87.6% (95% CI, 85.5%-89.5%; P < .001). When stratified into likelihood groups, the HR-B/V test had an NPV of 98.9% (95% CI, 96.1%-100%) for bacterial infection in the viral very likely group and a positive predictive value of 63.4% (95% CI, 47.2%-77.9%) for bacterial infection in the bacterial very likely group. The HR-B/V test correctly identified 30 of 33 participants (90.9%) with acute COVID-19 as having a viral infection. CONCLUSIONS AND RELEVANCE: In this study, the HR-B/V test accurately discriminated bacterial from viral infection among patients with febrile ARI and was superior to procalcitonin measurement. The findings suggest that an accurate point-of-need host response test with high NPV may offer an opportunity to improve antibiotic stewardship and patient outcomes.

Pharmacy

Amerine LB, Pasour T, Johnson SJ, Higgins JP, **Pyle J**, and Gehring C. Evaluation of density variations to determine impact on sterile compounding. *Am J Health Syst Pharm* 2022; 79(8):689-695. PMID: 34940808. Full Text

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PURPOSE: To determine the density variation between (1) the measured density and manually calculated density, (2) density variation of different lots, and (3) density variation of different drug manufacturers in order to support institutions using gravimetric compounding methods. SUMMARY: Seventeen sterile injectable ingredient (drug) vials frequently used to make compounded sterile products (CSPs) were identified based on the ability to ensure that for each drug there were vials produced by 2 different manufacturers and 2 lots produced by the same manufacturer. Each drug's density was measured using a density meter and by manual calculation using the institution's density formula. Density differences were compared between the 2 different methods. Overall, the average drug density difference between the measured versus calculated density was determined to be 0.022. Further analysis revealed the average difference between the different lot numbers of the same manufacturers was 0.005 for the nonhazardous drugs and 0.0001 for the hazardous drugs. The average difference between the different manufacturers of the same drug was determined to be 0.008 for the nonhazardous drugs and 0.001 for hazardous drugs. CONCLUSION: No clinically meaningful difference exists when manually calculating a drug's density compared to measuring a drug's density using a density meter. In addition, there does not appear to be a sizeable density variation between the same drugs in separate lots or produced by different manufacturers.

Pharmacy

Chung D, **Efta J**, **Brunsman A**, **Gabriel J**, **Johnson J**, **Martz C**, **Stuart M**, **Kenney R**, and **Smith Z**. Evaluation of pharmacist time dedicated to vancomycin dosing in adult patients using a 24-hour AUC nomogram or trough monitoring approach: A time motion study. *Am J Health Syst Pharm* 2022; Epub ahead of print. PMID: 35403665. Full Text

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DISCLAIMER: In an effort to expedite the publication of articles, AJHP is posting manuscripts online as soon as possible after acceptance. Accepted manuscripts have been peer-reviewed and copyedited, but are posted online before technical formatting and author proofing. These manuscripts are not the final version of record and will be replaced with the final article (formatted per AJHP style and proofed by the authors) at a later time. PURPOSE: Evidence-based guideline recommendations for vancomycin dosing recently shifted from a trough-based strategy to an area under the curve (AUC) approach. While several AUC dosing methods exist, the optimal approach has not been determined. Literature characterizing time requirements for various vancomycin dosing strategies remains limited. METHODS: A time and motion study was conducted to measure the time spent by clinical pharmacists dosing vancomycin using an AUC nomogram. Pharmacists who dosed and monitored vancomycin for adult patients on the general medical ward (GMW) or intensive care unit (ICU) of a large academic medical center consented to study participation. Vulnerable patients and vancomycin orders for surgical infection prophylaxis were excluded. The primary outcome was the median amount of time clinical pharmacists dedicated to vancomycin-related clinical activities during an 8-hour weekday shift. Secondary outcomes included the proportion of patients prescribed vancomycin at the beginning of each shift and factors contributing to greater than average time spent on vancomycin-related responsibilities. RESULTS: Seven clinical pharmacists collected data on 178 vancomycin orders. The estimated amount of time a clinical pharmacist spent on daily vancomycin responsibilities averaged 10.45 minutes (interquartile range [IQR], 6.94-15.8 minutes). The overall median time requirement per vancomycin assessment was 3.45 minutes (IQR, 1.95-6.7 minutes). The only factor independently associated with prolonged dosing time was follow-up dosing from a previous day. CONCLUSION: The study elucidated time requirements associated with an AUC nomogram-based vancomycin dosing approach. This data could be used to compare time requirements associated with other existing vancomycin dosing strategies, which may help healthcare systems determine the optimal AUC dosing method for their specific practice model.

Pharmacy

Soreide KK, **Solomon O**, **Farhat NM**, **Kolander S**, **Gottschall T**, **George DL**, **Szandzik EG**, **Kalus JS**, and **Thomas E**. Pharmacist hypertension management using an electronic health record-based approach. *Am J Manag Care* 2022; 28(4):e121-e125. PMID: 35420749. Full Text

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OBJECTIVES: To evaluate the impact of the chronic medication optimization pharmacist (CMOP) program on blood pressure (BP) control and time to goal compared with usual care in the ambulatory care setting. STUDY DESIGN: This was a retrospective cohort study that included patients from June 2018 to June 2020 who were seen in an ambulatory care clinic for hypertension management. METHODS: Patients aged 18 to 80 years were divided into 2 cohorts based on hypertension management by usual care or the CMOP program. Patients were enrolled in the CMOP program either by referral or identification via a data analytics tool. The primary outcome assessed the proportion of patients within BP goal (< 140/90 mm Hg) at 3 months. Secondary outcomes assessed the proportion of patients within goal at 6 months, time and number of visits to goal, and adherence (CMOP cohort only). RESULTS: The primary end point demonstrated a greater proportion of patients within goal in the CMOP cohort compared with usual care (69.4% vs 42.3%; P < .001). The CMOP cohort also displayed a greater proportion of patients achieving goal within 6 months (75.7% vs 60.4%; P = .014) and faster time to goal (42.99 vs 63.12 days; P = .002), but more visits (1.67 vs 1.18; P = .001). Lastly, adherence improved from 50.4% to 72.1% in the patients with a documented adherence assessment in the pharmacist group (P = .03). CONCLUSIONS: The pharmacist intervention improved BP control in a primarily African American patient population compared with usual care. Future studies should assess the sustainability of this intervention.

Public Health Sciences

Boakye EA, Polednik KM, Deshields TL, Sharma A, Molina Y, Schapira L, Barnes JM, and Osazuwa-Peters N. Emotional distress among survivors of Adolescent and Young Adult cancer or adult cancer. *Ann Epidemiol* 2022; Epub ahead of print. PMID: 35405345. Full Text

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Department of Radiation Oncology, Washington University School of Medicine in St. Louis, St. Louis, MO.
Department of Head and Neck Surgery & Communication Sciences, Duke University School of Medicine, Durham, NC; Department of Population Health Sciences, Duke University School of Medicine, Durham, NC.

PURPOSE: We examined emotional distress in cancer survivors diagnosed as adolescents or young adults (AYAs) vs. cancer survivors diagnosed as middle/older adults and vs. the general population without a history of cancer. METHODS: Using the 2014-2017 National Health Interview Surveys, 2,500 AYA survivors (initial cancer diagnosed between aged 15-39 years) were matched with 2,500 middle/older adult survivors (initial cancer diagnosed at aged ≥40 years) as well as with 1,609 from the general population without a history of cancer. Multinomial logistic regression models estimated the risk of emotional distress (measured using the validated Kessler distress (K6) scale) in the study population (AYA vs. middle/older adult cancer survivors and vs. general population without cancer), adjusting for known covariates. RESULTS: Emotional distress was more prevalent among AYAs (average age 52.8 ± 19.1 years) than middle/older adult (average age 67.4 ± 14.0 years) cancer survivors (moderate: 25.5%

vs. 19.4%; and severe: 6.4% vs. 4.4% [P<.0001]); however, there was no difference in emotional distress between AYA cancer survivors (moderate: 26.8% and severe: 7.5%) vs. general population without cancer (moderate: 23.7% and severe: 6.2%). In the multivariable multinomial analyses, AYA cancer survivors had higher risk of reporting emotional distress (aRR = 1.45; 95% CI 1.13, 1.86) than middle/older adult cancer survivors. CONCLUSION: Psychosocial support may be especially needed for cancer survivors diagnosed as adolescents or young adults to mitigate adverse psychosocial outcomes.

Public Health Sciences

Cassidy-Bushrow AE, **Sitarik AR**, **Johnson CC**, **Johnson-Hooper TM**, **Kassem Z**, **Levin AM**, Lynch SV, Ownby DR, **Phillips JM**, Yong GJM, **Wegienka G**, and **Straughen JK**. Early-life gut microbiota and attention deficit hyperactivity disorder in preadolescents. *Pediatr Res* 2022; Epub ahead of print. PMID: 35440767. Request Article

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Department of Psychiatry and Behavioral Health Services, Division of Neuropsychology, Henry Ford Hospital, Detroit, MI, USA.

BACKGROUND: Gut microbiota maturation coincides with nervous system development. Cross-sectional data suggest gut microbiota of individuals with and without attention deficit hyperactivity disorder (ADHD) differs. We hypothesized that infant gut microbiota composition is associated with later ADHD development in our on-going birth cohort study, WHEALS. METHODS: Gut microbiota was profiled using 16S ribosomal RNA and the internal transcribed spacer region 2 (ITS2) sequencing in stool samples from 1 month and 6 months of age. ADHD was defined by parent-reported or medical record doctor diagnosis at age 10. RESULTS: A total of 314 children had gut microbiota and ADHD data; 59 (18.8%) had ADHD. After covariate adjustment, bacterial phylogenetic diversity (p = 0.017) and bacterial composition (unweighted UniFrac p = 0.006, R(2) = 0.9%) at age 6 months were associated with development of ADHD. At 1 month of age, 18 bacterial and 3 fungal OTUs were associated with ADHD development. At 6 months of age, 51 bacterial OTUs were associated with ADHD; 14 of the order Lactobacillales. Three fungal OTUs at 6 months of age were associated with ADHD development. CONCLUSIONS: Infant gut microbiota is associated with ADHD development in pre-adolescents. Further studies replicating these findings and evaluating potential mechanisms of the association are needed. IMPACT: Cross-sectional studies suggest that the gut microbiota of individuals with and without ADHD differs. We found evidence that the bacterial gut microbiota of infants at 1 month and 6 months of age is associated with ADHD at age 10 years. We also found novel evidence that the fungal gut microbiota in infancy (ages 1 month and 6 months) is associated with ADHD at age 10 years. This study addresses a gap in the literature in providing longitudinal evidence for an association of the infant gut microbiota with later ADHD development.

Public Health Sciences

Dumancas G, and **Adrianto I**. A stacked regression ensemble approach for the quantitative determination of biomass feedstock compositions using near infrared spectroscopy. *Spectrochim Acta A Mol Biomol Spectrosc* 2022; 276:121231. PMID: 35427923. Request Article

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Rapid, robust, and accurate biomass compositional analyses are required in the bioenergy industry to accurately determine the chemical composition of biomass feedstocks. A stacked regression ensemble approach using near infrared spectroscopic method was developed for the quantitative determination of glucan, xylan, lignin, ash, and extract in biomass feedstocks. A comprehensive comparison of the performance of various machine learning techniques including support vector regression (linear and radial), least absolute shrinkage and selection operator (LASSO), ridge regression, elastic net, partial least squares, random forests, recursive partitioning and regression trees, gradient boosting, and gaussian process regression was assessed in the training set data (n = 188). The predictive performance of the aforementioned machine learning approaches was then compared with stacked regression, an ensemble learning algorithm which collates the performance of the abovementioned machine learning regression techniques. Results show that the stacked regression primarily outperformed other machine learning techniques (Root mean square error of prediction (RMSEP)(average)=1.660%wt,R(2)=0.907) across all five constituents in the validation set data (n = 81). Further results also show that the RMSEP of the stacked ensemble technique is significantly different than that of the partial least squares (PLS) approach in predicting glucan, ash, lignin, and extract components in biomass samples. The stacked ensemble learning approach offers an alternative method for a more accurate prediction of biomass compositions than the traditional PLS technique.

Public Health Sciences

Franca MC, Boyer VE, Gerend MA, Lee M, Whittington KD, McKinney SL, Collins SK, McKinnies RC, and **Adjei Boakye E**. College Students' Awareness of the Link Between Human Papillomavirus (HPV) and HPV-Associated Cancers. *J Cancer Educ* 2022; Epub ahead of print. PMID: 35459979. Request Article

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We describe the level of awareness of the link between HPV and HPV-associated cancers and identify demographic and lifestyle factors associated with awareness. This was a cross-sectional study of college students (n = 862) at a public Midwestern university conducted between February and May 2021. The outcomes were student's awareness-accessed by asking students if they knew whether HPV was causally link with anal, cervical, vaginal, oropharyngeal, vulvar, and penile cancers. Logistic regression models estimated the association between sociodemographic and sexual behavior and awareness of the link between HPV and HPV-associated cancers. Approximately 70% were aware that HPV causes cervical, 53% were aware HPV causes vaginal, 40% were aware HPV causes vulvar cancers, 39% were aware HPV causes oropharyngeal, 38% were aware HPV causes penile, and 34% were aware HPV causes anal cancers. In multivariable analyses, men were less likely to be aware that HPV causes vaginal (aOR = 0.42, 95% CI 0.30-0.59) or vulvar cancers (aOR = 0.54, 95% CI 0.38-0.77) compared to women. Compared with sexually naïve students, those who had have oral and vaginal sex were more likely to be aware that HPV causes anal (aOR = 1.98, 95% CI 1.17-3.34), penile (aOR = 1.82, 95% CI 1.11-2.97), vaginal (aOR = 1.81, 95% CI 1.14-2.88), or vulvar (aOR = 2.05, 95% CI 1.24-3.40) cancers. Awareness of the link between HPV and HPV-associated cancers was low, except cervical. This

underscores the need for more tailored interventions to increase knowledge about HPV and its association with cancer. Increasing students' levels of awareness may impact HPV vaccine uptake.

Public Health Sciences
Jehangir Q, Lee Y, **Latack K**, **Poisson L**, **Wang DD**, **Song S**, Apala DR, Patel K, Halabi AR, Krishnamoorthy G, and Sule AA. Incidence, Mortality, and Imaging Outcomes of Atrial Arrhythmias in COVID-19. *Am J Cardiol* 2022; Epub ahead of print. PMID: 35382929. Full Text

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Atrial arrhythmias (AAs) are common in hospitalized patients with COVID-19; however, it remains uncertain if AAs are a poor prognostic factor in SARS-CoV-2 infection. In this retrospective cohort study from 2014 to 2021, we report in-hospital mortality in patients with new-onset AA and history of AA. The incidence of new-onset congestive heart failure (CHF), hospital length of stay and readmission rate, intensive care unit admission, arterial and venous thromboembolism, and imaging outcomes were also analyzed. We further compared the clinical outcomes with a propensity-matched influenza cohort. Generalized linear regression was performed to identify the association of AA with mortality and other outcomes, relative to those without an AA diagnosis. Predictors of new-onset AA were also modeled. A total of 6,927 patients with COVID-19 were included (626 with new-onset AA, 779 with history of AA). We found that history of AA (adjusted relative risk [aRR] 1.38, confidence interval [CI], 1.11 to 1.71, p = 0.003) and new-onset AA (aRR 2.02, 95% CI 1.68 to 2.43, p <0.001) were independent predictors of in-hospital mortality. The incidence of new-onset CHF was 6.3% in history of AA (odds ratio 1.91, 95% CI 1.30 to 2.79, p <0.001) and 11.3% in new-onset AA (odds ratio 4.01, 95% CI 3.00 to 5.35, p <0.001). New-onset AA was shown to be associated with worse clinical outcomes within the propensity-matched COVID-19 and influenza cohorts. The risk of new-onset AA was higher in patients with COVID-19 than influenza (aRR 2.02, 95% CI 1.76 to 2.32, p <0.0001), but mortality associated with new-onset AA was higher in influenza (aRR 12.58, 95% CI 4.27 to 37.06, p <0.0001) than COVID-19 (aRR 1.86, 95% CI 1.55 to 2.22, p <0.0001). In a subset of the patients with COVID-19 for which echocardiographic data were captured, abnormalities were common, including valvular abnormalities (40.9%), right ventricular dilation (29.6%), and elevated pulmonary artery systolic pressure (16.5%); although there was no evidence of a difference in incidence among the 3 groups. In conclusion, new-onset AAs are associated with poor clinical outcomes in patients with COVID-19.

Public Health Sciences
Jehangir Q, Lee Y, Latack K, **Poisson L**, **Wang DD**, **Song S**, Apala DR, Patel K, Halabi AR, Krishnamoorthy G, and Sule AA. Data of atrial arrhythmias in hospitalized COVID-19 and influenza patients. *Data Brief* 2022; 42:108177. PMID: 35449710. Full Text

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Atrial arrhythmias (AA) are common in hospitalized COVID-19 patients with limited data on their association with COVID-19 infection, clinical and imaging outcomes. In the related research article using retrospective research data from one quaternary care and five community hospitals, patients aged 18 years and above with positive SARS-CoV-2 polymerase chain reaction test were included. 6927 patients

met the inclusion criteria. The data in this article provides demographics, home medications, in-hospital events and COVID-19 treatments, multivariable generalized linear regression regression models using a log link with a Poisson distribution (multi-parameter regression [MPR]) to determine predictors of new-onset AA and mortality in COVID-19 patients, computerized tomography chest scan findings, echocardiographic findings, and International Classification of Diseases-Tenth Revision codes. The clinical outcomes were compared to a propensity-matched cohort of influenza patients. For influenza, data is reported on baseline demographics, comorbid conditions, and in-hospital events. Generalized linear regression models were built for COVID-19 patients using demographic characteristics, comorbid conditions, and presenting labs which were significantly different between the groups, and hypoxia in the emergency room. Statistical analysis was performed using R programming language (version 4, ggplot2 package). Multivariable generalized linear regression model showed that, relative to normal sinus rhythm, history of AA (adjusted relative risk [RR]: 1.38; 95% CI: 1.11-1.71; p = 0.003) and newly-detected AA (adjusted RR: 2.02 95% CI: 1.68-2.43; p < 0.001) were independently associated with higher in-hospital mortality. Age in increments of 10 years, male sex, White race, prior history of coronary artery disease, congestive heart failure, end-stage renal disease, presenting leukocytosis, hypermagnesemia, and hypomagnesemia were found to be independent predictors of new-onset AA in the MPR model. The dataset reported is related to the research article entitled "Incidence, Mortality, and Imaging Outcomes of Atrial Arrhythmias in COVID-19" [Jehangir et al. Incidence, Mortality, and Imaging Outcomes of Atrial Arrhythmias in COVID-19, American Journal of Cardiology] [1].

Public Health Sciences

Joseph CLM, **Tang A**, Chesla DW, Epstein MM, Pawloski PA, Stevens AB, Waring SC, **Ahmedani BK**, **Johnson CC**, and **Peltz-Rauchman CD**. Demographic differences in willingness to share electronic health records in the All of Us Research Program. *J Am Med Inform Assoc* 2022; Epub ahead of print. PMID: 35472083. Full Text

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OBJECTIVE: Participant willingness to share electronic health record (EHR) information is central to success of the National Institutes of Health All of Us Research Program (AoURP). We describe the demographic characteristics of participants who decline access to their EHR data. MATERIALS AND METHODS: We included participants enrolling in AoURP between June 6, 2017 and December 31, 2019 through the Trans-American Consortium for the Health Care Systems Research Network (TACH). TACH is a consortium of health care systems spanning 6 states, and an AoURP research partner. RESULTS: We analyzed data for 25852 participants (89.3% of those enrolled). Mean age = 52.0 years (SD 16.8), with 66.5% White, 18.7% Black/African American, 7.7% Hispanic, 32.5% female, and 76% with >a high school diploma. Overall, 2.3% of participants declined to share access to their EHR data (range across TACH sites = 1.3% to 3.5%). Younger age, female sex, and education >high school were significantly associated with decline to share EHR data, odds ratio (95% confidence interval) = 1.26 (1.19-1.33), 1.74 (1.42-2.14), and 2.44 (1.86-3.21), respectively. Results were similar when several sensitivity analyses were performed. DISCUSSION: AoURP seeks a dataset reflecting our nation's diversity in all aspects of participation. Those under-represented in biomedical research may be reluctant to share access to their EHR data. CONCLUSION: In our data, race and ethnicity were not independently related to participant decision to decline access to their EHR information. Results suggest that the value of the AoURP dataset is unlikely to be constrained by the size or the racial/ethnic composition of this subgroup.

Public Health Sciences

Lamerato L, James G, van Haalen H, Hedman K, Sloand JA, **Tang A**, Wittbrodt ET, and **Yee J**. Epidemiology and outcomes in patients with anemia of CKD not on dialysis from a large US healthcare system database: a retrospective observational study. *BMC Nephrol* 2022; 23(1):166. PMID: 35490226. Full Text

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BACKGROUND: Optimal management of anemia of chronic kidney disease (CKD) remains controversial. This retrospective study aimed to describe the epidemiology and selected clinical outcomes of anemia in patients with CKD in the US. METHODS: Data were extracted from Henry Ford Health System databases. Adults with stages 3a-5 CKD not on dialysis (estimated glomerular filtration rate < 60 mL/min/1.73m(2)) between January 1, 2013 and December 31, 2017 were identified. Patients on renal replacement therapy or with active cancer or bleeding were excluded. Patients were followed for ≥12 months until December 31, 2018. Outcomes included incidence rates per 100 person-years (PY) of anemia (hemoglobin < 10 g/dL), renal and major adverse cardiovascular events, and of bleeding and hospitalization outcomes. Adjusted Cox proportional hazards models identified factors associated with outcomes after 1 and 5 years. RESULTS: Among the study cohort (N = 50,701), prevalence of anemia at baseline was 23.0%. Treatments used by these patients included erythropoiesis-stimulating agents (4.1%), iron replacement (24.2%), and red blood cell transfusions (11.0%). Anemia incidence rates per 100 PY in patients without baseline anemia were 7.4 and 9.7 after 1 and 5 years, respectively. Baseline anemia was associated with increased risk of renal and major cardiovascular events, hospitalizations (all-cause and for bleeding), and transfusion requirements. Increasing CKD stage was associated with increased risk of incident anemia, renal and major adverse cardiovascular events, and hospitalizations. CONCLUSIONS: Anemia was a prevalent condition associated with adverse renal, cardiovascular, and bleeding/hospitalization outcomes in US patients with CKD. Anemia treatment was infrequent.

Public Health Sciences

Lyons A, **Narla S**, **Kohli I**, **Zubair R**, **Jacobsen G**, **Ceresnie M**, **Parks-Miller A**, and **Hamzavi I**. Safety and Efficacy of Intense Pulsed Light With Radiofrequency in United States Hidradenitis Suppurativa Patients. *J Drugs Dermatol* 2022; 21(4):430-432. PMID: 35389583. Full Text

The combination of intense pulsed light and radiofrequency has been described in German populations to be a noninvasive therapy option for patients with hidradenitis suppurativa, demonstrating significant improvements in the quality of life and reduction in number of inflammatory lesions. OBJECTIVE: To evaluate the efficacy and safety of combination intense pulsed light and radiofrequency therapy in patients with hidradenitis suppurativa in the United States. METHODS: A prospective split body was conducted in the United States on patients with bilateral hidradenitis suppurativa. Subjects received 3 passes of intense pulsed light and radiofrequency per treatment session to a single involved body region on a randomized side of the body at least 2 weeks apart over 9 to 10 treatment sessions. RESULTS:

When measured from baseline to final visit, the overall mean difference in Dermatology Life Quality Index was found to be statistically significant (-2.8, P=0.043, n = 9). Patients reported mild discomfort during therapy and no adverse events occurred during or after treatment sessions. CONCLUSIONS: Although statistically significant, the mean difference in Dermatology Life Quality Index in treated patients found in this study did not reach the minimal clinically important difference for inflammatory skin disease. J Drugs Dermatol. 2022;21(4):430-432. .doi:10.36849/JDD.6562.

Public Health Sciences
Lyons AB, **Ozog DM**, **Lim HW**, **Viola K**, **Tang A**, and **Jones LR**. The Detroit Keloid Scale: A Validated Tool for Rating Keloids. *Facial Plast Surg Aesthet Med* 2022; Epub ahead of print. PMID: 35394356. Full Text

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Background: Comparing keloid treatment modalities and assessing response to treatments may be predicted by a better classification system. Objectives: To develop and validate the Detroit Keloid Scale (DKS), a standardized method of keloid assessment. Methods: Forty-seven physicians were polled to develop the DKS. The scale was validated in 52 patients against the Vancouver Scar Scale (VSS), Patient and Observer Scar Assessment Scale (POSAS), and Dermatology Life Quality Index (DLQI). Results: The inter-rater reliability was "substantial" for observer DKS and only "moderate" for VSS and observer POSAS (intraclass correlation coefficient were 0.80, 0.60, and 0.47, respectively). Pearson's correlation indicated "moderate" association between observer DKS with observer POSAS ($\rho = 0.56$, $p < 0.001$) and "substantial" relationship between observer DKS and VSS ($\rho = 0.63$, $p < 0.001$). Pearson's correlation indicated "moderate" association between patient portion of DKS and patient portion of POSAS and patient portion of the DKS and DLQI (0.61 and 0.60, respectively, $p < 0.05$). DKS total score consistently showed significant "substantial" relationship with POSAS total score ($\rho = 0.65$, $p < 0.001$). Conclusions: The DKS offers a validated keloid-specific outcome measure for comparing keloid treatments.

Public Health Sciences
Oravec D, **Kim W**, **Flynn MJ**, and **Yeni YN**. The relationship of whole human vertebral body creep to bone density and texture via clinically available imaging modalities. *J Biomech* 2022; 135:111021. PMID: 35245836. Full Text

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Creep deformation of human vertebrae accumulates under physiological levels of load and is understood to contribute to the progression toward clinically observable vertebral fracture. However, little information is available in terms of clinically measurable predictors of creep behavior in human vertebrae. In this study, creep tests were performed on 22 human cadaveric T12 vertebrae (13 male, 9 female; age 41-90). Areal and volumetric bone density parameters were measured from the same specimens using dual x-ray absorptiometry and high resolution computed tomography. Image textural analyses (which probe the organization of image intensities within the cancellous bone in low resolution clinical imaging) were performed using digital tomosynthesis (DTS) images. Multiple regression models were constructed to examine the relationship between creep properties and bone density and DTS image textural parameters. For the standard clinical imaging configuration, models including DTS derived image textural parameters alone were generally more explanatory (adjusted R(2): 0.14-0.68) than those with bone density parameters forced in the models (adjusted R(2): 0.17-0.61). Metrics of textural heterogeneity and anisotropy presented as the most explanatory imaging markers for creep deformation and recovery from creep. These metrics of image texture may help provide, independent from bone mass, important clinically measurable indicators of the time dependent deformation of human vertebrae.

Public Health Sciences

Stefanou AJ, **Kalu RU**, **Tang A**, and **Reickert CA**. Bowel Preparation for Elective Hartmann Operation: Analysis of the National Surgical Quality Improvement Program Database. *Surg Infect (Larchmt)* 2022; Epub ahead of print. PMID: 35451876. Request Article

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Background: Use of pre-operative bowel preparation in colorectal resection has not been examined solely in patients who have had colorectal resection with primary colostomy (Hartmann procedure). We aimed to evaluate the association of bowel preparations with short-term outcomes after non-emergent Hartmann procedure. Patients and Methods: The National Surgical Quality Improvement Program Participant Use File colectomy database was queried for patients who had elective open or laparoscopic Hartmann operation. Patients were grouped by pre-operative bowel preparation: no bowel preparation, oral antibiotic agents, mechanical preparation, or both mechanical and oral antibiotic agent preparation (combined). Propensity analysis was performed, and outcomes were compared by type of pre-operative bowel preparation. The primary outcome was rate of any surgical site infection (SSI). Secondary outcomes included overall complication, re-operation, re-admission, Clostridioides difficile colitis, and length of stay. Results: Of the 4,331 records analyzed, 2,040 (47.1%) patients received no preparation, 251 (4.4%) received oral antibiotic preparation, 1,035 (23.9%) received mechanical bowel preparation, and 1,005 (23.2%) received combined oral antibiotic and mechanical bowel preparation. After propensity adjustment, rates of any SSI, overall complication, and length of hospital stay varied significantly between pre-operative bowel regimens ($p < 0.005$). The use of combined bowel preparation was associated with decreased rate of SSI, overall complication, and length of stay. No difference in rate of re-operation or post-operative Clostridioides difficile infection was observed based on bowel preparation. Conclusions: Compared with no pre-operative bowel preparation, any bowel preparation was associated with reduced rate of SSI, but not rate of re-operation or post-operative Clostridioides difficile infection.

Public Health Sciences

Xiang J, Durance PW, Griffes LC, **Chen Y**, and Bakshi RR. Measuring case severity: a novel tool for benchmarking and clinical documentation improvement. *BMC Health Serv Res* 2022; 22(1):513. PMID: 35428299. Full Text

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BACKGROUND: Severity of illness (SOI) is an All Patients Refined Diagnosis Related Groups (APR DRG) modifier based on comorbidity capture. Tracking SOI helps hospitals improve performance and resource distribution. Furthermore, benchmarking SOI plays a key role in Quality Improvement (QI) efforts such as Clinical Documentation Improvement (CDI) programs. The current SOI system highly relies on the 3 M APR DRG grouper that is updated annually, making it difficult to track severity longitudinally and benchmark against hospitals with different patient populations. Here, we describe an alternative SOI scoring system that is grouper-independent and that can be tracked longitudinally. METHODS: Admission data for 2019-2020 U.S. News and World Report Honor Roll facilities were downloaded from the Vizient Clinical Database and split into training and testing datasets. Elixhauser comorbidities, body systems developed from the Healthcare Cost and Utilization Project (HCUP), and ICD-10-CM complication and comorbidity (CC/MCC) indicators were selected as the predictors for orthogonal polynomial regression

models to predict patients' admission and discharge SOI. Receiver operating characteristic (ROC) and Precision-Recall (PR) analysis, and prediction accuracy were used to evaluate model performance. RESULTS: In the training dataset, the full model including both Elixhauser comorbidities and body system CC/MCC indicators had the highest ROC AUC, PR AUC and predication accuracy for both admission (ROC AUC: 92.9%; PR AUC: 91.0%; prediction accuracy: 85.4%) and discharge SOI (ROC AUC: 93.6%; PR AUC: 92.8%; prediction accuracy: 86.2%). The model including only body system CC/MCC indicators had similar performance for admission (ROC AUC: 92.4%; PR AUC: 90.4%; prediction accuracy: 84.8%) and discharge SOI (ROC AUC: 93.1%; PR AUC: 92.2%; prediction accuracy: 85.6%) as the full model. The model including only Elixhauser comorbidities exhibited the lowest performance. Similarly, in the validation dataset, the prediction accuracy was 86.2% for the full model, 85.6% for the body system model, and 79.3% for the comorbidity model. With fewer variables and less model complexity, the body system model was more efficient and was determined to be the optimal model. The probabilities generated from this model, named J_Score and J_Score_POA, successfully measured SOI and had practical applications in assessment of CDI performance. CONCLUSIONS: The J_Scores generated from the body system model have significant value in evaluating admission and discharge severity of illness. We believe that this new scoring system will provide a useful tool for healthcare institutions to benchmark patients' illness severity and augment Quality Improvement (QI) efforts.

Pulmonary and Critical Care Medicine

Beran A, Altorok N, Srour O, Malhas SE, Khokher W, Mhanna M, Ayesh H, Aladamat N, Abuhelwa Z, **Srour K**, Mahmood A, Altorok N, Taleb M, and Assaly R. Balanced Crystalloids versus Normal Saline in Adults with Sepsis: A Comprehensive Systematic Review and Meta-Analysis. *J Clin Med* 2022; 11(7). PMID: 35407578. Full Text

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The crystalloid fluid of choice in sepsis remains debatable. We aimed to perform a comprehensive meta-analysis to compare the effect of balanced crystalloids (BC) vs. normal saline (NS) in adults with sepsis. A systematic search of PubMed, EMBASE, and Web of Sciences databases through 22 January 2022, was performed for studies that compared BC vs. NS in adults with sepsis. Our outcomes included mortality and acute kidney injury (AKI), need for renal replacement therapy (RRT), and ICU length of stay (LOS). Pooled risk ratio (RR) and mean difference (MD) with the corresponding 95% confidence intervals (CIs) were obtained using a random-effect model. Fifteen studies involving 20,329 patients were included. Overall, BC showed a significant reduction in the overall mortality (RR 0.88, 95% CI 0.81-0.96), 28/30-day mortality (RR 0.87, 95% CI 0.79-0.95), and AKI (RR 0.85, 95% CI 0.77-0.93) but similar 90-day mortality (RR 0.96, 95% CI 0.90-1.03), need for RRT (RR 0.91, 95% CI 0.76-1.08), and ICU LOS (MD -0.25 days, 95% CI -3.44, 2.95), were observed between the two groups. However, subgroup analysis of randomized controlled trials (RCTs) showed no statistically significant differences in overall mortality (RR 0.92, 95% CI 0.82-1.02), AKI (RR 0.71, 95% CI 0.47-1.06), and need for RRT (RR 0.71, 95% CI 0.36-1.41). Our meta-analysis demonstrates that overall BC was associated with reduced mortality and AKI in sepsis compared to NS among patients with sepsis. However, subgroup analysis of RCTs showed no significant differences in both overall mortality and AKI between the groups. There was no significant difference in the need for RRT or ICU LOS between BC and NS. Pending further data, our study supports using BC over NS for fluid resuscitation in adults with sepsis. Further large-scale RCTs are necessary to validate our findings.

Radiation Oncology

Al-Jumayli M, **Brown SL**, **Chetty IJ**, Extermann M, and **Movsas B**. The Biological Process of Aging and the Impact of Ionizing Radiation. *Semin Radiat Oncol* 2022; 32(2):172-178. PMID: 35307120. Full Text

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Ionizing radiation is used to create models of accelerated aging because the processes of aging and radiation injury share common elements. In this chapter we review the biological processes of aging and the similarities and impact of ionizing radiation on those processes. The information draws on data from laboratory studies and from epidemiology studies of radiation exposure victims. The chapter reviews the effects of radiation on DNA, cells, and organs systems on aged adults. The science of aging and the effect of radiation on the aging process are areas of active research and our understanding is evolving.

Radiation Oncology

Amini A, Morris L, Ludmir EB, **Movsas B**, Jagsi R, and VanderWalde NA. Radiation Therapy in Older Adults With Cancer: A Critical Modality in Geriatric Oncology. *J Clin Oncol* 2022; Epub ahead of print. PMID: 35417248. Full Text

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Radiation therapy (RT) is a commonly used modality in the treatment of older adults with cancer, and RT represents an attractive oncologic treatment option, providing a noninvasive local therapy with limited systemic side effects. The Journal of Clinical Oncology (JCO) recently published a special series on Geriatric Oncology providing a comprehensive overview of multiple treatment modalities available to older adults with cancer. The purpose of this short review is to highlight the importance of RT in the treatment of older adults and encourage multidisciplinary participation in their care.

Radiation Oncology

Bharati S, Anjaly K, **Thoidingjam S**, and Tiku AB. Oil Red O based method for exosome labelling and detection. *Biochem Biophys Res Commun* 2022; 611:179-182. PMID: 35490657. Full Text

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With the realization of the role of exosomes in diseases, especially cancer, exosome research is gaining popularity in biomedical sciences. To understand exosome biology, their labelling and tracking studies are important. New and improved methods of exosome labelling for detection and tracking of exosomes need to be developed to harness their therapeutic and diagnostic potential. In this paper, we report a novel, simple and effective method of labelling and detecting exosomes using Oil Red O (ORO), a dye commonly used for lipid staining. Using ORO is a cost effective and easy approach with an intense red coloration of exosomes. Further, the issues faced with commonly used lipophilic dyes for exosome labelling like long-term persistence of dyes, aggregation and micelle formation of dyes, difficulty in distinguishing dye particles from labelled exosomes, and detection of large aggregates of dye or dye-exosome, are also resolved with ORO dye. This method shows good labelling efficacy with very sensitive detection and real-time tracking of the cellular uptake of exosomes.

Radiation Oncology

Bismack B, **Dolan J**, **Laugeman E**, **Gopal A**, **Wen N**, and **Chetty I**. Model refinement increases confidence levels and clinical agreement when commissioning a three-dimensional secondary dose calculation system. *J Appl Clin Med Phys* 2022;e13590. Epub ahead of print. PMID: 35389554. Full Text

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PURPOSE: Evaluate custom beam models for a second check dose calculation system using statistically verifiable passing criteria for film analysis, DVH, and 3D gamma metrics. METHODS: Custom beam models for nine linear accelerators for the Sun Nuclear Dose Calculator algorithm (SDC, Sun Nuclear) were evaluated using the AAPM-TG119 test suite (5 Intensity Modulated Radiation Therapy (IMRT) and 5 Volumetric Modulated Arc Therapy (VMAT) plans) and a set of clinical plans. Where deemed necessary, adjustments to Multileaf Collimator (MLC) parameters were made to improve results. Comparisons to the Analytic Anisotropic Algorithm (AAA), and gafchromic film measurements were performed. Confidence intervals were set to 95% per TG-119. Film gamma criteria were 3%/3 mm (conventional beams) or 3%/1 mm (Stereotactic Radiosurgery [SRS] beams). Dose distributions in solid water phantom were evaluated based on DVH metrics (e.g., D95, V20) and 3D gamma criteria (3%/3 mm or 3%/1 mm). Film passing rates, 3D gamma passing rates, and DVH metrics were reported for HD MLC machines and Millennium MLC Machines. RESULTS: For HD MLC machines, SDC gamma film agreement was 98.76% ± 2.30% (5.74% CL) for 6FFF/6srs (3%/1 mm), and 99.80% ± 0.32% (0.83% CL) for 6x (3%/3 mm). For Millennium MLC machines, film passing rates were 98.20% ± 3.14% (7.96% CL), 99.52% ± 1.14% (2.71% CL), and 99.69% ± 0.82% (1.91% CL) for 6FFF, 6x, and 10x, respectively. For SDC to AAA comparisons: HD MLC Linear Accelerators (LINACs); DVH point agreement was 0.97% ± 1.64% (4.18% CL) and 1.05% ± 2.12% (5.20% CL); 3D gamma agreement was 99.97% ± 0.14% (0.30% CL) and 100.00% ± 0.02% (0.05% CL), for 6FFF/6srs and 6x, respectively; Millennium MLC LINACs: DVH point agreement was 0.77% ± 2.40% (5.47% CL), 0.80% ± 3.40% (7.47% CL), and 0.07% ± 2.15% (4.30% CL); 3D gamma agreement was 99.97% ± 0.13% (0.29% CL), 99.97% ± 0.17% (0.36% CL), and 99.99% ± 0.06% (0.12% CL) for 6FFF, 6x, and 10x, respectively. CONCLUSION: SDC shows agreement well within TG119 CLs for film and redundant dose calculation comparisons with AAA. In some models (SRS), this was achieved using stricter criteria. TG119 plans can be used to help guide model adjustments and to establish clinical baselines for DVH and 3D gamma criteria.

Radiation Oncology

Bryant AK, Yin H, Schipper MJ, Paximadis PA, Boike TP, Bergsma DP, **Movsas B**, Dess RT, Mietzel MA, Kendrick R, Seferi M, Dominello MM, Matuszak MM, Jagsi R, Hayman JA, Pierce LJ, and Jolly S. Uptake of Adjuvant Durvalumab After Definitive Concurrent Chemoradiotherapy for Stage III Nonsmall-cell Lung Cancer. *Am J Clin Oncol* 2022; 45(4):142-145. PMID: 35271524. Full Text

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OBJECTIVES: The addition of adjuvant durvalumab improves overall survival in locally advanced nonsmall-cell lung cancer (NSCLC) patients treated with definitive chemoradiation, but the real-world uptake of adjuvant durvalumab is unknown. MATERIALS AND METHODS: We identified patients with stage III NSCLC treated with definitive concurrent chemoradiation from January 2018 to October 2020 from a statewide radiation oncology quality consortium, representing a mix of community (n=22 centers) and academic (n=5) across the state of Michigan. Use of adjuvant durvalumab was ascertained at the time of routine 3-month or 6-month follow-up after completion of chemoradiation. RESULTS: Of 421 patients with stage III NSCLC who completed chemoradiation, 322 (76.5%) initiated adjuvant durvalumab. The percentage of patients initiating adjuvant durvalumab increased over time from 66% early in the

study period to 92% at the end of the study period. There was substantial heterogeneity by treatment center, ranging from 53% to 90%. In multivariable logistic regression, independent predictors of durvalumab initiation included more recent month (odds ratio [OR]: 1.05 per month, 95% confidence interval [CI]: 1.02-1.08, P=0.003), lower Eastern Cooperative Oncology Group score (OR: 4.02 for ECOG 0 vs. 2+, 95% CI: 1.67-9.64, P=0.002), and a trend toward significance for female sex (OR: 1.66, 95% CI: 0.98-2.82, P=0.06). CONCLUSION: Adjuvant durvalumab for stage III NSCLC treated with definitive chemoradiation was rapidly and successfully incorporated into clinical care across a range of community and academic settings in the state of Michigan, with over 90% of potentially eligible patients starting durvalumab in more recent months.

Radiation Oncology
Extermann M, **Chetty IJ**, **Brown SL**, Al-Jumayli M, and **Movsas B**. Predictors of Toxicity Among Older Adults with Cancer. *Semin Radiat Oncol* 2022; 32(2):179-185. PMID: 35307121. Full Text

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An increasing number of cancer patients are of advanced age as the incidence of cancer increases with age. In this article, the clinical predictors of toxicity that may help in treatment selection are addressed, as well as mitigators of toxicity. The potential of artificial intelligence to enable further progress in the understanding of the interaction of age and tolerance to radiation is reviewed. The final section reviews the literature on patient-related outcomes for older patients.

Radiation Oncology
Jagsi R, Griffith KA, Vicini F, Boike T, Dominello M, Gustafson G, Hayman JA, Moran JM, Radawski JD, **Walker E**, and Pierce L. Identifying Patients Whose Symptoms Are Underrecognized During Treatment With Breast Radiotherapy. *JAMA Oncol* 2022; Epub ahead of print. PMID: 35446337. Full Text

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IMPORTANCE: Understanding whether physicians accurately detect symptoms in patients with breast cancer is important because recognition of symptoms facilitates supportive care, and clinical trials often rely on physician assessments using Common Toxicity Criteria for Adverse Events (CTCAE). OBJECTIVE: To compare the patient-reported outcomes (PROs) of patients with breast cancer who received radiotherapy from January 1, 2012, to March 31, 2020, with physicians' CTCAE assessments to assess underrecognition of symptoms. DESIGN, SETTING, AND PARTICIPANTS: This cohort study included a total of 29 practices enrolled in the Michigan Radiation Oncology Quality Consortium quality initiative. Of 13 725 patients with breast cancer who received treatment with radiotherapy after undergoing lumpectomy, 9941 patients (72.4%) completed at least 1 PRO questionnaire during treatment with radiotherapy and were evaluated for the study. Of these, 9868 patients (99.3%) were matched to physician CTCAE assessments that were completed within 3 days of the PRO questionnaires. EXPOSURES: Patient and physician ratings of 4 symptoms (pain, pruritus, edema, and fatigue) were compared. MAIN OUTCOMES AND MEASURES: We used multilevel multivariable logistic regression to

evaluate factors associated with symptom underrecognition, hypothesizing that it would be more common in racial and ethnic minority groups. RESULTS: Of 9941 patients, all were female, 1655 (16.6%) were Black, 7925 (79.7%) were White, and 361 (3.6%) had Other race and ethnicity (including American Indian/Alaska Native, Arab/Middle Eastern, and Asian), either as self-reported or as indicated in the electronic medical record. A total of 1595 (16.0%) were younger than 50 years, 2874 (28.9%) were age 50 to 59 years, 3353 (33.7%) were age 60 to 69 years, and 2119 (21.3%) were 70 years or older. Underrecognition of symptoms existed in 2094 of 6781 (30.9%) observations of patient-reported moderate/severe pain, 748 of 2039 observations (36.7%) of patient-reported frequent pruritus, 2309 of 4492 observations (51.4%) of patient-reported frequent edema, and 390 of 2079 observations (18.8%) of patient-reported substantial fatigue. Underrecognition of at least 1 symptom occurred at least once for 2933 of 5510 (53.2%) of those who reported at least 1 substantial symptom. Factors independently associated with underrecognition were younger age (younger than 50 years compared with 60-69 years: odds ratio [OR], 1.35; 95% CI, 1.14-1.59; P < .001; age 50-59 years compared with 60-69 years: OR, 1.19; 95% CI, 1.03-1.37; P = .02), race (Black individuals compared with White individuals: OR, 1.56; 95% CI 1.30-1.88; P < .001; individuals with Other race or ethnicity compared with White individuals: OR, 1.52; 95% CI, 1.12-2.07; P = .01), conventional fractionation (OR, 1.26; 95% CI, 1.10-1.45; P = .002), male physician sex (OR, 1.54; 95% CI, 1.20-1.99; P = .002), and 2-field radiotherapy (without a supraclavicular field) (OR, 0.80; 95% CI, 0.67-0.97; P = .02). CONCLUSIONS AND RELEVANCE: The results of this cohort study suggest that PRO collection may be essential for trials because relying on the CTCAE to detect adverse events may miss important symptoms. Moreover, since physicians in this study systematically missed substantial symptoms in certain patients, including younger patients and Black individuals or those of Other race and ethnicity, improving symptom detection may be a targetable mechanism to reduce disparities.

Radiation Oncology

Sarria GR, Timmerman R, Hermansen M, Malhotra S, Chang B, Carter R, Martinez DA, Sarria GJ, Giordano FA, **Chetty IJ**, Roa D, and Li B. Longitudinal Remote SBRT/SRS Training in Latin America: A Prospective Cohort Study. *Front Oncol* 2022; 12:851849. PMID: 35480106. Full Text

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BACKGROUND: Continuing medical education in stereotactic technology are scarcely accessible in developing countries. We report the results of upscaling a longitudinal telehealth training course on stereotactic body radiation therapy (SBRT) and stereotactic radiosurgery (SRS), after successfully developing a pilot course in Latin America. METHODS: Longitudinal training on SBRT and SRS was provided to radiation oncology practitioners in Peru and Colombia at no cost. The program included sixteen weekly 1-hour live conferencing sessions with interactive didactics and a cloud-based platform for case-based learning. Participant-reported confidence was measured in 16 SBRT/SRS practical domains, based on a 1-to-5 Likert scale. Pre- and post-curriculum exams were required for participation credit. Knowledge-baseline, pre- and post-curriculum surveys, overall and single professional-group confidence changes, and exam results were assessed. RESULTS: One hundred and seventy-three radiotherapy professionals participated. An average of 56 (SD ±18) attendees per session were registered. Fifty (29.7%) participants completed the pre- and post-curriculum surveys, of which 30% were radiation

oncologists (RO), 26% radiation therapists (RTT), 20% residents, 18% medical physicists and 6% neurosurgeons. Significant improvements were found across all 16 domains with overall mean +0.55 (SD ±0.17, p<0.001) Likert-scale points. Significant improvements in individual competences were most common among medical physicists, RTT and residents. Pre- and post-curriculum exams yielded a mean 16.15/30 (53.8 ± 20.3%) and 23.6/30 (78.7 ± 19.3%) correct answers (p<0.001). CONCLUSION: Longitudinal telehealth training is an effective method for improving confidence and knowledge on SBRT/SRS amongst professionals. Remote continuing medical education should be widely adopted in lower-middle income countries.

Radiation Oncology

VanderWalde N, and **Movsas B**. Introduction: Personalization of Cancer Care for Older Adults. *Semin Radiat Oncol* 2022; 32(2):95-97. PMID: 35307122. Full Text

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Sleep Medicine

Roth T, Dauvilliers Y, Thorpy MJ, Kushida C, Corser BC, Bogan R, Rosenberg R, Dubow J, and Seiden D. Effect of FT218, a Once-Nightly Sodium Oxybate Formulation, on Disrupted Nighttime Sleep in Patients with Narcolepsy: Results from the Randomized Phase III REST-ON Trial. *CNS Drugs* 2022; 36(4):377-387. PMID: 35380374. Full Text

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BACKGROUND: Sodium oxybate has been recognized as a gold standard for the treatment of disrupted nighttime sleep due to narcolepsy. Its short half-life and immediate-release formulation require patients to awaken 2.5-4 h after their bedtime dose to take a second dose. A novel extended-release, once-nightly sodium oxybate formulation (ON-SXB; FT218) is under US Food and Drug Administration review for the treatment of adults with narcolepsy. OBJECTIVE: A phase III trial of ON-SXB in individuals with narcolepsy type 1 (NT1) or 2 (NT2) [the REST-ON trial; NCT02720744] has been conducted and the primary results reported elsewhere. Secondary objectives from REST-ON were to assess the efficacy of ON-SXB on disrupted nighttime sleep; the results of this analysis are reported here. METHODS: In the double-blind, phase III REST-ON trial, patients aged ≥ 16 years were randomly assigned 1:1 to ON-SXB (1 week, 4.5 g; 2 weeks, 6 g; 5 weeks, 7.5 g; 5 weeks, 9 g) or placebo. Secondary endpoints included polysomnographic measures of sleep stage shifts and nocturnal arousals and patient-reported assessments of sleep quality and refreshing nature of sleep at 6, 7.5, and 9 g; post hoc analyses included changes in time spent in each sleep stage, delta power, and assessments in stimulant-use subgroups for prespecified endpoints. RESULTS: In total, 190 participants (n = 97, ON-SXB; n = 93, placebo) were included in the efficacy analyses. All three ON-SXB doses demonstrated a clinically meaningful, statistically significant decrease vs placebo in the number of transitions to wake/N1 from N1, N2, and rapid eye movement (REM) stages (all doses p < 0.001) and the number of nocturnal arousals (p < 0.05 ON-SXB 6 g; p < 0.001 7.5 and 9 g). Sleep quality and refreshing nature of sleep were significantly improved with all three ON-SXB doses vs placebo (p < 0.001). Post hoc analyses revealed a significant

reduction in time spent in N1 ($p < 0.05$ ON-SXB 6 g; $p < 0.001$ 7.5 and 9 g) and REM (all $p < 0.001$) and increased time spent in N3 with ON-SXB vs placebo (all $p < 0.001$), with a significant increase in delta power ($p < 0.01$ ON-SXB 6 g; $p < 0.05$ 7.5 g; $p < 0.001$ 9 g) and increased REM latency (ON-SXB 7.5 g vs placebo; $p < 0.05$). Significant improvements in disrupted nighttime sleep were observed regardless of concomitant stimulant use. CONCLUSIONS: The clinically beneficial, single nighttime dose of ON-SXB significantly improved disrupted nighttime sleep in patients with narcolepsy. CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov NCT02720744.

Surgery
Ivanics T, Claasen MP, Patel MS, Hansen BE, and Sapisochin G. Reply. *Hepatology* 2022; Epub ahead of print. PMID: 35435274. Full Text

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Surgery
Khachfe HH, Habib JR, Salhab HA, Fares MY, **Chahrour MA**, and Jamali FR. American college of surgeons NSQIP pancreatic surgery publications: A critical appraisal of the quality of methodological reporting. *Am J Surg* 2022; 223(4):705-714. PMID: 34218930. Full Text

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BACKGROUND: The use of ACS-NSQIP has increased in pancreatic surgery (PS) research. The aim of this study is to critically appraise the methodological reporting of PS publications utilizing the ACS-NSQIP database. STUDY DESIGN: PubMed was queried for all PS studies employing the ACS-NSQIP database published between 2004 and 2021. Critical appraisal was performed using the JAMA-Surgery Checklist, STROBE Statement, and RECORD Statement. RESULTS: A total of 86 studies were included. Median scores for number of fulfilled criteria for the JAMA-Surgery Checklist, STROBE Statement, and RECORD Statement were 6, 20, and 6 respectively. The most commonly unfulfilled criteria were those relating to discussion of missed data, compliance with IRB, unadjusted and adjusted outcomes, providing supplementary/raw information, and performing subgroup analyses. CONCLUSION: An overall satisfactory reporting of methodology is present among PS studies utilizing the ACS-NSQIP database. Areas for improved adherence include discussing missed data, providing supplementary information, and performing subgroup analysis. Due to the increasing role of large-scale databases, enhanced adherence to reporting guidelines may advance PS research.

Surgery
Natour AK, **Kabbani L**, **Rteil A**, **Nypaver T**, **Weaver M**, **Lee A**, **Mohammad F**, **Shepard A**, and **Omar Z**. Cross-clamp location and perioperative outcomes after open infrarenal abdominal aortic aneurysm repair: A Vascular Quality Initiative(®) review. *Vascular* 2022; Epub ahead of print. PMID: 35435780. Full Text

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OBJECTIVES: By analyzing national Vascular Quality Initiative (VQI) data for patients undergoing open infrarenal abdominal aortic aneurysms (AAA) repair, we sought to better characterize the effects of different suprarenal clamping positions on postoperative outcomes. METHODS: We performed a retrospective analysis of a prospectively collected national VQI database for all open infrarenal AAA repairs performed between 2003 and 2017. Patients were initially divided into proximal (above 1 renal, above 2 renals, and supraceliac) and infrarenal clamp groups. Patients were then subdivided into those who underwent surgery between 2003-2010 and those who had surgery between 2011-2017. Univariate followed by multivariate analyses were done to compare the baseline characteristics, preoperative, intraoperative, and postoperative outcomes between the two groups. RESULTS: During the study period, 9068 open AAA repairs were recorded in the VQI; of these, 5043 met the inclusion criteria. Aortic clamp level was infrarenal in 59% (N = 2975), above 1 renal in 15% (N = 735), above both renals in 21% (N = 1053), and supraceliac in 5% (N = 280). The average age was 69 years, and males comprised 73% (N = 3701) of the cohort. The overall 30-day mortality for the entire study group was 2.7%. On univariate analysis, patients who underwent proximal clamping had significantly higher 30-day mortality than those undergoing infrarenal clamping (3.7 vs 2.0%, $p < 0.001$). After adjusting for preoperative and intraoperative variables, this difference became nonsignificant. On multivariate analysis, clamping above both renals or the celiac artery was associated with an increased occurrence of postoperative myocardial infarction (odds ratio = 1.44, $p = 0.037$ and odds ratio = 1.78, $p = 0.023$, respectively). All proximal clamp positions were associated with a significant increase in the incidence of AKI and renal failure requiring dialysis. There was no significant difference when looking at overall survival times comparing the suprarenal and infrarenal clamp position groups ($p = 0.1$). Patients who underwent surgery in the latter half of the study period had longer intraoperative renal ischemia time, increased in estimated blood loss, and longer total procedure time. CONCLUSIONS: Suprarenal clamping, at any level, was associated with an increased risk of AKI and renal replacement therapy. Clamping above both renal and celiac arteries was associated with increased cardiac morbidity. Perioperative and long-term mortality was unaffected by clamp level. Patients operating in the latter half of the study had increased estimated blood loss, renal ischemia time, and operative time, which may reflect decreased training in open AAA repair. During open AAA repair, the proximal clamp site should be chosen based on anatomic considerations and not a perceived perioperative mortality benefit. Proximal aortic clamping should always be performed at the safest, distal-most level to reduce cardiac morbidity and the risk of postoperative dialysis.

Surgery

Sattler SS, Magro CM, Shapiro L, Merves JF, Levy R, **Veenstra J**, and **Patel P**. Gastrointestinal Kohlmeier-Degos disease: a narrative review. *Orphanet J Rare Dis* 2022; 17(1):172. PMID: 35443671. Full Text

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INTRODUCTION: Kohlmeier-Degos (K-D) disease is a rare obliterative vasculopathy that can present as a benign cutaneous form or with potentially malignant systemic involvement. The gastrointestinal tract is most frequently involved in systemic disease and mortality is often related to bowel perforations. Herein, we provide information to providers and patients regarding gastrointestinal K-D symptomology, pathology, treatment, and diagnosis, with a focus on the importance of timely diagnostic laparoscopy. We present three new cases of gastrointestinal K-D to highlight varying disease presentations and outcomes. BODY: Based on reviewed reports, perforation is preceded by at least one gastrointestinal symptom: abdominal pain/cramping, anorexia/weight loss, vomiting, diarrhea, nausea, gastrointestinal bleeding, obstipation, constipation, and abdominal fullness. Perforation most commonly occurs in the small intestine and often

results in sepsis and death. Although underutilized, laparoscopy is the most sensitive and specific diagnostic technique, demonstrating serosal porcelain plaques similar to those on the skin and characteristic for K-D. The combination of eculizumab and treprostinil is presently the most effective treatment option for gastrointestinal K-D. The pathology of gastrointestinal K-D is characterized by an obliterative intimal arteriopathy eventuating in occlusive acellular deposits of mucin and collagen along with an extravascular pauci-cellular sclerosing process resembling scleroderma confined to the subserosal fat. C5b-9 and interferon-alpha are both expressed in all caliber of vessels in the affected intestine. While C5b-9 blockade does not prevent the intimal expansion, enhanced type I interferon signaling is likely a key determinant to intimal expansion by, causing an influx of monocytes which transdifferentiate into procollagen-producing myofibroblast-like cells. CONCLUSION: Prompt laparoscopic evaluation is necessary in any K-D patient with an abdominal symptom to facilitate diagnosis and treatment initiation, as well as to hopefully decrease mortality. Those with gastrointestinal K-D should start on eculizumab as soon as possible, as onset of action is immediate.

Surgery
Schwartz T. Personal Systemic Therapy Decision-Making has Officially Arrived for Node-Positive Breast Cancer. *Ann Surg Oncol* 2022; Epub ahead of print. PMID: 35430658. Full Text

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Surgery
Shamaa TM, **Shamaa O**, **Crombez C**, **Konel JM**, **Kitajima T**, **Shimada S**, **Ivanics T**, **Mohamed A**, **Collins K**, **Nagai S**, **Yoshida A**, **Abouljoud M**, and **Rizzari M**. The use of normothermic liver preservation in combined liver and lung transplantation: A single-center experience. *Am J Transplant* 2022; Epub ahead of print. PMID: 35384271. Full Text

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Combined liver and lung transplantation (CLLT) is indicated in patients with both end-stage liver and lung disease. Ex-situ normothermic machine perfusion (NMP) has been previously used for extended normothermic lung preservation in CLLT. We aim to describe our single-center experience using ex-situ NMP for extended normothermic liver preservation in CLLT. Four CLLTs were performed from 2019 to 2020 with the lung transplanted first for all patients. Median ex-situ pump time for the liver was 413 min (IQR 400-424). Over a median follow-up of 15 months (IQR 14-19), all patients were alive and doing well. Normothermic extended liver preservation is a safe method to allow prolonged cold ischemia using normothermic perfusion of the liver during CLLT.

Surgery
Stefanou AJ, **Kalu RU**, **Tang A**, and **Reickert CA**. Bowel Preparation for Elective Hartmann Operation: Analysis of the National Surgical Quality Improvement Program Database. *Surg Infect (Larchmt)* 2022; Epub ahead of print. PMID: 35451876. Request Article

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Background: Use of pre-operative bowel preparation in colorectal resection has not been examined solely in patients who have had colorectal resection with primary colostomy (Hartmann procedure). We aimed to evaluate the association of bowel preparations with short-term outcomes after non-emergent Hartmann procedure. Patients and Methods: The National Surgical Quality Improvement Program Participant Use File colectomy database was queried for patients who had elective open or laparoscopic Hartmann operation. Patients were grouped by pre-operative bowel preparation: no bowel preparation, oral antibiotic agents, mechanical preparation, or both mechanical and oral antibiotic agent preparation (combined). Propensity analysis was performed, and outcomes were compared by type of pre-operative

bowel preparation. The primary outcome was rate of any surgical site infection (SSI). Secondary outcomes included overall complication, re-operation, re-admission, Clostridioides difficile colitis, and length of stay. Results: Of the 4,331 records analyzed, 2,040 (47.1%) patients received no preparation, 251 (4.4%) received oral antibiotic preparation, 1,035 (23.9%) received mechanical bowel preparation, and 1,005 (23.2%) received combined oral antibiotic and mechanical bowel preparation. After propensity adjustment, rates of any SSI, overall complication, and length of hospital stay varied significantly between pre-operative bowel regimens ($p < 0.005$). The use of combined bowel preparation was associated with decreased rate of SSI, overall complication, and length of stay. No difference in rate of re-operation or post-operative Clostridioides difficile infection was observed based on bowel preparation. Conclusions: Compared with no pre-operative bowel preparation, any bowel preparation was associated with reduced rate of SSI, but not rate of re-operation or post-operative Clostridioides difficile infection.

Surgery

Tinney F, **Ivanics T**, Stracke J, **Malinzak L**, Elsabbagh AM, **McEvoy T**, **Nagai S**, and **Yoshida A**. Robotic-assisted Versus Open Technique for Living Donor Kidney Transplantation: A Comparison Using Propensity Score Matching for Intention to Treat. *Transplant Direct* 2022; 8(5):e1320. PMID: 35434284. Full Text

Division of Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, MI.
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Living donor robotic-assisted kidney transplantation (RAKT) is an alternative to open kidney transplantation (OKT), but experience with this technique is limited in the United States. METHODS: A retrospective review of living donor kidney transplants performed between 2016 and 2018 compared RAKT with OKT with regard to recipient, donor, and perioperative parameters. A 1:1 propensity score matching was performed on recipient/donor age, sex, body mass index, race, preoperative dialysis, and calculated panel reactive antibodies. RESULTS: Outcomes of patient survival, graft survival, and postoperative complications were assessed for 139 transplants (47 RAKT and 92 OKT). Propensity score analysis (47:47) showed that RAKT recipients had longer warm ischemic times (49 versus 40 min; $P < 0.001$) and less blood loss (100 versus 150 mL; $P = 0.005$). Operative time and length of stay were similar between groups. Postoperative serum creatinine was similar during a 2-y follow-up. Post hoc analysis excluding 4 open conversions showed lower operative time with RAKT (297 versus 320 min; $P = 0.04$) and lower 30-d (4.7% versus 23.4%; $P = 0.02$) and 90-d (7% versus 27.7%; $P = 0.01$) Clavien-Dindo grade ≥3 complications. CONCLUSIONS: Our findings suggest that RAKT is a safe alternative to OKT.

Surgery

Vijayanarayanan A, **Wlosinski L**, **El-Bashir J**, **Galusca D**, **Nagai S**, **Yoshida A**, **Abouljoud MS**, and **Otrock ZK**. Lack of alloimmunization to the D antigen in D-negative orthotopic liver transplant recipients receiving D-positive red blood cells perioperatively. *Vox Sang* 2022; Epub ahead of print. PMID: 35393659. Full Text

Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Michigan, USA.
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BACKGROUND AND OBJECTIVES: D-negative patients undergoing orthotopic liver transplantation (OLT) might require a large number of red blood cell (RBC) units, which can impact the inventory of D-negative blood. The blood bank might need to supply these patients with D-positive RBCs because of inventory constraints. This study evaluates the prevalence of anti-D formation in D-negative OLT patients who received D-positive RBCs perioperatively, as this will assist in successful patient blood management. MATERIALS AND METHODS: This was a retrospective study performed at a single academic medical centre. Electronic medical records for all 1052 consecutive patients who underwent OLT from January 2007 through December 2017 were reviewed. D-negative patients who were transfused perioperatively

with D-positive RBCs and had antibody screening at least 30 days after transfusion were included. RESULTS: Of a total of 155 D-negative patients, 23 (14.8%) received D-positive RBCs perioperatively. Seventeen patients were included in the study. The median age was 54 years (range 36-67 years); 13 (76.5%) were male. The median number of D-positive RBC units transfused perioperatively was 7 (range 1-66 units). There was no evidence of D alloimmunization in any patient after a median serologic follow-up of 49.5 months (range 31 days to 127.7 months). The average number of antibody screening post OLT was 7.29. CONCLUSION: Our study showed that transfusion of D-positive RBCs in D-negative OLT recipients is a safe and acceptable practice in the setting of immunosuppression. This practice allows the conservation of D-negative RBC inventory.

Surgery

Yang P, Bonham AJ, **Carlin AM**, Finks JF, Ghaferi AA, and Varban OA. Patient characteristics and outcomes among bariatric surgery patients with high narcotic overdose scores. *Surg Endosc* 2022; Epub ahead of print. PMID: 35411461. Full Text

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BACKGROUND: Obesity-related chronic pain can increase the risk of narcotic abuse in bariatric surgery patients. However, assessment of overdose risk has not been evaluated to date. METHODS: A NARxCHECK® overdose score ("Narx score") was obtained preoperatively on all patients undergoing bariatric surgery (n = 306) between 2018 and 2020 at a single-center academic bariatric surgery program. The 3-digit score ranges from 000 to 999 and is based on patient risk factors found within the Prescription Drug Monitoring Program. A Narx score ≥ 200 indicates tenfold increased risk of narcotic overdose. Patient characteristics, comorbidities, and emergency room (ER) visits were compared between patients in the upper (≥ 200) and lower (000) terciles of Narx scores. Morphine milligram equivalent (MME) prescribed at discharge and refills was also evaluated. RESULTS: Patients in the upper tercile represented 32% (n = 99) of the study population, and compared to the lower tercile (n = 101, 33%), were more likely to have depression (63.6% vs 38.6%, p = 0.0004), anxiety (47.5% vs 30.7%, p = 0.0150), and bipolar disorder (6.1% vs 0.0%, p = 0.0120). Median MME prescribed at discharge was the same between both groups (75); however, high-risk patients were more likely to be prescribed more than 10 tablets of a secondary opioid (83.3% vs 0.0%, p = 0.0111), which was prescribed by another provider in 67% of cases. ER visits among patients who did not have a complication or require a readmission was also higher among high-risk patients (7.8% vs 0.0%, p = 0.0043). There were no deaths or incidents of mental health-related ER visits in either group. CONCLUSION: Patients with a Narx score ≥ 200 were more likely to have mental health disorders and have potentially avoidable ER visits in the setting of standardized opioid prescribing practices. Narx scores can help reduce ER visits by identifying at-risk patients who may benefit from additional clinic or telehealth follow-up.

Urology

Agarwal A, Sharma RK, Gupta S, Boitrelle F, Finelli R, Parekh N, Durairajanayagam D, Saleh R, Arafa M, Cho CL, Farkouh A, **Rambhatla A**, Henkel R, Vogiatzi P, Tadros N, Kavoussi P, Ko E, Leisegang K, Kandil H, Palani A, Salvio G, Mostafa T, Rajmil O, Banihani SA, Schon S, Le TV, Birowo P, Çeker G, Alvarez J, Molina JMC, Ho CCK, Calogero AE, Khalafalla K, Duran MB, Kuroda S, Colpi GM, Zini A, Anagnostopoulou C, Pescatori E, Chung E, Caroppo E, Dimitriadis F, Pinggera GM, Busetto GM, Balercia G, Elbardisi H, Taniguchi H, Park HJ, Maldonado Rosas I, de la Rosette J, Ramsay J, Bowa K, Simopoulou M, Rodriguez MG, Sabbaghian M, Martinez M, Gilani MAS, Al-Marhoon MS, Kosgi R, Cannarella R, Micic S, Fukuhara S, Parekattil S, Jindal S, Abdel-Meguid TA, Morimoto Y, and Shah R. Sperm Vitality and Necrozoospermia: Diagnosis, Management, and Results of a Global Survey of Clinical Practice. *World J Mens Health* 2022; 40(2):228-242. PMID: 34666422. Full Text

Sperm vitality testing is a basic semen examination that has been described in the World Health Organization (WHO) Laboratory Manual for the Examination and Processing of Human Semen from its primary edition, 40 years ago. Several methods can be used to test sperm vitality, such as the eosin-

nigrosin (E-N) stain or the hypoosmotic swelling (HOS) test. In the 6th (2021) edition of the WHO Laboratory Manual, sperm vitality assessment is mainly recommended if the total motility is less than 40%. Hence, a motile spermatozoon is considered alive, however, in certain conditions an immotile spermatozoon can also be alive. Therefore, the differentiation between asthenozoospermia (pathological decrease in sperm motility) and necrozoospermia (pathological decrease in sperm vitality) is important in directing further investigation and management of infertile patients. The causes leading to necrozoospermia are diverse and can either be local or general, testicular or extra-testicular. The andrological management of necrozoospermia depends on its etiology. However, there is no standardized treatment available presently and practice varies among clinicians. In this study, we report the results of a global survey to understand current practices regarding the physician order of sperm vitality tests as well as the management practices for necrozoospermia. Laboratory and clinical scenarios are presented to guide the reader in the management of necrozoospermia with the overall objective of establishing a benchmark ranging from the diagnosis of necrozoospermia by sperm vitality testing to its clinical management.

Urology
Agochukwu-Mmonu N, Qi J, Dunn RL, Montie J, Wittmann D, Miller D, Martin R, Kim T, Johnston WK, and **Peabody J**. Re: Patient- and Surgeon-Level Variation in Patient-Reported Sexual Function Outcomes following Radical Prostatectomy over 2 Years: Results from a Statewide Surgical Improvement Collaborative. *J Urol* 2022; 207(4):928-928. PMID: Not assigned. Full Text

Urology
Elsayed AS, Iqbal U, Jing Z, Houenstein HA, Wijburg C, Wiklund P, Kim E, Stöckle M, Kelly J, Dasgupta P, Wagner AA, Kaouk J, Badani KK, Redorta JP, Mottrie A, **Peabody JO**, Rouprêt M, Balbay D, Richstone L, Rha KH, Aboumohamed A, Li Q, Hussein AA, and Guru KA. Relapses Rates and Patterns for Pathological T0 after Robot-Assisted Radical Cystectomy: Results from the International Robotic Cystectomy Consortium. *Urology* 2022; Epub ahead of print. PMID: 35461914. Full Text

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Henry Ford Health System, MI, USA.
Sorbonne University, GRC 5 Predictive Onco-Uro, AP-HP, Urology, Pitie-Salpetriere Hospital, F-75013 PARIS, France.
Koç University Hospital, Istanbul, Turkey.
Arthur Smith Institute for Urology, NY, USA.
Yonsei Medical Health Care System (Severance Hospital), Gyeonggi-do, South Korea.
Montefiore Medical Center (Albert Einstein College of Medicine), NY, USA.
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OBJECTIVES: To investigate the oncologic outcomes of pT0 after robot-assisted radical cystectomy (RARC). METHODS: A retrospective review of the International Robotic Cystectomy Consortium database was performed. Patients with pT0 after RARC were identified and analyzed. Data were reviewed for demographics and pathologic outcomes. Kaplan Meier(KM) curves were used to depict recurrence free survival(RFS), disease specific survival(DSS), and overall survival(OS). Multivariate stepwise Cox regression models were used to identify variables associated with RFS and OS. RESULTS:

471 patients (18%) with pT0 were identified. Median age was 68 years (IQR 60-73), with a median follow up of 20 months (IQR 6-47). Thirty-seven percent received neoadjuvant chemotherapy (NAC) and 5% had pN+ disease. Seven percent of patients experienced disease relapse; 3% had local and 5% had distant recurrence. Most common sites of local and distant recurrences were pelvis (1%) and lungs (2%). Five-year RFS, DSS, and OS were 88%, 93% and 79%, respectively. Age (HR 1.05, 95% CI 1.01-1.09, p=0.02), pN+ve (HR 11.48, 95%CI 4.47 - 29.49, p<0.01), and reoperations within 30 days (HR 5.53, 95% CI 2.08-14.64, p<0.01) were associated with RFS. Chronic kidney disease (HR 3.24, 95% CI 1.45 - 7.23,p<0.01), neoadjuvant chemotherapy (HR 0.41, 95%CI 0.18-0.92, p=0.03), pN+ve (HR 4.37, 95% CI 1.46-13.06, p<0.01), and reoperations within 30 days (HR 2.64, 95% CI, 1.08 - 6.43, p=0.03) were associated with OS. CONCLUSIONS: Despite pT0 status at RARC, 5% had pN+ disease and 7% of patients relapsed. Node status was the strongest variable associated with RFS and OS in pT0.

Urology

Goldenthal SB, Reimers MA, Singhal U, Farha M, Mehra R, Piert M, Tosoian JJ, Modi PK, Curci N, **Peabody J**, Kleer E, Smith DC, and Morgan TM. Prostate Cancer with Peritoneal Carcinomatosis: A robotic-assisted radical prostatectomy-based Case Series. *Urology* 2022; Epub ahead of print. PMID: 35472327. Full Text

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OBJECTIVE: To aid in the diagnosis and treatment of patients with metastatic tumor seeding, an exceedingly phenomenon following minimally invasive urological surgery, additional case reports are needed. MATERIALS AND METHODS: We report our experience with patients determined to have peritoneal carcinomatosis following robotic-assisted radical prostatectomy (RARP) and provide a descriptive summary of these unique cases. RESULTS: Five cases of peritoneal carcinomatosis were identified, all of which occurred relatively late - between 8-13 years - following RARP. Four of the five cases had T3 disease at the time of prostatectomy. (68)Ga-PSMA PET identified peritoneal carcinomatosis in three of five cases. CONCLUSIONS: Certain clinical factors, such as advanced pathologic stage at the time of prostatectomy, may predict risk for carcinomatosis following RARP. Additionally, next generation imaging modalities, such as PSMA PET, may aid in identifying these metastases and are likely to identify increasing numbers of these patients as next generation imaging becomes more widely available. Continued documentation and classification of this atypical presentation are needed to improve our understanding and management of this phenomenon.

Urology

Hakimi K, Carbonara U, Djaladat H, Mehrazin R, Eun D, Reese A, Gonzalgo ML, Margulis V, Uzzo RG, Porter J, Sundaram CP, **Abdollah F**, Mottrie A, Tellini R, Ferro M, Walia A, Saidian A, Soliman S, Yuan J, Veccia A, Ghoreifi A, Cacciamani G, Bhattu AS, Meng X, Farrow JM, **Jamil M**, Minervini A, Rha KH, Wu Z, Simone G, Autorino R, and Derweesh IH. Outcomes of Lymph Node Dissection in Nephroureterectomy in the Treatment of Upper Tract Urothelial Carcinoma: Analysis of the ROBUUST Registry. *J Urol* 2022; Epub ahead of print. PMID: 35377778. Full Text

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Urology
König F, Grossmann NC, Soria F, D'Andrea D, Juvet T, Potretzke A, Djaladat H, Ghoreifi A, Kikuchi E, Hayakawa N, Mari A, Khene ZE, Fujita K, Raman JD, Breda A, Fontana M, Sfakianos JP, Pfail JL, Laukhtina E, Rajwa P, Pallauf M, Cacciamani GE, van Doeveren T, Boormans JL, Antonelli A, **Jamil M**, **Abdollah F**, **Budzyn J**, Ploussard G, Heidenreich A, Daneshmand S, Boorjian SA, Rouprêt M, Rink M, Shariat SF, and Pradere B. Pentafecta for Radical Nephroureterectomy in Patients with High-Risk Upper Tract Urothelial Carcinoma: A Proposal for Standardization of Quality Care Metrics. *Cancers (Basel)* 2022; 14(7). PMID: 35406553. Full Text

BACKGROUND: Measuring quality of care indicators is important for clinicians and decision making in health care to improve patient outcomes. OBJECTIVE: The primary objective was to identify quality of care indicators for patients with upper tract urothelial carcinoma (UTUC) and to validate these in an international cohort treated with radical nephroureterectomy (RNU). The secondary objective was to assess the factors associated with failure to validate the pentafecta. DESIGN: We performed a retrospective multicenter study of patients treated with RNU for EAU high-risk (HR) UTUC. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Five quality indicators were consensually approved, including a negative surgical margin, a complete bladder-cuff resection, the absence of hematological complications, the absence of major complications, and the absence of a 12-month postoperative recurrence. After multiple imputations and propensity-score matching, log-rank tests and a Cox regression were used to assess the survival outcomes. Logistic regression analyses assessed predictors for pentafecta failure. RESULTS: Among the 1718 included patients, 844 (49%) achieved the pentafecta. The median follow-up was 31 months. Patients who achieved the pentafecta had superior 5-year overall- (OS) and cancer-specific survival (CSS) compared to those who did not (68.7 vs. 50.1% and 79.8 vs. 62.7%, respectively, all p < 0.001). On multivariable analyses, achieving the pentafecta was associated with improved recurrence-free survival (RFS), CSS, and OS. No preoperative clinical factors predicted a failure to validate the pentafecta. CONCLUSIONS: Establishing quality indicators for UTUC may help define prognosis and improve patient care. We propose a pentafecta quality criteria in RNU patients. Approximately half of the patients evaluated herein reached this endpoint, which in turn was independently associated with survival outcomes. Extended validation is needed.

Conference Abstracts

Anesthesiology
Franco-Palacios DJ, **Allenspach L**, **Stagner L**, **Pinto-Corrales J**, **Hanlon K**, **Nappo T**, **Sherbin E**, **Sternberg D**, **Dillon W**, **Simanovski J**, and **Alangaden G**. Early Outcomes of Lung Transplantation for COVID-19 Related Lung Disease. Single Center Experience. *J Heart Lung Transplant* 2022; 41(4):S393. PMID: Not assigned. Full Text

D.J. Franco-Palacios, Pulmonary and Critical Care, Henry Ford Hospital, Detroit, MI, United States

Purpose: Lung transplantation (LT) is a lifesaving treatment for Covid-19 related lung disease with early outcomes similar to other indications. Methods: Seven patients underwent LT for Covid-19 related lung disease at our center: 5 for ARDS and 2 for IPF exacerbation post SARS-CoV-2 infection. Results: Seven patients (5 men) with single organ failure underwent bilateral LT. Median age was 47 years old. All ARDS cases had poor lung mechanics on invasive mechanical ventilation with radiographic evidence of lung fibrosis: pneumatocele, GGO, consolidations, subpleural reticulations and traction bronchiectasis. vvECMO was bridge to transplant in 5 cases (bridge to recovery in 2). Median ECMO duration for ARDS was 32 days (range 7-99). Median time to LT from Covid diagnosis was 59 days (Q1-IQ3, 54-62). Two patients were post-partum women with ARDS. Explanted pathology showed UIP, DAD, diffuse hemorrhage and one case of fibrosing NSIP. Pulmonary hypertension was seen in 4 cases. One patient did not survive. Organizing pneumonia and granuloma were present in this patient. Most ARDS patients were unable to tolerate lower sedation and consent by a substitute decision-makers was obtained. Post operative ECMO decannulation was possible in all cases. Induction, maintenance immunosuppression and antimicrobials were standard for our program. Donated grafts were from deceased brain death donors and negative for 2019-nCoV. Rehabilitation potential and strong social support were absolute inclusion criteria. All survivors have excellent lung function. Conclusion: In the USA, over 130 LT have listed Covid-19 as the diagnosis indication. Although Covid-19 ARDS makes up for the majority of these LT, other diagnosis are post Covid pulmonary fibrosis and underlying fibrosis with SARS-CoV-2 induced exacerbation. LT for ARDS poses several challenges and is reserved for the minority of carefully selected patients dependent on extracorporeal life support. As others have reported, good short-term survival is described.

Behavioral Health Services/Psychiatry/Neuropsychology
Talati N, **Toledo T**, and **Akinyemi E**. MANAGEMENT OF DEPRESSION IN ALS WITH THE USE OF METHYLPHENIDATE AND SERTRALINE. *Am J Geriatr Psychiatry* 2022; 30(4):S123-S124. PMID: Not assigned. Full Text

Behavioral Health Services/Psychiatry/Neuropsychology
Triemstra J, Bartiss M, Bourassa E, Beltz E, Lickiss S, Lowery L, and **Felton J**. THE FEASIBILITY AND ACCEPTABILITY OF BEHAVIORAL ACTIVATION IN AN ADOLESCENT CLINICAL SETTING. *J Adolesc Health* 2022; 70(4):S68-S69. PMID: Not assigned. Full Text

Cardiology/Cardiovascular Research
Al-Darzi W, **Aurora L**, **Cowger J**, **Tanaka D**, **Lemor A**, **Koenig G**, and **Parikh S**. Hemodynamic and Echocardiographic Assessment of Left Ventricle Recovery with Left Ventricular Assist Devices: Do We Explant? *J Heart Lung Transplant* 2022; 41(4):S234-S235. PMID: Not assigned. Full Text

W. Al-Darzi, Cardiology, Henry Ford Hospital, Detroit, MI, United States

Introduction: Explantation of left ventricular assist devices (LVAD) after left ventricular (LV) recovery is estimated to occur in 1-2% of cases. Herein, we present a case of hemodynamic and echocardiographic assessment of LV recovery during outflow graft balloon occlusion leading to LVAD explantation. Case Report: A 56-year-old female with medical history of systolic heart failure due to non-ischemic cardiomyopathy with LVEF 25%. She underwent an urgent HeartMate 3 LVAD implant after an admission for cardiogenic shock. Post LVAD course was complicated by driveline infection. History was notable for admissions due to low-flow alarms in the setting of dehydration. On echocardiogram, progressive LVEF

improvement was noted although with suboptimal images. CT angiography did not demonstrate any occlusion of the cannulas. Right heart catheterization showed stable cardiac index despite minimal flow on LVAD. Cardiopulmonary testing was favorable. After multi-disciplinary discussion, patient underwent LVAD wean study in the cath lab under hemodynamic and transesophageal echo (TEE) guidance with therapeutic anticoagulation. LVAD was turned off for 10 minutes with outflow graft occluded by Armada 14 mm x 20 cm peripheral balloon. Wiring of the outflow graft from aorta and balloon occlusion were visualized by TEE (Figure). The left and right ventricular function were similar to baseline with no change in mitral regurgitation. Cardiac index was normal (Figure). Patient subsequently underwent successful LVAD explant. She is doing well with NYHA class I symptoms and LVEF 45-50% noted upon 3-months follow-up LVAD explantation is a feasible option in LV recovery after appropriate hemodynamic and echocardiographic assessment. TEE is an essential tool, especially in patients with suboptimal windows. Outflow graft balloon occlusion can be used if there is concern about falsely poor results related to backflow or ongoing LVAD support at low speed leading to falsely improved results

Cardiology/Cardiovascular Research

Al-Darzi W, **Mukherjee A**, **Cowger J**, and **Hannawi B**. A Case of Muscular Dystrophy with Dilated Cardiomyopathy: Do Not Forget Your Basics. *J Heart Lung Transplant* 2022; 41(4):S456. PMID: Not assigned. Full Text

W. Al-Darzi, Cardiology, Henry Ford Hospital, Detroit, MI, United States

Introduction: Becker muscular dystrophy (BMD) is an X-linked recessive disorder with dystrophin mutation. Dilated Cardiomyopathy (DCM) is a leading cause of death in BMD patients. Herein, we are presenting a patient with BMD that initially sought medical attention for acute onset of systolic heart failure that highlights the importance of careful clinical assessment and appropriate work up. Case Report: A 29-year-old male with medical history of asthma presented to the hospital with progressive dyspnea and leg swelling. He was diagnosed with DCM with an LVIDD of 6.5 cm and LV ejection fraction of 20-25% by echocardiogram. Coronary angiogram revealed no coronary artery disease. Initial blood work and electrocardiogram are below (Figure). Cardiac MRI showed severely reduced biventricular systolic function with near circumferential, sub-epicardial to mid-myocardial delayed gadolinium enhancement (Figure). Initial differential diagnosis included prior myocarditis vs. burnt out sarcoidosis. It was subsequently noted that patient began recurrently falling with muscle weakness from age 20 years with chronically elevated AST and CK. His exam was notable for atrophy of the bilateral quadriceps muscles, decreased muscular strength and bilateral calves hypertrophy. Electromyography showed evidence of chronic proximal and distal myopathy, predominantly affecting the lower extremity. Skeletal muscle biopsy showed fascicular atrophy and hypertrophy, focal endomyosial fibrosis and an increase of central nuclei without evidence of inflammation or granuloma which was most suggestive of a muscular dystrophy. Genetic testing was then completed and showed hemizygous dystrophin mutation confirming diagnosis of BMD. BMD has a diffuse phenotype and should be considered in young patients with cardiomyopathy and chronically elevated CK and AST. A thorough clinical history, exam, and CMR can assist in directing need for skeletal muscle biopsy and subsequent genetic testing.

Cardiology/Cardiovascular Research

Boshara A, **Ananthasubramaniam K**, **Russell C**, **Bradley P**, **Nadeem O**, and **Cowger J**. Sarcoidosis: Hiding in Plain Sight. *J Heart Lung Transplant* 2022; 41(4):S345. PMID: Not assigned. Full Text

A. Boshara, Advanced Heart Failure and Transplant Cardiology, Henry Ford Hospital, Detroit, MI, United States

Introduction: Sarcoidosis is a systemic disease that can masquerade as many conditions. Due to its often patchy distribution, myocardial biopsy is only ~30% sensitive. Herein we present a case of sarcoidosis diagnosed from an extra-cardiac biopsy years after the onset of cardiomyopathy. Case Report: A 54 year old man initially presented with dyspnea and fatigue due to new onset HFrEF of 20%. He had a significant family history of SCD. His workup revealed non-obstructive CAD, a myxomatous mitral valve with bileaflet prolapse and moderate regurgitation, and a cystic structure attached to the tricuspid valve. Given his frequent ventricular ectopy, he was discharged on guideline therapy for HFrEF and a wearable

cardioverter defibrillator. Genetic testing for dilated cardiomyopathies revealed EYA4 and TTN variants of unknown significance. A cardiac MRI a few months later demonstrated no abnormal late gadolinium enhancement and persistent systolic dysfunction, so he underwent AICD implant. His course was further complicated by recurrent admissions for supraventricular and ventricular tachyarrhythmias. A cardiopulmonary exercise stress test demonstrated low-risk results. Further evaluation noted prolonged AV conduction. A RHC revealed mild post-capillary pulmonary hypertension and a mildly decreased cardiac index at 2.01 L/min/m2. Months later, he underwent CRT-D upgrade. He started improving functionally until he developed left eyelid swelling, initially thought to be lymphoma. An orbital biopsy revealed non-caseating granulomas. A PET/CT demonstrated FDG uptake within subcarinal lymph nodes but no cardiac uptake. Initially he declined immunomodulatory therapy, but as his symptoms worsened, he started corticosteroids and transitioned to mycophenolate mofetil due to intolerance of methotrexate. Due to disease progression on repeat FDG-PET, he was switched to infliximab. The diagnosis of sarcoidosis can be difficult due to its variable presentation, including heart block, heart failure, ventricular arrhythmias and sudden cardiac death. Cardiac involvement occurs in 25% of cases. Our case was complicated by a cMRI that was negative for cardiac involvement, which emphasizes the importance of complimentary inflammatory imaging with FDG-PET. A multidisciplinary approach is needed that engages sarcoid specialists for earlier diagnosis to ensure rapid initiation of therapy to reduce end-organ dysfunction.

Cardiology/Cardiovascular Research
Chamogeorgakis T, Toumpoulis I, **Lanfear D**, **Williams C**, Koliopoulou A, Adamopoulos S, and **Cowger J**. Right Ventricular Failure Following Left Ventricular Assist Device Implant: An Intermacs Analysis. *J Heart Lung Transplant* 2022; 41(4):S31. PMID: Not assigned. Full Text

T. Chamogeorgakis, Henry Ford Health System/Transplant Institute, Detroit, MI, United States

Purpose: Right heart failure (RHF) management following LVAD include inotropes, right ventricular mechanical support and heart transplant. We analyzed the outcomes of severe RHF following implant of a fully magnetically levitated or hybrid magnetic centrifugal durable LVAD. Methods: In this INTERMACS analysis we identified patients who developed severe RHF following LVAD from 2013 until 2020 as bridge to recovery or transplant. Patients were categorized in three groups based on RHF treatment strategy: inotrope support (group 1), temporary mechanical support (group 2), and durable centrifugal RVAD (group 3). Kaplan Meier and Cox-regression survival analysis between groups was undertaken. Logistic regression analysis for new onset dialysis was conducted. Results: 2509 patients developed severe RHF after LVAD. 2199 (87.6%) patients were managed with inotropes (group 1), 233 (9.3%) with temporary RVAD (group 2) and 77 (3.1%) with durable RVAD (group 3). Group 1 had fewer patients with INTERMACS profile 1 and 2 (21.6%, $p<0.001$). One year survival was 84.6%, 59.3%, and 63.8% in groups 1,2, and 3 (mortality HR=2.4 and 3.3 for groups 2 and 3 vs. group 1, $p<0.05$). One year survival to transplant was 27%, 36.5%, and 53.6% in groups 1, 2, and 3, respectively ($p<0.05$). Group 2 had higher incidence of new onset dialysis (42.6%, $p=0.049$). Conclusion: Survival with RHF following LVAD implant varies based on treatment strategy; inotrope support is associated with increased survival. Patients with durable RVAD are more likely to survive to transplant. Patient selection studies for durable RVAD with contraindications for transplant are necessary.

Cardiology/Cardiovascular Research
Hencken L, **Grafton G**, **To L**, **Nemeh H**, and **Cowger J**. Peri-Operative Warfarin Protocol to Decrease Length of Stay After Left Ventricular Assist Device Implantation. *J Heart Lung Transplant* 2022; 41(4):S462. PMID: Not assigned. Full Text

L. Hencken, Pharmacy, Henry Ford Hospital, Detroit, MI, United States

Purpose: A limitation to left ventricular assist device (LVAD) implantation is cost with fixed reimbursement rates for the LVAD implantation hospitalization regardless of hospital length of stay and costs. Patients must have a therapeutic INR on warfarin prior to discharge which can take days and delay discharge. The purpose of this study is to evaluate the impact of a peri-operative warfarin protocol on decreasing length of stay during index LVAD implantation. Methods: This is a retrospective single center study of adult

patients undergoing LVAD implantation between January 1, 2019 and December 31, 2020. Patients who died during the admission were excluded. Patients in the intervention group (INT) underwent LVAD between January 1-December 31, 2020. The peri-operative warfarin protocol included pre-operative vitamin K dosing according to INR, initiation of warfarin by post-operative day (POD) 3, and warfarin titration scheme. The historical control group (CON) included patients receiving LVADs between January 1-December 31, 2019. Warfarin start date was at the discretion of providers. All patients had a goal INR of 2-3. Endpoints included length of stay, post-operative warfarin start date, time to therapeutic INR, warfarin dosing requirements, pre-operative vitamin K dosing and bleeding complications. Results: Seventy-seven patients were included; n=41 (53.2%) CON and n=36 (46.8%) INT. Total hospital length of stay was 35 [26,43] days in the CON group compared to 27.5 [24,35] days in the INT group (p=0.095). Warfarin was started earlier in the INT group (POD 5.5 [2.8,7.0]) compared to the CON group (POD 8 [6,14]) (p=0.004). Time to therapeutic INR remained the same between the two groups with a median of 6 days. Pre-operative vitamin K decreased from 15 [10,15] mg in the CON group to 5 [0.0,11.3] mg in the INT group (p=<0.001). There was no increase in bleeding with the peri-operative warfarin interventions: 8 bleeds in the CON group and 4 bleeds in the INT group. Conclusion: Initiating warfarin earlier post-operatively may help decrease hospital length of stay after LVAD implantation without increasing bleeding events.

Cardiology/Cardiovascular Research

John R, Kanwar MK, Cleveland JC, Uriel N, Naka Y, Salerno C, Horstmanshof D, Hall SA, **Cowger J**, Heatley G, Somo SI, and Mehra MR. Concomitant Valvular Procedures During LVAD Implantation and Outcomes: An Analysis of the MOMENTUM 3 Trial Portfolio. *J Heart Lung Transplant* 2022; 41(4):S24. PMID: Not assigned. Full Text

R. John, University of Minnesota Medical Center, Minneapolis, MN, United States

Purpose: Correction of valvular pathology is often undertaken in patients undergoing LVAD implantation but impact on outcomes is uncertain. We compared clinical outcomes with HeartMate 3 (HM3) LVAD implantation in those with concurrent valve procedures (VP) to those with an isolated LVAD implant within the MOMENTUM3 trial portfolio, including the Pivotal Trial (n=515, NCT02224755) and Continued Access Protocol/ CAP (n=1685, NCT02892955). Methods: The study included 2200 HM3 implanted patients. Among 820 concurrent procedures (including VP, CABG, RVAD, LAA closure), 466 (21.8%) were VPs (HM3+VP), including 81 aortic, 61 mitral, 163 tricuspid, and 85 patients with multiple VPs. Short and Long-term outcomes including peri-operative complications and healthcare resource use, major adverse events and survival were analyzed. Results: Patients undergoing HM3+VP were older (63[54-70] vs. 62[52-68] yrs), with a sicker INTERMACS profile (1-2:41% vs.31%) and higher central venous pressure (11[8-16] vs. 9[6-14] mmHg) compared to HM3 alone (all p<0.05). The cardiopulmonary bypass time (124[97-158] vs.76[59-96] mins); ICU (8.5 [5-16] vs. 7 [5-13]) and hospital length of stay (20 [15-30] vs. 18 [14-24] days) were longer in HM3+VP (all p<0.0001). A significantly higher incidence of stroke (4.9% vs. 2.4%), bleeding (33.9% vs. 23.8%) and right heart failure (41.5% vs. 29.6%) was noted in HM3+VP for 0-30 days post-implant (all p<0.01), but 30-day survival was similar between groups (96.7% vs. 96.1%). There was no difference in 2-year survival in HM3+VP vs HM3 alone patients (HR[95%CI]:0.93 [0.71-1.21];p=0.60). Analysis of individual VPs showed no significant differences in survival compared to HM3 alone (Figure). Conclusion: Concurrent VPs are commonly performed during LVAD implantation, are associated with increased morbidity during the index hospitalization, but short and long-term survival are not impacted adversely when compared with those that undergo an isolated LVAD procedure.

Cardiology/Cardiovascular Research

Kaczorowski DJ, Kanwar MK, Molina EJ, Dardas TF, Cogswell R, Rogers JG, Deng L, Cantor RS, Estep JD, Cleveland JC, Gosev I, Sandau KE, McIlvennan C, Pagani FD, and **Cowger JA**. Defining Metrics for Short Term Success After LVAD Implant: An Analysis of the Society of Thoracic Surgeons Intermacs Registry. *J Heart Lung Transplant* 2022; 41(4):S350-S351. PMID: Not assigned. Full Text

J.A. Cowger, Cardiovascular Medicine, Henry Ford Health System, Detroit, MI, United States

Purpose: While clinical trials evaluating left ventricular assist device (LVAD) technology typically use composite outcomes to assess efficacy, composite outcomes including patient reported outcomes (PROs) have not been utilized as benchmarks for LVAD implant center performance improvement initiatives or quality ranking. The objective of the study was to assess the feasibility of generating a patient composite outcome measure including PROs from a real world registry. Methods: Short term (ST, 180 days) adverse events (AEs) and mortality were tallied for Intermacs patients undergoing LVAD implant between 1/2012 and 12/2019. ST postoperative events included mortality on first device and frequencies of stroke, reoperation (device malfunction/other), right heart failure (RHF), prolonged respiratory failure, and/or dialysis on first device. Logistic regression was used to generate odds ratios for mortality for each AE. Separately, the EuroQOL visual analog scale (VAS) was assessed at baseline and 180 days in ST survivors. Results: Of 20,115 patients, 37% suffered at least one event, most commonly death, reoperation and stroke (Table, column A). Stroke, prolonged respiratory failure, and dialysis attributed the most to ST mortality (Table, column B). Of the 16725 patients alive at 180 days, 43% completed a VAS with 82.0% showing VAS improvement. Renal failure and RHF contributed most to failure to improve VAS (Figure). Conclusion: Assessment of a ST composite outcome metric after LVAD implant from a real world data source is feasible but limited by incomplete PRO reporting. ST adverse events display differential effects on mortality and PROs that can be used in development of global rank outcome scores. While reoperation is common, stroke, prolonged respiratory failure and renal failure conferred highest risks of ST deaths within Intermacs. Assessment of PROs should become a priority for LVAD centers to allow the field to generate a complete assessment of patient-centered outcomes.

Cardiology/Cardiovascular Research

Kanwar M, Pagani FD, Estep JD, Pinney SP, Silvestry SC, Uriel N, Goldstein DJ, Mehra MR, Cleveland JC, Kormos RL, Wang A, Chuang J, and **Cowger JA**. Variability Across Implanting Centers in Short and Long-Term Mortality and Adverse Events in Patients on HeartMate 3 Support: A Momentum 3 Secondary Analysis. *J Heart Lung Transplant* 2022; 41(4):S120. PMID: Not assigned. Full Text

J.A. Cowger, Cardiovascular Medicine, Henry Ford Health System, Detroit, MI, United States

Purpose: We aimed to characterize center-specific variability in HeartMate 3 (HM3) patient survival within the MOMENTUM 3 studies and to examine the correlation between implanting center survival and major adverse events (AEs). Methods: Center HM3 implant volume during the MOMENTUM 3 pivotal (n=515) and continued access protocol (n=1685) trials were tallied. Centers implanting ≤16 HM3 patients (25th percentile) were excluded. De-identified center variability in mortality was assessed at 90 days and 2 years using direct adjusted survival while accounting for key baseline risk factors. The 90-day frequency and 2-year rates of stroke, bleeding, and infection were compared across centers and correlations between survival and event rate variability were assessed. Results: Among 48 centers, 1957 HM3 patients were included in this analysis with site implants ranging between 17 to 103 patients. Patient cohorts differed across the sites by age (average 52-68 years), sex (60-95% male), destination therapy intent (25-100%), and %INTERMACS profile 1-2 (2-81%). At 90 days, center adjusted median mortality was 6.5%, nadiring at ≤3.2% (25th percentile) and peaking at ≥10.5% (75th percentile). Median 2-year center adjusted mortality was 18.6%, nadiring at ≤14.0% and peaking at ≥25.2% (figure A). AEs were also highly variable across centers; centers with low mortality tended to have lower AE rates at 2 years (figure B). Conclusion: Patient characteristics and outcomes were highly variable across MOMENTUM 3 centers despite trial preoperative inclusion/exclusion criteria. Many centers had exemplary risk-adjusted HM3 patient outcomes. Studies are needed to improve our understanding of top performing centers' best practices as they relate to HM3 care in the pre, interoperative, and chronic support stages in an effort to further improve HM3 LVAD-associated clinical outcomes.

Cardiology/Cardiovascular Research

McCarthy S, Molina E, **Nemeh H**, Chaudhry S, Pinney S, Srivastava A, Grinstein J, Hackett I, and **Cowger JA**. Characterizing Outflow Graft Narrowing over Time. *J Heart Lung Transplant* 2022; 41(4):S138. PMID: Not assigned. Full Text

S. McCarthy, Wayne State School of Medicine, Wayne State, Detroit, MI, United States

Purpose: Cases of pump dysfunction due to outflow graft (OG) anastomosis obstruction related to serous fluid accumulation have been reported but the rate of occlusion and actual frequency of asymptomatic OG diminution is not known. Methods: This was a multicenter retrospective analysis of patients on HeartMate II (HMII) or HeartMate 3 (HM3) support surviving at least 180 days with at least one chest computed tomography (CT) scan at 6 months, 1, 2, and/or 3 years postoperative. Patients with OG obstruction due to torsion were excluded. The outflow graft (OG) diameter was measured at its narrowest region; region was categorized as external outflow graft (EOG), mid-graft, or within 2 cm of the aortic anastomosis. Mixed models with repeated measure linear regression was used to assess OG diameter change over time, with 14 mm as reference. Using the narrowest measure, OG diameter was modelled for freedom from death, admission for HF and low flow alarms with hazard ratio [95% CI presented]. Results: Of 71 patients included herein, 25% and 75% were on HMII and HM3 support for a median [25th, 75th] 1230 [703,1592] days. The median CT count was 2 [1,2] per patient. At follow-up, small (1-3 mm, table), but statistically significant reductions in OG diameter were noted (Figure). The median OG narrowing was 7% [0%, 20%]. Time from device implant was the most significant contributing factor ($p<0.001$) while wrapping of the outflow was nonsignificantly correlated with OG narrowing ($p=0.071$). Device model was not correlative ($p=0.16$). OG diameter was not correlated with survival (HR 1.04 [0.81-1.3]), stroke (HR 0.94 [0.78-1.1]) or admissions for heart failure (HR 1.06 [0.88-1.3]), or VAD alarms (HR 0.93 [0.79-1.1]). Conclusion: Minor narrowing of the OG was noted over time, irrespective of LVAD model. The observed degrees of non-twist related-OG narrowing herein did not lead to increase mortality or events. OG wrapping may be associated with OG narrowing over time. Larger sample analyses aim to define degrees of narrowing that elicit device dysfunction.

Cardiology/Cardiovascular Research

Mehra MR, Nayak A, Morris A, **Lanfear DE**, **Nemeh H**, Desai S, Bansal A, Guerrero-Miranda C, Hall S, Cleveland JC, Goldstein DJ, Uriel N, Chen L, Bailey S, Anyanwu A, Heatley G, Chuang J, and Estep JD. Development and Validation of a Personalized Risk Score for Prediction of Patient-Specific Clinical Experiences with HeartMate 3 LVAD Implantation: An Analysis from the MOMENTUM 3 Trial Portfolio. *J Heart Lung Transplant* 2022; 41(4):S23-S24. PMID: Not assigned. Full Text

M.R. Mehra, Brigham and Women's Hospital, Boston, MA, United States

Purpose: Although clinical trials inform on efficacy of left ventricular assist device (LVAD) therapy, individualized risk assessments for outcome prediction are important in guiding implementation of such treatment. In this analysis based on the MOMENTUM 3 trial portfolio (studies sponsored by Abbott), we seek to develop and validate patient-specific risk scores to facilitate the evaluation of candidates for HeartMate 3 (HM3) LVAD implantation. Methods: The MOMENTUM 3 trial portfolio includes 2200 patients that underwent HM3 LVAD implantation in the pivotal trial and Continued Access Protocol (CAP) study, between 2014-2018. Patients were followed for 2 years, and the primary results were presented at ISHLT 2021 and published in Eur J Heart Fail. 2021;23:1392-1400. In this analysis, we shall randomly assign all enrolled patients implanted with the HM3 LVAD to a Derivation Cohort or an internal Validation Cohort. The Derivation Cohort will be used to develop multivariate regression models incorporating common, pre-implant patient parameters that are typically assessed when an informed decision is established. Calculation of the risk scores will be based on the parameter estimates of the final derived models. Receiver operating characteristic curve analysis will be used to evaluate the discriminatory ability of each risk score. The ability of the risk scores to predict outcomes after HM3 LVAD implantation will be tested independently in the Validation Cohort (results expected by February 2022). To avoid bias in the development of the scores, the Validation Cohort will only be analyzed after the risk models are derived. The risk scores will include estimates (and range of individual outcomes) for endpoints including short and long-term survival, hospitalization burden, quality of life, hemocompatibility and non-hemocompatibility related adverse events. Endpoints: The scientific discovery and validation of personalized risk scores will inform clinicians on expectations of individualized outcomes through the clinical journey following HM3 LVAD implantation. Such risk scores and individualized estimates for outcomes will facilitate enhanced decision-making and guide communication among clinicians and patients when considering LVAD therapy in advanced heart failure.

Cardiology/Cardiovascular Research
Nayak A, Hu Y, Patel KJ, Ko Y, Okoh AK, Wang J, Mehta A, Liu C, Pennington J, Xie R, Kirklin JK, Kormos RL, Simon MA, **Cowger J**, and Morris AA. Machine Learning Algorithms Identify Distinct Phenotypes of Right Heart Failure After Left Ventricular Assist Device Implant. *J Heart Lung Transplant* 2022; 41(4):S39. PMID: Not assigned. Full Text

A. Nayak, Emory University, Atlanta, GA, United States

Purpose: The challenges of predicting right heart failure (RHF) post-Left Ventricular Assist Device (LVAD) may reflect heterogenous underlying pathophysiology. We hypothesized that 1) machine learning (ML) algorithms applied to multidimensional phenotypic data from patients with confirmed post-LVAD RHF will allow identification of distinct RHF phenotypes, 2) identified phenotypes will have unique clinical trajectories. Methods: Patients with acute post-LVAD RHF (RVAD and/or ≥ 14 days inotropes post-implant, n=2,550) were identified from the ISHLT Mechanically Assisted Circulatory Support database (n=15,428); and divided into a derivation (DC, n=1,531) and validation cohort (VC, n=1,019). First, unsupervised ML (blinded to clinical outcomes) was applied to 41 pre-implant variables to identify distinct phenotypes. Then, resultant phenotypes were clinically validated by comparing outcomes of 1) RVAD/ death during index hospitalization 2) ICU Length of Stay. Results were validated in the VC. Risk discrimination of existing RHF risk scores was compared between phenotypes. Results: Four distinct RHF phenotypes were identified. (Figure 1) Phenotype I had the worst, and Phenotype III had the best outcomes. Results were validated in the VC. RHF risk scores were modestly accurate at predicting RHF in those with severe shock (Phenotype I) pre-implant; but performed poorly for phenotypes without prominent shock. (Table 1) Conclusion: ML identifies novel pathophysiological phenotypes of RHF, among which current risk scores were useful to predict RHF only in patients in severe shock prior to implant.

Cardiology/Cardiovascular Research
Qutob O, **Rama S**, **Black L**, **Zubalik M**, **Bensenhaver J**, **Petersen L**, **Nathanson SD**, **Tepper D**, **Yoho D**, **Evangelista M**, and **Atisha D**. The effect of lymphatic microsurgical preventive healing approach (LYMPHA) on the development of upper-extremity lymphedema following axillary lymph node dissection in breast cancer patients. *Ann Surg Oncol* 2022; 29(SUPPL 1):40-41. PMID: Not assigned. Full Text

Hematology-Oncology
Besse B, Johnson M, Ou SHI, **Gadgeel S**, Spira A, Lin J, Felip E, van der Wekken AJ, Calles A, de Miguel MJ, Camidge DR, Elamin Y, Lopes GDL, Liu S, Bauman J, Haggstrom D, Riley G, Pelish HE, Zhu VW, and Drilon A. Clinical evaluation of NVL-520, a highly selective ROS1 inhibitor in patients with advanced ROS1-positive solid tumors: The phase I/II ARROS-1 study. *Ann Oncol* 2022; 33:S68-S69. PMID: Not assigned. Full Text

Hematology-Oncology
Ghanem AI, **Maahs L**, **Gutta R**, **Tang A**, **Gilbert M**, **Arya S**, **Saheli ZA**, **Tam S**, **Sheqwara J**, and **Siddiqui F**. Does Cetuximab Reduce the Risk of Anemia in Patients Undergoing Radiation Therapy for Head and Neck Cancers? *Int J Radiat Oncol Biol Phys* 2022; 112(5):e61-e62. PMID: Not assigned. Full Text

A.I. Ghanem, Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, United States

Purpose/Objective(s): Epidermal growth factor receptor (EGFR) activation is associated with increased production of interleukin 6 (IL6), which is intensified by radiotherapy (RT) induced inflammatory response. Elevated IL6 levels promote RT-induced anemia by upregulating hepcidin causing functional iron deficiency. Cetuximab, an EGFR inhibitor, resulted in significantly lower rates of RT induced anemia for locally advanced head and neck squamous cell carcinoma (HNSCC) patients receiving definitive RT vs RT-alone according to Bonner et al; and other studies compared to concomitant chemotherapy. However, little is known for cases receiving cetuximab with RT in the adjuvant setting. Materials/Methods: We queried our institutional HNSCC database for surgically staged non-metastatic cases that received adjuvant RT with or without concomitant cetuximab between 2006-2018. Cetuximab was administered for

some high-risk cases medically unfit for platinum agents per multidisciplinary team evaluation. All included patients need to have at least one complete blood count pre- and post-RT end. We compared RT-cetuximab vs RT-alone for prevalence of baseline and post-RT anemia, defined as Hb below 12g/dL in females and 13g/dL in males, and mean hemoglobin (Hb) levels. We also assessed the improvement in Hb level post-RT (resolution of baseline anemia or Hb increase of at least 1g/dL above baseline), in addition to overall survival (OS) in relation to anemia/Hb dynamics. Results: We were able to identify 66 patients who fit our inclusion criteria, of which 27 (41%) received RT-cetuximab, with the remaining receiving RT-alone (n=39, 59%). Median age was 62.5 years (range, 34-88 years), males 80%, black 29%, and 85% had a smoking history. The majority of cases (73%) were locally advanced. Oral cavity and oropharynx were the most common subsites (37.5% each), with HPV+ve cases representing 52% of the later. The study groups were well-balanced, except for higher rates of positive final surgical margins, and extracapsular space invasion and median RT dose ($p<0.05$). Baseline anemia was diagnosed in 70.4% in RT-cetuximab vs 76.9% in the RT-alone, $p=0.76$; with similar mean Hb level (11.7g/dL in both). Meanwhile, baseline iron, vitamin-B12 and folate deficiencies, and chronic kidney disease were non-different. After completion of RT, mean Hb was significantly higher in the RT-alone (12.9±1.4 g/dL) compared to RT-Cetuximab (11.9±2.1 g/dL), $p=0.02$. Nevertheless, higher anemia levels (70% vs 51%) and lower improvement of Hb post-RT (81.5% vs 92.3%) were both non-significant for RT-cetuximab vs RT-alone respectively, $p>0.05$ for both. On multivariate analysis, baseline anemia was associated with worse OS ($p=0.0052$), unlike improvement of Hb post-RT ($p=0.14$) with a corresponding better improvement of Hb (56.4% vs. 25.9%, $p=0.014$), albeit lower anemia levels (70% vs. 51%), was non significant ($p=0.195$). On multivariate analysis, lack of baseline anemia was associated with better OS ($p=0.0052$), whereas improvement of Hb post-RT was only marginal ($p=0.068$). Conclusion: In a homogenous cohort of HNSCC patients treated postoperatively, concomitant cetuximab was not associated with lower RT-induced anemia, in contrast to previous studies.

Infectious Diseases

Franco-Palacios DJ, **Allenspach L**, **Stagner L**, **Pinto-Corrales J**, **Hanlon K**, **Nappo T**, **Sherbin E**, **Sternberg D**, **Dillon W**, **Simanovski J**, and **Alangaden G**. Early Outcomes of Lung Transplantation for COVID-19 Related Lung Disease. Single Center Experience. *J Heart Lung Transplant* 2022; 41(4):S393. PMID: Not assigned. Full Text

D.J. Franco-Palacios, Pulmonary and Critical Care, Henry Ford Hospital, Detroit, MI, United States

Purpose: Lung transplantation (LT) is a lifesaving treatment for Covid-19 related lung disease with early outcomes similar to other indications. Methods: Seven patients underwent LT for Covid-19 related lung disease at our center: 5 for ARDS and 2 for IPF exacerbation post SARS-CoV-2 infection. Results: Seven patients (5 men) with single organ failure underwent bilateral LT. Median age was 47 years old. All ARDS cases had poor lung mechanics on invasive mechanical ventilation with radiographic evidence of lung fibrosis: pneumatocele, GGO, consolidations, subpleural reticulations and traction bronchiectasis. vvECMO was bridge to transplant in 5 cases (bridge to recovery in 2). Median ECMO duration for ARDS was 32 days (range 7-99). Median time to LT from Covid diagnosis was 59 days (Q1-IQ3, 54-62). Two patients were post-partum women with ARDS. Explanted pathology showed UIP, DAD, diffuse hemorrhage and one case of fibrosing NSIP. Pulmonary hypertension was seen in 4 cases. One patient did not survive. Organizing pneumonia and granuloma were present in this patient. Most ARDS patients were unable to tolerate lower sedation and consent by a substitute decision-makers was obtained. Post operative ECMO decannulation was possible in all cases. Induction, maintenance immunosuppression and antimicrobials were standard for our program. Donated grafts were from deceased brain death donors and negative for 2019-nCoV. Rehabilitation potential and strong social support were absolute inclusion criteria. All survivors have excellent lung function. Conclusion: In the USA, over 130 LT have listed Covid-19 as the diagnosis indication. Although Covid-19 ARDS makes up for the majority of these LT, other diagnosis are post Covid pulmonary fibrosis and underlying fibrosis with SARS-CoV-2 induced exacerbation. LT for ARDS poses several challenges and is reserved for the minority of carefully selected patients dependent on extracorporeal life support. As others have reported, good short-term survival is described.

Infectious Diseases

Franco-Palacios DJ, **Allenspach L**, **Stagner L**, **Pinto-Corrales J**, **Hanlon K**, **Waynick L**, **Nicholson D**, **Shaheen E**, **Spezia M**, **Nappo T**, **Dillon W**, **Sherbin EL**, and **Alangaden G**. Outcomes of SARS-CoV-2 Infection in Lung Transplant Recipients: A Single Center Experience. *J Heart Lung Transplant* 2022; 41(4):S523. PMID: Not assigned. Full Text

D.J. Franco-Palacios, Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI, United States

Purpose: Outcomes of Covid-19 in lung transplant recipients (LTr) were reported in the beginning of the pandemic. Only few centers reported on their experience since December 2020 when vaccines received emergency use authorization. We aim to investigate the outcome of SARS-CoV-2 infection in a cohort of LTr at our center in Detroit, Michigan. Methods: Retrospective chart review study of adult LTr with confirmed SARS-CoV-2 infection from March 2020 to August 2021. Results: Thirty LTr were diagnosed with SARS-CoV-2 infection confirmed by RT PCR of nasopharynx. Median age at diagnosis was 63; 53% were males; 57% Caucasians and 40% of African descendance. Most patients underwent bilateral LT for interstitial lung disease (46%) and for pulmonary sarcoidosis (23%). The median time post LT was 3.1 years. Most patients needed hospitalization for respiratory failure secondary to Covid-19 (73%). Eleven patients were initially managed as outpatient. Five patients received outpatient combination of monoclonal antibodies with three of them later requiring hospitalization for development of hypoxia. None of the patients with initial out of the hospital management died. Amongst 21 hospitalized LTr, six patients were diagnosed with severe pneumonia and ARDS requiring heated high flow and invasive mechanical ventilation (IMV) in 4 patients. 28-day mortality was 10% and ICU mortality was 25% (50% mortality in those on IMV). Twelve hospitalized patients (57%) were treated with remdesivir. Augmented systemic corticosteroids was used in 85% of cases. Cycle cell inhibitor was held in 71% of the cases. Bilateral ground glass opacities of the allografts were common. None of the patients that received at least one dose of mRNA vaccine died. Conclusion: Outcomes in LTr infected with SARS-CoV-2 varies. Early reports showed high mortality rate in severe and critical Covid-19 in LTr. Although hospitalization rate in this cohort was high, only four patients in our cohort required IMV during acute Covid-19. Two of them died; both were unvaccinated. Another unvaccinated patient died due to allograft rejection two months after testing positive to SARS-CoV-2. Most cases were mild to moderate despite frequent radiographic findings of pneumonia. Underreporting and exclusion of mild cases as well as likely protective effect of vaccination and use of monoclonal antibodies may explain our different outcomes.

Infectious Diseases

Simanovski J, **Nemeh HM**, **Allenspach LL**, **Mei LL**, **Stagner LD**, **Pinto JC**, **Olexsey KM**, **Franco-Palacios DJ**, and **Alangaden GJ**. Risks and Outcomes Associated with Pleural Space Infections After Lung Transplantation. *J Heart Lung Transplant* 2022; 41(4):S394. PMID: Not assigned. Full Text

J. Simanovski, Transplant Institute, Henry Ford Health System, Detroit, MI, United States

Purpose: Pleural space infections (PSI) are a serious complication after lung transplantation (LT) however there is limited data on the associated risk factors and outcomes of PSI. We examined: 1) risk factors associated with PSI after LT; 2) effect of PSI on LT outcomes. Methods: This is a retrospective single center cohort study of 74 consecutive LT recipients (1/2018- 6/2020). Patients were divided into infected and non-infected groups, where PSI were defined as post-LT pleural effusions with pathogen(s) isolated from pleural fluid. Data were collected and compared between two groups with two-sample t-test or Fisher-exact. Multivariable logit model was performed with estimations of odds ratio (OR) and its confidence interval [CI]. Results: Among 74 LT recipients, 38 (51%) developed pleural effusions requiring drainage; of them 16 (42%) had PSI. Baseline demographics were similar in patients with and without PSI (Table). Notably, 88% of PSI group received steroids pre-LT compared to 55% in the non-infected group ($p<0.05$); 88% of the PSI group had an underlying diagnosis of interstitial lung disease versus 45% of the non-infected group ($p<0.01$). Overall post-operative complications occurred more frequently in the PSI group vs. non-infected group 77% vs. 25% ($p<0.01$) and airway complications in 86% vs. 44% ($p<0.01$). Hospital length of stay was longer in the PSI group with the median of 78 versus 31 days in the non-infected group ($p<0.01$). Results of logistical modeling showed high risk of PSI with presence of post-LT

airway complications (OR =10.8 95% CI 1.7- 72.5) and presence of post operative complications (OR=10.6, 95% CI 1.8-63.5). There was no difference in the incidence of readmissions, acute cellular rejection or 1 year mortality between the two cohorts. Conclusion: PSI remain a prevalent yet under-studied complication. Airway or post-operative complications after LT were associated with PSI. One-year outcomes were similar in LT recipients with and without PSI.

Internal Medicine

Ghanem AI, **Maahs L**, **Gutta R**, **Tang A**, **Gilbert M**, **Arya S**, **Saheli ZA**, **Tam S**, **Sheqwara J**, and **Siddiqui F**. Does Cetuximab Reduce the Risk of Anemia in Patients Undergoing Radiation Therapy for Head and Neck Cancers? *Int J Radiat Oncol Biol Phys* 2022; 112(5):e61-e62. PMID: Not assigned. Full Text

A.I. Ghanem, Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, United States

Purpose/Objective(s): Epidermal growth factor receptor (EGFR) activation is associated with increased production of interleukin 6 (IL6), which is intensified by radiotherapy (RT) induced inflammatory response. Elevated IL6 levels promote RT-induced anemia by upregulating hepcidin causing functional iron deficiency. Cetuximab, an EGFR inhibitor, resulted in significantly lower rates of RT induced anemia for locally advanced head and neck squamous cell carcinoma (HNSCC) patients receiving definitive RT vs RT-alone according to Bonner et al; and other studies compared to concomitant chemotherapy. However, little is known for cases receiving cetuximab with RT in the adjuvant setting. Materials/Methods: We queried our institutional HNSCC database for surgically staged non-metastatic cases that received adjuvant RT with or without concomitant cetuximab between 2006-2018. Cetuximab was administered for some high-risk cases medically unfit for platinum agents per multidisciplinary team evaluation. All included patients need to have at least one complete blood count pre- and post-RT end. We compared RT-cetuximab vs RT-alone for prevalence of baseline and post-RT anemia, defined as Hb below 12g/dL in females and 13g/dL in males, and mean hemoglobin (Hb) levels. We also assessed the improvement in Hb level post-RT (resolution of baseline anemia or Hb increase of at least 1g/dL above baseline), in addition to overall survival (OS) in relation to anemia/Hb dynamics. Results: We were able to identify 66 patients who fit our inclusion criteria, of which 27 (41%) received RT-cetuximab, with the remaining receiving RT-alone (n=39, 59%). Median age was 62.5 years (range, 34-88 years), males 80%, black 29%, and 85% had a smoking history. The majority of cases (73%) were locally advanced. Oral cavity and oropharynx were the most common subsites (37.5% each), with HPV+ve cases representing 52% of the later. The study groups were well-balanced, except for higher rates of positive final surgical margins, and extracapsular space invasion and median RT dose ($p<0.05$). Baseline anemia was diagnosed in 70.4% in RT-cetuximab vs 76.9% in the RT-alone, $p=0.76$; with similar mean Hb level (11.7g/dL in both). Meanwhile, baseline iron, vitamin-B12 and folate deficiencies, and chronic kidney disease were non-different. After completion of RT, mean Hb was significantly higher in the RT-alone (12.9±1.4 g/dL) compared to RT-Cetuximab (11.9±2.1 g/dL), $p=0.02$. Nevertheless, higher anemia levels (70% vs 51%) and lower improvement of Hb post-RT (81.5% vs 92.3%) were both non-significant for RT-cetuximab vs RT-alone respectively, $p>0.05$ for both. On multivariate analysis, baseline anemia was associated with worse OS ($p=0.0052$), unlike improvement of Hb post-RT ($p=0.14$) with a corresponding better improvement of Hb (56.4% vs. 25.9%, $p=0.014$), albeit lower anemia levels (70% vs. 51%), was non significant ($p=0.195$). On multivariate analysis, lack of baseline anemia was associated with better OS ($p=0.0052$), whereas improvement of Hb post-RT was only marginal ($p=0.068$). Conclusion: In a homogenous cohort of HNSCC patients treated postoperatively, concomitant cetuximab was not associated with lower RT-induced anemia, in contrast to previous studies.

Nephrology

Kumbar L, Astor B, and **Yee J**. SURVEILLANCE-BASED RISK SCORE PREDICTS STENOTIC HEMODIALYSIS ARTERIOVENOUS ACCESSES. *Am J Kidney Dis* 2022; 79(4):S54-S54. PMID: Not assigned. Full Text

Nursing

Franco-Palacios DJ, **Allenspach L**, **Stagner L**, **Pinto-Corrales J**, **Hanlon K**, **Nappo T**, **Sherbin E**, **Sternberg D**, **Dillon W**, **Simanovski J**, and **Alangaden G**. Early Outcomes of Lung Transplantation for

COVID-19 Related Lung Disease. Single Center Experience. *J Heart Lung Transplant* 2022; 41(4):S393. PMID: Not assigned. Full Text

D.J. Franco-Palacios, Pulmonary and Critical Care, Henry Ford Hospital, Detroit, MI, United States

Purpose: Lung transplantation (LT) is a lifesaving treatment for Covid-19 related lung disease with early outcomes similar to other indications. Methods: Seven patients underwent LT for Covid-19 related lung disease at our center: 5 for ARDS and 2 for IPF exacerbation post SARS-CoV-2 infection. Results: Seven patients (5 men) with single organ failure underwent bilateral LT. Median age was 47 years old. All ARDS cases had poor lung mechanics on invasive mechanical ventilation with radiographic evidence of lung fibrosis: pneumatocele, GGO, consolidations, subpleural reticulations and traction bronchiectasis. vvECMO was bridge to transplant in 5 cases (bridge to recovery in 2). Median ECMO duration for ARDS was 32 days (range 7-99). Median time to LT from Covid diagnosis was 59 days (Q1-IQ3, 54-62). Two patients were post-partum women with ARDS. Explanted pathology showed UIP, DAD, diffuse hemorrhage and one case of fibrosing NSIP. Pulmonary hypertension was seen in 4 cases. One patient did not survive. Organizing pneumonia and granuloma were present in this patient. Most ARDS patients were unable to tolerate lower sedation and consent by a substitute decision-makers was obtained. Post operative ECMO decannulation was possible in all cases. Induction, maintenance immunosuppression and antimicrobials were standard for our program. Donated grafts were from deceased brain death donors and negative for 2019-nCoV. Rehabilitation potential and strong social support were absolute inclusion criteria. All survivors have excellent lung function. Conclusion: In the USA, over 130 LT have listed Covid-19 as the diagnosis indication. Although Covid-19 ARDS makes up for the majority of these LT, other diagnosis are post Covid pulmonary fibrosis and underlying fibrosis with SARS-CoV-2 induced exacerbation. LT for ARDS poses several challenges and is reserved for the minority of carefully selected patients dependent on extracorporeal life support. As others have reported, good short-term survival is described.

Orthopedics/Bone and Joint Center

Wilson T, **Kaur N**, **Loveless I**, **Datta I**, Potla P, **Baker K**, **Davis J**, and **Ali SA**. CIRCULATING MIR-126-3P IS ELEVATED IN LATE-STAGE RADIOGRAPHIC KNEE OSTEOARTHRITIS. *Osteoarthritis Cartilage* 2022; 30:S130-S131. PMID: Not assigned. Full Text

Purpose: There is an outstanding need to identify minimally invasive biomarkers for reliable detection of knee osteoarthritis (OA). Current clinical diagnostic methods are limited since OA symptoms do not always correlate with structural degeneration in the joint. Soluble biochemical markers provide a better readout of disease activity, and a variety of blood, synovial fluid, and urine biomarkers have been explored in OA, including microRNAs. As small, non-coding RNAs, microRNAs are promising biomarker candidates since they are easy to detect in biofluids, are relatively stable (i.e. resistant to enzymatic degradation), and can be reliably quantified such that levels can be linked to disease. Furthermore, microRNAs are known drivers of OA pathology, and their expression may precede joint degeneration, when opportunities for intervention still exist. Based on this, circulating microRNAs have strong potential to serve as biomarkers for knee OA, but a major limitation is lack of reproducibility across studies profiling circulating microRNAs in OA. While sequencing is the gold standard method for unbiased profiling of microRNAs, there are critical experimental design and analysis parameters that can impact the results. The objectives of this study are to identify circulating microRNAs in late-stage radiographic knee OA compared to non-OA controls using existing microRNA-sequencing data, and to validate the findings using our recently established Henry Ford Health System (HFHS) Osteoarthritis cohort. Methods: We searched the literature for microRNA-sequencing studies profiling circulating microRNAs in OA versus non-OA participants and identified two studies, one conducted in Norway (Aae et al., 2020) and the other in France (Rousseau et al., 2020). We obtained raw sequencing data from the authors and re-analyzed the data by applying our recently reported method for microRNA-sequencing analysis. Among other changes (e.g. normalization method), we re-defined the cohorts to include participants with only Kellgren-Lawrence (KL) grades 3 and 4 in the OA group (compared to KL 0 to 4 and total knee arthroplasty in the original Norway study and KL 2 and 3 in the original France study) and with KL grade 0 in the non-OA group (consistent with the original Norway study and compared to KL 0 and 1 in the original France study). Following differential expression analysis using a multivariate model adjusted for age, sex, and

body mass index, we prioritized microRNAs that were common to the OA groups in both cohorts. We next performed validation by real-time PCR in the HFHS Osteoarthritis cohort utilizing plasma samples from participants with unilateral and/or bilateral knee and/or hip OA and non-OA controls. Results: As reported by the two original microRNA-sequencing studies, there were no significant differences in the Norway cohort and 3 differentially expressed microRNAs in OA (miR-139-5p, miR-1299, miR-200a-3p) in the France cohort, though none achieved validation in real-time PCR experiments. Following our re-analysis, we identified 23 and 82 differentially expressed microRNAs ($p<0.1$) in the Norway and France cohorts, respectively, with 3 microRNAs in common between the OA groups: miR-126-3p, miR-30c-2-3p, and miR-144-5p. Of these, miR-126-3p had the highest counts-per-million in both cohorts, showed an increased fold change in OA in both cohorts ($p<0.05$; Figure 1A and 1B), and was found in 100% and 91% of OA samples and 0% and 35% of non-OA samples in the Norway and France cohorts, respectively. Furthermore, a report in 2014 by Borgonio Cuadra et al. identified circulating miR-126 to be elevated in OA (KL 2 and 3) compared to non-OA (KL 0) by both real-time PCR array and real-time PCR validation experiments (Figure 1C). This led us to explore miR-126-3p expression in plasma samples from the HFHS Osteoarthritis cohort where we found a consistent increase in knee OA (symptomatic, KL 3 or 4), irrespective of unilateral or bilateral, compared to non-OA controls (asymptomatic, KL 0), yet no significant increase in hip OA (Figure 1D) Conclusions: Through application of our microRNA-sequencing analysis method, we identified circulating miR-126-3p to be increased in late-stage radiographic knee OA compared to non-OA controls in two studies originally reporting no validated differences. This finding is supported by previous literature identifying circulating miR-126 to be elevated in knee OA compared to non-OA controls and is extended by our data showing that the increase may be unique to knee OA and not hip OA. Taken together, there are now data from four independent cohorts demonstrating an increase in circulating miR-126-3p in knee OA, suggesting that this microRNA may have utility as a biomarker for OA. [Formula presented]

Otolaryngology – Head and Neck Surgery

Ghanem AI, **Maahs L**, **Gutta R**, **Tang A**, **Gilbert M**, **Arya S**, **Saheli ZA**, **Tam S**, **Sheqwara J**, and **Siddiqui F**. Does Cetuximab Reduce the Risk of Anemia in Patients Undergoing Radiation Therapy for Head and Neck Cancers? *Int J Radiat Oncol Biol Phys* 2022; 112(5):e61-e62. PMID: Not assigned. Full Text

A.I. Ghanem, Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, United States

Purpose/Objective(s): Epidermal growth factor receptor (EGFR) activation is associated with increased production of interleukin 6 (IL6), which is intensified by radiotherapy (RT) induced inflammatory response. Elevated IL6 levels promote RT-induced anemia by upregulating hepcidin causing functional iron deficiency. Cetuximab, an EGFR inhibitor, resulted in significantly lower rates of RT induced anemia for locally advanced head and neck squamous cell carcinoma (HNSCC) patients receiving definitive RT vs RT-alone according to Bonner et al; and other studies compared to concomitant chemotherapy. However, little is known for cases receiving cetuximab with RT in the adjuvant setting. Materials/Methods: We queried our institutional HNSCC database for surgically staged non-metastatic cases that received adjuvant RT with or without concomitant cetuximab between 2006-2018. Cetuximab was administered for some high-risk cases medically unfit for platinum agents per multidisciplinary team evaluation. All included patients need to have at least one complete blood count pre- and post-RT end. We compared RT-cetuximab vs RT-alone for prevalence of baseline and post-RT anemia, defined as Hb below 12g/dL in females and 13g/dL in males, and mean hemoglobin (Hb) levels. We also assessed the improvement in Hb level post-RT (resolution of baseline anemia or Hb increase of at least 1g/dL above baseline), in addition to overall survival (OS) in relation to anemia/Hb dynamics. Results: We were able to identify 66 patients who fit our inclusion criteria, of which 27 (41%) received RT-cetuximab, with the remaining receiving RT-alone (n=39, 59%). Median age was 62.5 years (range, 34-88 years), males 80%, black 29%, and 85% had a smoking history. The majority of cases (73%) were locally advanced. Oral cavity and oropharynx were the most common subsites (37.5% each), with HPV+ve cases representing 52% of the later. The study groups were well-balanced, except for higher rates of positive final surgical margins, and extracapsular space invasion and median RT dose ($p<0.05$). Baseline anemia was diagnosed in 70.4% in RT-cetuximab vs 76.9% in the RT-alone, $p=0.76$; with similar mean Hb level (11.7g/dL in both). Meanwhile, baseline iron, vitamin-B12 and folate deficiencies, and chronic kidney disease were non-

different. After completion of RT, mean Hb was significantly higher in the RT-alone (12.9±1.4 g/dL) compared to RT-Cetuximab (11.9±2.1 g/dL), p=0.02. Nevertheless, higher anemia levels (70% vs 51%) and lower improvement of Hb post-RT (81.5% vs 92.3%) were both non-significant for RT-cetuximab vs RT-alone respectively, p>0.05 for both. On multivariate analysis, baseline anemia was associated with worse OS (p=0.0052), unlike improvement of Hb post-RT (p=0.14) with a corresponding better improvement of Hb (56.4% vs. 25.9%, p=0.014), albeit lower anemia levels (70% vs. 51%), was non significant (p=0.195). On multivariate analysis, lack of baseline anemia was associated with better OS (p=0.0052), whereas improvement of Hb post-RT was only marginal (p=0.068). Conclusion: In a homogenous cohort of HNSCC patients treated postoperatively, concomitant cetuximab was not associated with lower RT-induced anemia, in contrast to previous studies.

Pathology and Laboratory Medicine

Al-Darzi W, **Mukherjee A**, **Cowger J**, and **Hannawi B**. A Case of Muscular Dystrophy with Dilated Cardiomyopathy: Do Not Forget Your Basics. *J Heart Lung Transplant* 2022; 41(4):S456. PMID: Not assigned. Full Text

W. Al-Darzi, Cardiology, Henry Ford Hospital, Detroit, MI, United States

Introduction: Becker muscular dystrophy (BMD) is an X-linked recessive disorder with dystrophin mutation. Dilated Cardiomyopathy (DCM) is a leading cause of death in BMD patients. Herein, we are presenting a patient with BMD that initially sought medical attention for acute onset of systolic heart failure that highlights the importance of careful clinical assessment and appropriate work up. Case Report: A 29-year-old male with medical history of asthma presented to the hospital with progressive dyspnea and leg swelling. He was diagnosed with DCM with an LVIDD of 6.5 cm and LV ejection fraction of 20-25% by echocardiogram. Coronary angiogram revealed no coronary artery disease. Initial blood work and electrocardiogram are below (Figure). Cardiac MRI showed severely reduced biventricular systolic function with near circumferential, sub-epicardial to mid-myocardial delayed gadolinium enhancement (Figure). Initial differential diagnosis included prior myocarditis vs. burnt out sarcoidosis. It was subsequently noted that patient began recurrently falling with muscle weakness from age 20 years with chronically elevated AST and CK. His exam was notable for atrophy of the bilateral quadriceps muscles, decreased muscular strength and bilateral calves hypertrophy. Electromyography showed evidence of chronic proximal and distal myopathy, predominantly affecting the lower extremity. Skeletal muscle biopsy showed fascicular atrophy and hypertrophy, focal endomyosial fibrosis and an increase of central nuclei without evidence of inflammation or granuloma which was most suggestive of a muscular dystrophy. Genetic testing was then completed and showed hemizygous dystrophin mutation confirming diagnosis of BMD. BMD has a diffuse phenotype and should be considered in young patients with cardiomyopathy and chronically elevated CK and AST. A thorough clinical history, exam, and CMR can assist in directing need for skeletal muscle biopsy and subsequent genetic testing.

Pharmacy

Hencken L, **Grafton G**, **To L**, **Nemeh H**, and **Cowger J**. Peri-Operative Warfarin Protocol to Decrease Length of Stay After Left Ventricular Assist Device Implantation. *J Heart Lung Transplant* 2022; 41(4):S462. PMID: Not assigned. Full Text

L. Hencken, Pharmacy, Henry Ford Hospital, Detroit, MI, United States

Purpose: A limitation to left ventricular assist device (LVAD) implantation is cost with fixed reimbursement rates for the LVAD implantation hospitalization regardless of hospital length of stay and costs. Patients must have a therapeutic INR on warfarin prior to discharge which can take days and delay discharge. The purpose of this study is to evaluate the impact of a peri-operative warfarin protocol on decreasing length of stay during index LVAD implantation. Methods: This is a retrospective single center study of adult patients undergoing LVAD implantation between January 1, 2019 and December 31, 2020. Patients who died during the admission were excluded. Patients in the intervention group (INT) underwent LVAD between January 1-December 31, 2020. The peri-operative warfarin protocol included pre-operative vitamin K dosing according to INR, initiation of warfarin by post-operative day (POD) 3, and warfarin titration scheme. The historical control group (CON) included patients receiving LVADs between January

1-December 31, 2019. Warfarin start date was at the discretion of providers. All patients had a goal INR of 2-3. Endpoints included length of stay, post-operative warfarin start date, time to therapeutic INR, warfarin dosing requirements, pre-operative vitamin K dosing and bleeding complications. Results: Seventy-seven patients were included; n=41 (53.2%) CON and n=36 (46.8%) INT. Total hospital length of stay was 35 [26,43] days in the CON group compared to 27.5 [24,35] days in the INT group (p=0.095). Warfarin was started earlier in the INT group (POD 5.5 [2.8,7.0]) compared to the CON group (POD 8 [6,14]) (p=0.004). Time to therapeutic INR remained the same between the two groups with a median of 6 days. Pre-operative vitamin K decreased from 15 [10,15] mg in the CON group to 5 [0.0,11.3] mg in the INT group (p=<0.001). There was no increase in bleeding with the peri-operative warfarin interventions: 8 bleeds in the CON group and 4 bleeds in the INT group. Conclusion: Initiating warfarin earlier post-operatively may help decrease hospital length of stay after LVAD implantation without increasing bleeding events.

Public Health Sciences
Cheung WL, **Cannella C**, **Chen YL**, **Rama S**, **Yono S**, **Romano I**, **Bensenhaver J**, **Yoho D**, and **Atisha D**. Patient factors that affect pre-operative patient-reported outcomes in women undergoing breast cancer surgery. *Ann Surg Oncol* 2022; 29(SUPPL 1):230-230. PMID: Not assigned. Full Text

Public Health Sciences
Cheung WL, **Cannella C**, **Chen YL**, **Rama S**, **Yono S**, **Romano I**, **Bensenhaver J**, **Yoho D**, and **Atisha D**. Patient and disease pre-operative factors influencing surgical procedure choice for breast cancer treatment. *Ann Surg Oncol* 2022; 29(SUPPL 1):226-226. PMID: Not assigned. Full Text

Public Health Sciences
Ghanem AI, **Maahs L**, **Gutta R**, **Tang A**, **Gilbert M**, **Arya S**, **Saheli ZA**, **Tam S**, **Sheqwara J**, and **Siddiqui F**. Does Cetuximab Reduce the Risk of Anemia in Patients Undergoing Radiation Therapy for Head and Neck Cancers? *Int J Radiat Oncol Biol Phys* 2022; 112(5):e61-e62. PMID: Not assigned. Full Text

A.I. Ghanem, Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, United States

Purpose/Objective(s): Epidermal growth factor receptor (EGFR) activation is associated with increased production of interleukin 6 (IL6), which is intensified by radiotherapy (RT) induced inflammatory response. Elevated IL6 levels promote RT-induced anemia by upregulating hepcidin causing functional iron deficiency. Cetuximab, an EGFR inhibitor, resulted in significantly lower rates of RT induced anemia for locally advanced head and neck squamous cell carcinoma (HNSCC) patients receiving definitive RT vs RT-alone according to Bonner et al; and other studies compared to concomitant chemotherapy. However, little is known for cases receiving cetuximab with RT in the adjuvant setting. Materials/Methods: We queried our institutional HNSCC database for surgically staged non-metastatic cases that received adjuvant RT with or without concomitant cetuximab between 2006-2018. Cetuximab was administered for some high-risk cases medically unfit for platinum agents per multidisciplinary team evaluation. All included patients need to have at least one complete blood count pre- and post-RT end. We compared RT-cetuximab vs RT-alone for prevalence of baseline and post-RT anemia, defined as Hb below 12g/dL in females and 13g/dL in males, and mean hemoglobin (Hb) levels. We also assessed the improvement in Hb level post-RT (resolution of baseline anemia or Hb increase of at least 1g/dL above baseline), in addition to overall survival (OS) in relation to anemia/Hb dynamics. Results: We were able to identify 66 patients who fit our inclusion criteria, of which 27 (41%) received RT-cetuximab, with the remaining receiving RT-alone (n=39, 59%). Median age was 62.5 years (range, 34-88 years), males 80%, black 29%, and 85% had a smoking history. The majority of cases (73%) were locally advanced. Oral cavity and oropharynx were the most common subsites (37.5% each), with HPV+ve cases representing 52% of the later. The study groups were well-balanced, except for higher rates of positive final surgical margins, and extracapsular space invasion and median RT dose (p<0.05). Baseline anemia was diagnosed in 70.4% in RT-cetuximab vs 76.9% in the RT-alone, p=0.76; with similar mean Hb level (11.7g/dL in both). Meanwhile, baseline iron, vitamin-B12 and folate deficiencies, and chronic kidney disease were non-different. After completion of RT, mean Hb was significantly higher in the RT-alone (12.9±1.4 g/dL) compared to RT-Cetuximab (11.9±2.1 g/dL), p=0.02. Nevertheless, higher anemia levels (70% vs 51%)

and lower improvement of Hb post-RT (81.5% vs 92.3%) were both non-significant for RT-cetuximab vs RT-alone respectively, p>0.05 for both. On multivariate analysis, baseline anemia was associated with worse OS (p=0.0052), unlike improvement of Hb post-RT (p=0.14) with a corresponding better improvement of Hb (56.4% vs. 25.9%, p=0.014), albeit lower anemia levels (70% vs. 51%), was non significant (p=0.195). On multivariate analysis, lack of baseline anemia was associated with better OS (p=0.0052), whereas improvement of Hb post-RT was only marginal (p=0.068). Conclusion: In a homogenous cohort of HNSCC patients treated postoperatively, concomitant cetuximab was not associated with lower RT-induced anemia, in contrast to previous studies.

Public Health Sciences
McDonough L, **Petersen L**, **Lehrberg A**, **Bensenhaver J**, **Qutob O**, **Susick L**, **Ekkel E**, **Thaker H**, and **Schwartz T**. Is nodal staging necessary for older patients with HER2-positive or triple-negative breast cancers? *Ann Surg Oncol* 2022; 29(SUPPL 1):305-305. PMID: Not assigned. Full Text

Public Health Sciences
Simanovski J, **Nemeh HM**, **Allenspach LL**, **Mei LL**, **Stagner LD**, **Pinto JC**, **Olexsey KM**, **Franco-Palacios DJ**, and **Alangaden GJ**. Risks and Outcomes Associated with Pleural Space Infections After Lung Transplantation. *J Heart Lung Transplant* 2022; 41(4):S394. PMID: Not assigned. Full Text

J. Simanovski, Transplant Institute, Henry Ford Health System, Detroit, MI, United States

Purpose: Pleural space infections (PSI) are a serious complication after lung transplantation (LT) however there is limited data on the associated risk factors and outcomes of PSI. We examined: 1) risk factors associated with PSI after LT; 2) effect of PSI on LT outcomes. Methods: This is a retrospective single center cohort study of 74 consecutive LT recipients (1/2018- 6/2020). Patients were divided into infected and non-infected groups, where PSI were defined as post-LT pleural effusions with pathogen(s) isolated from pleural fluid. Data were collected and compared between two groups with two-sample t-test or Fisher-exact. Multivariable logit model was performed with estimations of odds ratio (OR) and its confidence interval [CI]. Results: Among 74 LT recipients, 38 (51%) developed pleural effusions requiring drainage; of them 16 (42%) had PSI. Baseline demographics were similar in patients with and without PSI (Table). Notably, 88% of PSI group received steroids pre-LT compared to 55% in the non-infected group (p<0.05); 88% of the PSI group had an underlying diagnosis of interstitial lung disease versus 45% of the non-infected group (p<0.01). Overall post-operative complications occurred more frequently in the PSI group vs. non-infected group 77% vs. 25% (p<0.01) and airway complications in 86% vs. 44% (p<0.01). Hospital length of stay was longer in the PSI group with the median of 78 versus 31 days in the non-infected group (p<0.01). Results of logistical modeling showed high risk of PSI with presence of post-LT airway complications (OR =10.8 95% CI 1.7- 72.5) and presence of post operative complications (OR=10.6, 95% CI 1.8-63.5). There was no difference in the incidence of readmissions, acute cellular rejection or 1 year mortality between the two cohorts. Conclusion: PSI remain a prevalent yet under-studied complication. Airway or post-operative complications after LT were associated with PSI. One-year outcomes were similar in LT recipients with and without PSI.

Public Health Sciences
Wilson T, **Kaur N**, **Loveless I**, **Datta I**, Potla P, **Baker K**, **Davis J**, and **Ali SA**. CIRCULATING MIR-126-3P IS ELEVATED IN LATE-STAGE RADIOGRAPHIC KNEE OSTEOARTHRITIS. *Osteoarthritis Cartilage* 2022; 30:S130-S131. PMID: Not assigned. Full Text

Purpose: There is an outstanding need to identify minimally invasive biomarkers for reliable detection of knee osteoarthritis (OA). Current clinical diagnostic methods are limited since OA symptoms do not always correlate with structural degeneration in the joint. Soluble biochemical markers provide a better readout of disease activity, and a variety of blood, synovial fluid, and urine biomarkers have been explored in OA, including microRNAs. As small, non-coding RNAs, microRNAs are promising biomarker candidates since they are easy to detect in biofluids, are relatively stable (i.e. resistant to enzymatic degradation), and can be reliably quantified such that levels can be linked to disease. Furthermore, microRNAs are known drivers of OA pathology, and their expression may precede joint degeneration, when opportunities for intervention still exist. Based on this, circulating microRNAs have strong potential

to serve as biomarkers for knee OA, but a major limitation is lack of reproducibility across studies profiling circulating microRNAs in OA. While sequencing is the gold standard method for unbiased profiling of microRNAs, there are critical experimental design and analysis parameters that can impact the results. The objectives of this study are to identify circulating microRNAs in late-stage radiographic knee OA compared to non-OA controls using existing microRNA-sequencing data, and to validate the findings using our recently established Henry Ford Health System (HFHS) Osteoarthritis cohort. Methods: We searched the literature for microRNA-sequencing studies profiling circulating microRNAs in OA versus non-OA participants and identified two studies, one conducted in Norway (Aae et al., 2020) and the other in France (Rousseau et al., 2020). We obtained raw sequencing data from the authors and re-analyzed the data by applying our recently reported method for microRNA-sequencing analysis. Among other changes (e.g. normalization method), we re-defined the cohorts to include participants with only Kellgren-Lawrence (KL) grades 3 and 4 in the OA group (compared to KL 0 to 4 and total knee arthroplasty in the original Norway study and KL 2 and 3 in the original France study) and with KL grade 0 in the non-OA group (consistent with the original Norway study and compared to KL 0 and 1 in the original France study). Following differential expression analysis using a multivariate model adjusted for age, sex, and body mass index, we prioritized microRNAs that were common to the OA groups in both cohorts. We next performed validation by real-time PCR in the HFHS Osteoarthritis cohort utilizing plasma samples from participants with unilateral and/or bilateral knee and/or hip OA and non-OA controls. Results: As reported by the two original microRNA-sequencing studies, there were no significant differences in the Norway cohort and 3 differentially expressed microRNAs in OA (miR-139-5p, miR-1299, miR-200a-3p) in the France cohort, though none achieved validation in real-time PCR experiments. Following our re-analysis, we identified 23 and 82 differentially expressed microRNAs ($p<0.1$) in the Norway and France cohorts, respectively, with 3 microRNAs in common between the OA groups: miR-126-3p, miR-30c-2-3p, and miR-144-5p. Of these, miR-126-3p had the highest counts-per-million in both cohorts, showed an increased fold change in OA in both cohorts ($p<0.05$; Figure 1A and 1B), and was found in 100% and 91% of OA samples and 0% and 35% of non-OA samples in the Norway and France cohorts, respectively. Furthermore, a report in 2014 by Borgonio Cuadra et al. identified circulating miR-126 to be elevated in OA (KL 2 and 3) compared to non-OA (KL 0) by both real-time PCR array and real-time PCR validation experiments (Figure 1C). This led us to explore miR-126-3p expression in plasma samples from the HFHS Osteoarthritis cohort where we found a consistent increase in knee OA (symptomatic, KL 3 or 4), irrespective of unilateral or bilateral, compared to non-OA controls (asymptomatic, KL 0), yet no significant increase in hip OA (Figure 1D) Conclusions: Through application of our microRNA-sequencing analysis method, we identified circulating miR-126-3p to be increased in late-stage radiographic knee OA compared to non-OA controls in two studies originally reporting no validated differences. This finding is supported by previous literature identifying circulating miR-126 to be elevated in knee OA compared to non-OA controls and is extended by our data showing that the increase may be unique to knee OA and not hip OA. Taken together, there are now data from four independent cohorts demonstrating an increase in circulating miR-126-3p in knee OA, suggesting that this microRNA may have utility as a biomarker for OA. [Formula presented]

Pulmonary and Critical Care Medicine

Boshara A, **Ananthasubramaniam K**, **Russell C**, **Bradley P**, **Nadeem O**, and **Cowger J**. Sarcoidosis: Hiding in Plain Sight. *J Heart Lung Transplant* 2022; 41(4):S345. PMID: Not assigned. Full Text

A. Boshara, Advanced Heart Failure and Transplant Cardiology, Henry Ford Hospital, Detroit, MI, United States

Introduction: Sarcoidosis is a systemic disease that can masquerade as many conditions. Due to its often patchy distribution, myocardial biopsy is only ~30% sensitive. Herein we present a case of sarcoidosis diagnosed from an extra-cardiac biopsy years after the onset of cardiomyopathy. Case Report: A 54 year old man initially presented with dyspnea and fatigue due to new onset HFrEF of 20%. He had a significant family history of SCD. His workup revealed non-obstructive CAD, a myxomatous mitral valve with bileaflet prolapse and moderate regurgitation, and a cystic structure attached to the tricuspid valve. Given his frequent ventricular ectopy, he was discharged on guideline therapy for HFrEF and a wearable cardioverter defibrillator. Genetic testing for dilated cardiomyopathies revealed EYA4 and TTN variants of unknown significance. A cardiac MRI a few months later demonstrated no abnormal late gadolinium

enhancement and persistent systolic dysfunction, so he underwent AICD implant. His course was further complicated by recurrent admissions for supraventricular and ventricular tachyarrhythmias. A cardiopulmonary exercise stress test demonstrated low-risk results. Further evaluation noted prolonged AV conduction. A RHC revealed mild post-capillary pulmonary hypertension and a mildly decreased cardiac index at 2.01 L/min/m2. Months later, he underwent CRT-D upgrade. He started improving functionally until he developed left eyelid swelling, initially thought to be lymphoma. An orbital biopsy revealed non-caseating granulomas. A PET/CT demonstrated FDG uptake within subcarinal lymph nodes but no cardiac uptake. Initially he declined immunomodulatory therapy, but as his symptoms worsened, he started corticosteroids and transitioned to mycophenolate mofetil due to intolerance of methotrexate. Due to disease progression on repeat FDG-PET, he was switched to infliximab. The diagnosis of sarcoidosis can be difficult due to its variable presentation, including heart block, heart failure, ventricular arrhythmias and sudden cardiac death. Cardiac involvement occurs in 25% of cases. Our case was complicated by a cMRI that was negative for cardiac involvement, which emphasizes the importance of complimentary inflammatory imaging with FDG-PET. A multidisciplinary approach is needed that engages sarcoid specialists for earlier diagnosis to ensure rapid initiation of therapy to reduce end-organ dysfunction.

Pulmonary and Critical Care Medicine

Franco-Palacios DJ, **Allenspach L**, **Stagner L**, **Pinto-Corrales J**, **Hanlon K**, **Nappo T**, **Sherbin E**, **Sternberg D**, **Dillon W**, **Simanovski J**, and **Alangaden G**. Early Outcomes of Lung Transplantation for COVID-19 Related Lung Disease. Single Center Experience. *J Heart Lung Transplant* 2022; 41(4):S393. PMID: Not assigned. Full Text

D.J. Franco-Palacios, Pulmonary and Critical Care, Henry Ford Hospital, Detroit, MI, United States

Purpose: Lung transplantation (LT) is a lifesaving treatment for Covid-19 related lung disease with early outcomes similar to other indications. Methods: Seven patients underwent LT for Covid-19 related lung disease at our center: 5 for ARDS and 2 for IPF exacerbation post SARS-CoV-2 infection. Results: Seven patients (5 men) with single organ failure underwent bilateral LT. Median age was 47 years old. All ARDS cases had poor lung mechanics on invasive mechanical ventilation with radiographic evidence of lung fibrosis: pneumatocele, GGO, consolidations, subpleural reticulations and traction bronchiectasis. vvECMO was bridge to transplant in 5 cases (bridge to recovery in 2). Median ECMO duration for ARDS was 32 days (range 7-99). Median time to LT from Covid diagnosis was 59 days (Q1-IQ3, 54-62). Two patients were post-partum women with ARDS. Explanted pathology showed UIP, DAD, diffuse hemorrhage and one case of fibrosing NSIP. Pulmonary hypertension was seen in 4 cases. One patient did not survive. Organizing pneumonia and granuloma were present in this patient. Most ARDS patients were unable to tolerate lower sedation and consent by a substitute decision-makers was obtained. Post operative ECMO decannulation was possible in all cases. Induction, maintenance immunosuppression and antimicrobials were standard for our program. Donated grafts were from deceased brain death donors and negative for 2019-nCoV. Rehabilitation potential and strong social support were absolute inclusion criteria. All survivors have excellent lung function. Conclusion: In the USA, over 130 LT have listed Covid-19 as the diagnosis indication. Although Covid-19 ARDS makes up for the majority of these LT, other diagnosis are post Covid pulmonary fibrosis and underlying fibrosis with SARS-CoV-2 induced exacerbation. LT for ARDS poses several challenges and is reserved for the minority of carefully selected patients dependent on extracorporeal life support. As others have reported, good short-term survival is described.

Pulmonary and Critical Care Medicine

Franco-Palacios DJ, **Allenspach L**, **Stagner L**, **Pinto-Corrales J**, **Hanlon K**, **Waynick L**, **Nicholson D**, **Shaheen E**, **Spezia M**, **Nappo T**, **Dillon W**, **Sherbin EL**, and **Alangaden G**. Outcomes of SARS-CoV-2 Infection in Lung Transplant Recipients: A Single Center Experience. *J Heart Lung Transplant* 2022; 41(4):S523. PMID: Not assigned. Full Text

D.J. Franco-Palacios, Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI, United States

Purpose: Outcomes of Covid-19 in lung transplant recipients (LTr) were reported in the beginning of the pandemic. Only few centers reported on their experience since December 2020 when vaccines received emergency use authorization. We aim to investigate the outcome of SARS-CoV-2 infection in a cohort of LTr at our center in Detroit, Michigan. Methods: Retrospective chart review study of adult LTr with confirmed SARS-CoV-2 infection from March 2020 to August 2021. Results: Thirty LTr were diagnosed with SARS-CoV-2 infection confirmed by RT PCR of nasopharynx. Median age at diagnosis was 63; 53% were males; 57% Caucasians and 40% of African descendance. Most patients underwent bilateral LT for interstitial lung disease (46%) and for pulmonary sarcoidosis (23%). The median time post LT was 3.1 years. Most patients needed hospitalization for respiratory failure secondary to Covid-19 (73%). Eleven patients were initially managed as outpatient. Five patients received outpatient combination of monoclonal antibodies with three of them later requiring hospitalization for development of hypoxia. None of the patients with initial out of the hospital management died. Amongst 21 hospitalized LTr, six patients were diagnosed with severe pneumonia and ARDS requiring heated high flow and invasive mechanical ventilation (IMV) in 4 patients. 28-day mortality was 10% and ICU mortality was 25% (50% mortality in those on IMV). Twelve hospitalized patients (57%) were treated with remdesivir. Augmented systemic corticosteroids was used in 85% of cases. Cycle cell inhibitor was held in 71% of the cases. Bilateral ground glass opacities of the allografts were common. None of the patients that received at least one dose of mRNA vaccine died. Conclusion: Outcomes in LTr infected with SARS-CoV-2 varies. Early reports showed high mortality rate in severe and critical Covid-19 in LTr. Although hospitalization rate in this cohort was high, only four patients in our cohort required IMV during acute Covid-19. Two of them died; both were unvaccinated. Another unvaccinated patient died due to allograft rejection two months after testing positive to SARS-CoV-2. Most cases were mild to moderate despite frequent radiographic findings of pneumonia. Underreporting and exclusion of mild cases as well as likely protective effect of vaccination and use of monoclonal antibodies may explain our different outcomes.

Pulmonary and Critical Care Medicine

Simanovski J, **Nemeh HM**, **Allenspach LL**, **Mei LL**, **Stagner LD**, **Pinto JC**, **Olexsey KM**, **Franco-Palacios DJ**, and **Alangaden GJ**. Risks and Outcomes Associated with Pleural Space Infections After Lung Transplantation. *J Heart Lung Transplant* 2022; 41(4):S394. PMID: Not assigned. Full Text

J. Simanovski, Transplant Institute, Henry Ford Health System, Detroit, MI, United States

Purpose: Pleural space infections (PSI) are a serious complication after lung transplantation (LT) however there is limited data on the associated risk factors and outcomes of PSI. We examined: 1) risk factors associated with PSI after LT; 2) effect of PSI on LT outcomes. Methods: This is a retrospective single center cohort study of 74 consecutive LT recipients (1/2018- 6/2020). Patients were divided into infected and non-infected groups, where PSI were defined as post-LT pleural effusions with pathogen(s) isolated from pleural fluid. Data were collected and compared between two groups with two-sample t-test or Fisher-exact. Multivariable logit model was performed with estimations of odds ratio (OR) and its confidence interval [CI]. Results: Among 74 LT recipients, 38 (51%) developed pleural effusions requiring drainage; of them 16 (42%) had PSI. Baseline demographics were similar in patients with and without PSI (Table). Notably, 88% of PSI group received steroids pre-LT compared to 55% in the non-infected group ($p<0.05$); 88% of the PSI group had an underlying diagnosis of interstitial lung disease versus 45% of the non-infected group ($p<0.01$). Overall post-operative complications occurred more frequently in the PSI group vs. non-infected group 77% vs. 25% ($p<0.01$) and airway complications in 86% vs. 44% ($p<0.01$). Hospital length of stay was longer in the PSI group with the median of 78 versus 31 days in the non-infected group ($p<0.01$). Results of logistical modeling showed high risk of PSI with presence of post-LT airway complications (OR =10.8 95% CI 1.7- 72.5) and presence of post operative complications (OR=10.6, 95% CI 1.8-63.5). There was no difference in the incidence of readmissions, acute cellular rejection or 1 year mortality between the two cohorts. Conclusion: PSI remain a prevalent yet under-studied complication. Airway or post-operative complications after LT were associated with PSI. One-year outcomes were similar in LT recipients with and without PSI.

Radiation Oncology

Ghanem AI, **Maahs L**, **Gutta R**, **Tang A**, **Gilbert M**, **Arya S**, **Saheli ZA**, **Tam S**, **Sheqwara J**, and **Siddiqui F**. Does Cetuximab Reduce the Risk of Anemia in Patients Undergoing Radiation Therapy for

Head and Neck Cancers? *Int J Radiat Oncol Biol Phys* 2022; 112(5):e61-e62. PMID: Not assigned. Full Text

A.I. Ghanem, Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, United States

Purpose/Objective(s): Epidermal growth factor receptor (EGFR) activation is associated with increased production of interleukin 6 (IL6), which is intensified by radiotherapy (RT) induced inflammatory response. Elevated IL6 levels promote RT-induced anemia by upregulating hepcidin causing functional iron deficiency. Cetuximab, an EGFR inhibitor, resulted in significantly lower rates of RT induced anemia for locally advanced head and neck squamous cell carcinoma (HNSCC) patients receiving definitive RT vs RT-alone according to Bonner et al; and other studies compared to concomitant chemotherapy. However, little is known for cases receiving cetuximab with RT in the adjuvant setting. Materials/Methods: We queried our institutional HNSCC database for surgically staged non-metastatic cases that received adjuvant RT with or without concomitant cetuximab between 2006-2018. Cetuximab was administered for some high-risk cases medically unfit for platinum agents per multidisciplinary team evaluation. All included patients need to have at least one complete blood count pre- and post-RT end. We compared RT-cetuximab vs RT-alone for prevalence of baseline and post-RT anemia, defined as Hb below 12g/dL in females and 13g/dL in males, and mean hemoglobin (Hb) levels. We also assessed the improvement in Hb level post-RT (resolution of baseline anemia or Hb increase of at least 1g/dL above baseline), in addition to overall survival (OS) in relation to anemia/Hb dynamics. Results: We were able to identify 66 patients who fit our inclusion criteria, of which 27 (41%) received RT-cetuximab, with the remaining receiving RT-alone (n=39, 59%). Median age was 62.5 years (range, 34-88 years), males 80%, black 29%, and 85% had a smoking history. The majority of cases (73%) were locally advanced. Oral cavity and oropharynx were the most common subsites (37.5% each), with HPV+ve cases representing 52% of the later. The study groups were well-balanced, except for higher rates of positive final surgical margins, and extracapsular space invasion and median RT dose ($p<0.05$). Baseline anemia was diagnosed in 70.4% in RT-cetuximab vs 76.9% in the RT-alone, $p=0.76$; with similar mean Hb level (11.7g/dL in both). Meanwhile, baseline iron, vitamin-B12 and folate deficiencies, and chronic kidney disease were non-different. After completion of RT, mean Hb was significantly higher in the RT-alone (12.9±1.4 g/dL) compared to RT-Cetuximab (11.9±2.1 g/dL), $p=0.02$. Nevertheless, higher anemia levels (70% vs 51%) and lower improvement of Hb post-RT (81.5% vs 92.3%) were both non-significant for RT-cetuximab vs RT-alone respectively, $p>0.05$ for both. On multivariate analysis, baseline anemia was associated with worse OS ($p=0.0052$), unlike improvement of Hb post-RT ($p=0.14$) with a corresponding better improvement of Hb (56.4% vs. 25.9%, $p=0.014$), albeit lower anemia levels (70% vs. 51%), was non significant ($p=0.195$). On multivariate analysis, lack of baseline anemia was associated with better OS ($p=0.0052$), whereas improvement of Hb post-RT was only marginal ($p=0.068$). Conclusion: In a homogenous cohort of HNSCC patients treated postoperatively, concomitant cetuximab was not associated with lower RT-induced anemia, in contrast to previous studies.

Rehabilitation Services/Physical Therapy/Occupational Health
Qutob O, **Rama S**, **Black L**, **Zubalik M**, **Bensenhaver J**, **Petersen L**, **Nathanson SD**, **Tepper D**, **Yoho D**, **Evangelista M**, and **Atisha D**. The effect of lymphatic microsurgical preventive healing approach (LYMPHA) on the development of upper-extremity lymphedema following axillary lymph node dissection in breast cancer patients. *Ann Surg Oncol* 2022; 29(SUPPL 1):40-41. PMID: Not assigned. Full Text

Sleep Medicine
Drake C, Yardley J, Pinner K, and Moline M. SUBJECTIVE RATINGS OF MEDICATION STRENGTH OVER 6 MONTHS IN ELDERLY SUBJECTS WITH MODERATE OR SEVERE INSOMNIA TREATED WITH LEMBOREXANT. *Am J Geriatr Psychiatry* 2022; 30(4):S74-S75. PMID: Not assigned. Full Text

Sleep Medicine
Drake C, Yardley J, Pinner K, Perdomo C, and Moline M. LONG-TERM PERCEPTION OF MEDICATION EFFECTIVENESS IN ELDERLY SUBJECTS WITH INSOMNIA RECEIVING LEMBOREXANT FOR UP TO 12 MONTHS. *Am J Geriatr Psychiatry* 2022; 30(4):S74-S74. PMID: Not assigned. Full Text

Surgery

Al-Darzi W, **Aurora L**, **Cowger J**, **Tanaka D**, **Lemor A**, **Koenig G**, and **Parikh S**. Hemodynamic and Echocardiographic Assessment of Left Ventricle Recovery with Left Ventricular Assist Devices: Do We Explant? *J Heart Lung Transplant* 2022; 41(4):S234-S235. PMID: Not assigned. Full Text

W. Al-Darzi, Cardiology, Henry Ford Hospital, Detroit, MI, United States

Introduction: Explantation of left ventricular assist devices (LVAD) after left ventricular (LV) recovery is estimated to occur in 1-2% of cases. Herein, we present a case of hemodynamic and echocardiographic assessment of LV recovery during outflow graft balloon occlusion leading to LVAD explantation. Case Report: A 56-year-old female with medical history of systolic heart failure due to non-ischemic cardiomyopathy with LVEF 25%. She underwent an urgent HeartMate 3 LVAD implant after an admission for cardiogenic shock. Post LVAD course was complicated by driveline infection. History was notable for admissions due to low-flow alarms in the setting of dehydration. On echocardiogram, progressive LVEF improvement was noted although with suboptimal images. CT angiography did not demonstrate any occlusion of the cannulas. Right heart catheterization showed stable cardiac index despite minimal flow on LVAD. Cardiopulmonary testing was favorable. After multi-disciplinary discussion, patient underwent LVAD wean study in the cath lab under hemodynamic and transesophageal echo (TEE) guidance with therapeutic anticoagulation. LVAD was turned off for 10 minutes with outflow graft occluded by Armada 14 mm x 20 cm peripheral balloon. Wiring of the outflow graft from aorta and balloon occlusion were visualized by TEE (Figure). The left and right ventricular function were similar to baseline with no change in mitral regurgitation. Cardiac index was normal (Figure). Patient subsequently underwent successful LVAD explant. She is doing well with NYHA class I symptoms and LVEF 45-50% noted upon 3-months follow-up LVAD explantation is a feasible option in LV recovery after appropriate hemodynamic and echocardiographic assessment. TEE is an essential tool, especially in patients with suboptimal windows. Outflow graft balloon occlusion can be used if there is concern about falsely poor results related to backflow or ongoing LVAD support at low speed leading to falsely improved results

Surgery

Chamogeorgakis T, Toumpoulis I, **Lanfear D**, **Williams C**, Koliopoulou A, Adamopoulos S, and **Cowger J**. Right Ventricular Failure Following Left Ventricular Assist Device Implant: An Intermacs Analysis. *J Heart Lung Transplant* 2022; 41(4):S31. PMID: Not assigned. Full Text

T. Chamogeorgakis, Henry Ford Health System/Transplant Institute, Detroit, MI, United States

Purpose: Right heart failure (RHF) management following LVAD include inotropes, right ventricular mechanical support and heart transplant. We analyzed the outcomes of severe RHF following implant of a fully magnetically levitated or hybrid magnetic centrifugal durable LVAD. Methods: In this INTERMACS analysis we identified patients who developed severe RHF following LVAD from 2013 until 2020 as bridge to recovery or transplant. Patients were categorized in three groups based on RHF treatment strategy: inotrope support (group 1), temporary mechanical support (group 2), and durable centrifugal RVAD (group 3). Kaplan Meier and Cox-regression survival analysis between groups was undertaken. Logistic regression analysis for new onset dialysis was conducted. Results: 2509 patients developed severe RHF after LVAD. 2199 (87.6%) patients were managed with inotropes (group 1), 233 (9.3%) with temporary RVAD (group 2) and 77 (3.1%) with durable RVAD (group 3). Group 1 had fewer patients with INTERMACS profile 1 and 2 (21.6%, $p<0.001$). One year survival was 84.6%, 59.3%, and 63.8% in groups 1,2, and 3 (mortality HR=2.4 and 3.3 for groups 2 and 3 vs. group 1, $p<0.05$). One year survival to transplant was 27%, 36.5%, and 53.6% in groups 1, 2, and 3, respectively ($p<0.05$). Group 2 had higher incidence of new onset dialysis (42.6%, $p=0.049$). Conclusion: Survival with RHF following LVAD implant varies based on treatment strategy; inotrope support is associated with increased survival. Patients with durable RVAD are more likely to survive to transplant. Patient selection studies for durable RVAD with contraindications for transplant are necessary.

Surgery

Chang DD, Giraldo-Grueso M, Desai S, Marz K, Bansal A, Webre K, and Parrino P. Surgical Specialization and Standardization of Care Improves Outcomes in Mechanical Circulatory Support: A

Single Center Experience. *J Heart Lung Transplant* 2022; 41(4):S387-S388. PMID: Not assigned. Full Text

A. Bansal, Surgery, Ochsner Clinic Foundation, New Orleans, LA, United States

Purpose: Cardiac surgery continues to transform into areas of sub-specialization and expertise to reduce variability and have superior outcomes. We sought to analyze the impact of surgical sub-specialization and use of protocol and clinical pathways on outcomes with MCS at the time of LVAD implantation. Methods: A single center retrospective analysis of long term durable MCS patients between 2004-2019 was performed. The analysis was conducted comparing management of patients before (Era 1: 2004-2011) vs. after (Era 2: 2012-2019) based on before and after introduction of MCS sub-specialization. Since 2012, multiple initiatives were introduced namely recruitment of specialized MCS/transplant surgeons, multidisciplinary team rounds, establishment of a shock team, development of clinical care pathways, electronic medical record order sets and clinical practice guidelines. Results: A total of 542 patients were included. During Era 1, five cardiac surgeons implanted LVADs in 123 patients, while in Era 2, two MCS/transplant trained surgeons implanted LVADs in 419 patients. Era 2 included higher number of INTERMACS 1 and 2 profile patients (41% vs. 63%) reflecting higher-acuity patient population. With implementation of the sub-specialization services, 1-year survival improved from 70% to 90%. Median ICU stay decreased from 13 to 8 days and percent of patients discharged to home increased from 62% to 95%. Standardized protocols for management of high LDH, GI bleeding, and blood pressure management resulted in significant reduction in overall hospital length of stay. With introduction of clinical care pathways, the average time for workup from admission to LVAD implant decreased from 27.6 days to 8.5 days. Conclusion: Introduction of surgical sub-specialization and standardization of care with the use of clinical pathways and protocols in managing patients with LVADs can help improve survival, reduce variability in medical care, and reduce ICU length of stay.

Surgery
Cheung WL, **Cannella C**, **Chen YL**, **Rama S**, **Yono S**, **Romano I**, **Bensenhaver J**, **Yoho D**, and **Atisha D**. Patient factors that affect pre-operative patient-reported outcomes in women undergoing breast cancer surgery. *Ann Surg Oncol* 2022; 29(SUPPL 1):230-230. PMID: Not assigned. Full Text

Surgery
Cheung WL, **Cannella C**, **Chen YL**, **Rama S**, **Yono S**, **Romano I**, **Bensenhaver J**, **Yoho D**, and **Atisha D**. Patient and disease pre-operative factors influencing surgical procedure choice for breast cancer treatment. *Ann Surg Oncol* 2022; 29(SUPPL 1):226-226. PMID: Not assigned. Full Text

Surgery
Franco-Palacios DJ, **Allenspach L**, **Stagner L**, **Pinto-Corrales J**, **Hanlon K**, **Nappo T**, **Sherbin E**, **Sternberg D**, **Dillon W**, **Simanovski J**, and **Alangaden G**. Early Outcomes of Lung Transplantation for COVID-19 Related Lung Disease. Single Center Experience. *J Heart Lung Transplant* 2022; 41(4):S393. PMID: Not assigned. Full Text

D.J. Franco-Palacios, Pulmonary and Critical Care, Henry Ford Hospital, Detroit, MI, United States

Purpose: Lung transplantation (LT) is a lifesaving treatment for Covid-19 related lung disease with early outcomes similar to other indications. Methods: Seven patients underwent LT for Covid-19 related lung disease at our center: 5 for ARDS and 2 for IPF exacerbation post SARS-CoV-2 infection. Results: Seven patients (5 men) with single organ failure underwent bilateral LT. Median age was 47 years old. All ARDS cases had poor lung mechanics on invasive mechanical ventilation with radiographic evidence of lung fibrosis: pneumatocele, GGO, consolidations, subpleural reticulations and traction bronchiectasis. vvECMO was bridge to transplant in 5 cases (bridge to recovery in 2). Median ECMO duration for ARDS was 32 days (range 7-99). Median time to LT from Covid diagnosis was 59 days (Q1-IQ3, 54-62). Two patients were post-partum women with ARDS. Explanted pathology showed UIP, DAD, diffuse hemorrhage and one case of fibrosing NSIP. Pulmonary hypertension was seen in 4 cases. One patient did not survive. Organizing pneumonia and granuloma were present in this patient. Most ARDS patients were unable to tolerate lower sedation and consent by a substitute decision-makers was obtained. Post

operative ECMO decannulation was possible in all cases. Induction, maintenance immunosuppression and antimicrobials were standard for our program. Donated grafts were from deceased brain death donors and negative for 2019-nCoV. Rehabilitation potential and strong social support were absolute inclusion criteria. All survivors have excellent lung function. Conclusion: In the USA, over 130 LT have listed Covid-19 as the diagnosis indication. Although Covid-19 ARDS makes up for the majority of these LT, other diagnosis are post Covid pulmonary fibrosis and underlying fibrosis with SARS-CoV-2 induced exacerbation. LT for ARDS poses several challenges and is reserved for the minority of carefully selected patients dependent on extracorporeal life support. As others have reported, good short-term survival is described.

Surgery

Franco-Palacios DJ, **Allenspach L**, **Stagner L**, **Pinto-Corrales J**, **Hanlon K**, **Waynick L**, **Nicholson D**, **Shaheen E**, **Spezia M**, **Nappo T**, **Dillon W**, **Sherbin EL**, and **Alangaden G**. Outcomes of SARS-CoV-2 Infection in Lung Transplant Recipients: A Single Center Experience. *J Heart Lung Transplant* 2022; 41(4):S523. PMID: Not assigned. Full Text

D.J. Franco-Palacios, Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI, United States

Purpose: Outcomes of Covid-19 in lung transplant recipients (LTr) were reported in the beginning of the pandemic. Only few centers reported on their experience since December 2020 when vaccines received emergency use authorization. We aim to investigate the outcome of SARS-CoV-2 infection in a cohort of LTr at our center in Detroit, Michigan. Methods: Retrospective chart review study of adult LTr with confirmed SARS-CoV-2 infection from March 2020 to August 2021. Results: Thirty LTr were diagnosed with SARS-CoV-2 infection confirmed by RT PCR of nasopharynx. Median age at diagnosis was 63; 53% were males; 57% Caucasians and 40% of African descendance. Most patients underwent bilateral LT for interstitial lung disease (46%) and for pulmonary sarcoidosis (23%). The median time post LT was 3.1 years. Most patients needed hospitalization for respiratory failure secondary to Covid-19 (73%). Eleven patients were initially managed as outpatient. Five patients received outpatient combination of monoclonal antibodies with three of them later requiring hospitalization for development of hypoxia. None of the patients with initial out of the hospital management died. Amongst 21 hospitalized LTr, six patients were diagnosed with severe pneumonia and ARDS requiring heated high flow and invasive mechanical ventilation (IMV) in 4 patients. 28-day mortality was 10% and ICU mortality was 25% (50% mortality in those on IMV). Twelve hospitalized patients (57%) were treated with remdesivir. Augmented systemic corticosteroids was used in 85% of cases. Cycle cell inhibitor was held in 71% of the cases. Bilateral ground glass opacities of the allografts were common. None of the patients that received at least one dose of mRNA vaccine died. Conclusion: Outcomes in LTr infected with SARS-CoV-2 varies. Early reports showed high mortality rate in severe and critical Covid-19 in LTr. Although hospitalization rate in this cohort was high, only four patients in our cohort required IMV during acute Covid-19. Two of them died; both were unvaccinated. Another unvaccinated patient died due to allograft rejection two months after testing positive to SARS-CoV-2. Most cases were mild to moderate despite frequent radiographic findings of pneumonia. Underreporting and exclusion of mild cases as well as likely protective effect of vaccination and use of monoclonal antibodies may explain our different outcomes.

Surgery

Hencken L, **Grafton G**, **To L**, **Nemeh H**, and **Cowger J**. Peri-Operative Warfarin Protocol to Decrease Length of Stay After Left Ventricular Assist Device Implantation. *J Heart Lung Transplant* 2022; 41(4):S462. PMID: Not assigned. Full Text

L. Hencken, Pharmacy, Henry Ford Hospital, Detroit, MI, United States

Purpose: A limitation to left ventricular assist device (LVAD) implantation is cost with fixed reimbursement rates for the LVAD implantation hospitalization regardless of hospital length of stay and costs. Patients must have a therapeutic INR on warfarin prior to discharge which can take days and delay discharge. The purpose of this study is to evaluate the impact of a peri-operative warfarin protocol on decreasing length of stay during index LVAD implantation. Methods: This is a retrospective single center study of adult

patients undergoing LVAD implantation between January 1, 2019 and December 31, 2020. Patients who died during the admission were excluded. Patients in the intervention group (INT) underwent LVAD between January 1-December 31, 2020. The peri-operative warfarin protocol included pre-operative vitamin K dosing according to INR, initiation of warfarin by post-operative day (POD) 3, and warfarin titration scheme. The historical control group (CON) included patients receiving LVADs between January 1-December 31, 2019. Warfarin start date was at the discretion of providers. All patients had a goal INR of 2-3. Endpoints included length of stay, post-operative warfarin start date, time to therapeutic INR, warfarin dosing requirements, pre-operative vitamin K dosing and bleeding complications. Results: Seventy-seven patients were included; n=41 (53.2%) CON and n=36 (46.8%) INT. Total hospital length of stay was 35 [26,43] days in the CON group compared to 27.5 [24,35] days in the INT group (p=0.095). Warfarin was started earlier in the INT group (POD 5.5 [2.8,7.0]) compared to the CON group (POD 8 [6,14]) (p=0.004). Time to therapeutic INR remained the same between the two groups with a median of 6 days. Pre-operative vitamin K decreased from 15 [10,15] mg in the CON group to 5 [0.0,11.3] mg in the INT group (p=<0.001). There was no increase in bleeding with the peri-operative warfarin interventions: 8 bleeds in the CON group and 4 bleeds in the INT group. Conclusion: Initiating warfarin earlier post-operatively may help decrease hospital length of stay after LVAD implantation without increasing bleeding events.

Surgery
McCarthy S, Molina E, **Nemeh H**, Chaudhry S, Pinney S, Srivastava A, Grinstein J, Hackett I, and **Cowger JA**. Characterizing Outflow Graft Narrowing over Time. *J Heart Lung Transplant* 2022; 41(4):S138. PMID: Not assigned. Full Text

S. McCarthy, Wayne State School of Medicine, Wayne State, Detroit, MI, United States

Purpose: Cases of pump dysfunction due to outflow graft (OG) anastomosis obstruction related to serous fluid accumulation have been reported but the rate of occlusion and actual frequency of asymptomatic OG diminution is not known. Methods: This was a multicenter retrospective analysis of patients on HeartMate II (HMII) or HeartMate 3 (HM3) support surviving at least 180 days with at least one chest computed tomography (CT) scan at 6 months, 1, 2, and/or 3 years postoperative. Patients with OG obstruction due to torsion were excluded. The outflow graft (OG) diameter was measured at its narrowest region; region was categorized as external outflow graft (EOG), mid-graft, or within 2 cm of the aortic anastomosis. Mixed models with repeated measure linear regression was used to assess OG diameter change over time, with 14 mm as reference. Using the narrowest measure, OG diameter was modelled for freedom from death, admission for HF and low flow alarms with hazard ratio [95% CI presented]. Results: Of 71 patients included herein, 25% and 75% were on HMII and HM3 support for a median [25th, 75th] 1230 [703,1592] days. The median CT count was 2 [1,2] per patient. At follow-up, small (1-3 mm, table), but statistically significant reductions in OG diameter were noted (Figure). The median OG narrowing was 7% [0%, 20%]. Time from device implant was the most significant contributing factor (p<0.001) while wrapping of the outflow was nonsignificantly correlated with OG narrowing (p=0.071). Device model was not correlative (p=0.16). OG diameter was not correlated with survival (HR 1.04 [0.81-1.3]), stroke (HR 0.94 [0.78-1.1]) or admissions for heart failure (HR 1.06 [0.88-1.3]), or VAD alarms (HR 0.93 [0.79-1.1]). Conclusion: Minor narrowing of the OG was noted over time, irrespective of LVAD model. The observed degrees of non-twist related-OG narrowing herein did not lead to increase mortality or events. OG wrapping may be associated with OG narrowing over time. Larger sample analyses aim to define degrees of narrowing that elicit device dysfunction.

Surgery
McDonough L, **Petersen L**, **Lehrberg A**, **Bensenhaver J**, **Qutob O**, **Susick L**, **Ekkel E**, **Thaker H**, and **Schwartz T**. Is nodal staging necessary for older patients with HER2-positive or triple-negative breast cancers? *Ann Surg Oncol* 2022; 29(SUPPL 1):305-305. PMID: Not assigned. Full Text

Surgery
Mehra MR, Nayak A, Morris A, **Lanfear DE**, **Nemeh H**, Desai S, Bansal A, Guerrero-Miranda C, Hall S, Cleveland JC, Goldstein DJ, Uriel N, Chen L, Bailey S, Anyanwu A, Heatley G, Chuang J, and Estep JD. Development and Validation of a Personalized Risk Score for Prediction of Patient-Specific Clinical

Experiences with HeartMate 3 LVAD Implantation: An Analysis from the MOMENTUM 3 Trial Portfolio. *J Heart Lung Transplant* 2022; 41(4):S23-S24. PMID: Not assigned. Full Text

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Purpose: Although clinical trials inform on efficacy of left ventricular assist device (LVAD) therapy, individualized risk assessments for outcome prediction are important in guiding implementation of such treatment. In this analysis based on the MOMENTUM 3 trial portfolio (studies sponsored by Abbott), we seek to develop and validate patient-specific risk scores to facilitate the evaluation of candidates for HeartMate 3 (HM3) LVAD implantation. Methods: The MOMENTUM 3 trial portfolio includes 2200 patients that underwent HM3 LVAD implantation in the pivotal trial and Continued Access Protocol (CAP) study, between 2014-2018. Patients were followed for 2 years, and the primary results were presented at ISHLT 2021 and published in Eur J Heart Fail. 2021;23:1392-1400. In this analysis, we shall randomly assign all enrolled patients implanted with the HM3 LVAD to a Derivation Cohort or an internal Validation Cohort. The Derivation Cohort will be used to develop multivariate regression models incorporating common, pre-implant patient parameters that are typically assessed when an informed decision is established. Calculation of the risk scores will be based on the parameter estimates of the final derived models. Receiver operating characteristic curve analysis will be used to evaluate the discriminatory ability of each risk score. The ability of the risk scores to predict outcomes after HM3 LVAD implantation will be tested independently in the Validation Cohort (results expected by February 2022). To avoid bias in the development of the scores, the Validation Cohort will only be analyzed after the risk models are derived. The risk scores will include estimates (and range of individual outcomes) for endpoints including short and long-term survival, hospitalization burden, quality of life, hemocompatibility and non-hemocompatibility related adverse events. Endpoints: The scientific discovery and validation of personalized risk scores will inform clinicians on expectations of individualized outcomes through the clinical journey following HM3 LVAD implantation. Such risk scores and individualized estimates for outcomes will facilitate enhanced decision-making and guide communication among clinicians and patients when considering LVAD therapy in advanced heart failure.

Surgery
Qutob O, **Rama S**, **Black L**, **Zubalik M**, **Bensenhaver J**, **Petersen L**, **Nathanson SD**, **Tepper D**, **Yoho D**, **Evangelista M**, and **Atisha D**. The effect of lymphatic microsurgical preventive healing approach (LYMPHA) on the development of upper-extremity lymphedema following axillary lymph node dissection in breast cancer patients. *Ann Surg Oncol* 2022; 29(SUPPL 1):40-41. PMID: Not assigned. Full Text

Surgery
Sanchez PG, Chan EG, Davis RD, Hartwig M, Machuca T, Whitson B, Daneshmand M, Ovidio FD, Dcunha J, Weyant M, Jessen M, Bermudez C, Mulligan M, Wozniak T, Lynch W, **Nemeh H**, Caldeira C, Song T, Kreisel D, Camp P, Ramzy D, Griffith B, and Cantu E. Normothermic Ex Vivo Lung Perfusion (Novel) as an Assessment of Extended Criteria Donor Lungs: A Prospective Multi-Center Clinical Trial. *J Heart Lung Transplant* 2022; 41(4):S40-S41. PMID: Not assigned. Full Text

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Purpose: Ex vivo lung perfusion (EVLP) allows re-evaluation of extended criteria/marginal donor lungs. This can increase the number of lung transplants. However, the long-term outcomes of transplanting EVLP-screened lungs in a multicenter setting are unknown. We proposed to evaluate the short- and long-term outcomes of EVLP performed at multiple centers. Methods: This is a prospective, nonrandomized clinical trial. Seventeen lung transplant centers in the United States. Adult patients with end-stage pulmonary disease requiring lung transplant from May 2011 to December 2017 were eligible. Lung allografts initially deemed extended criteria/marginal (n=216) were placed on EVLP and re-evaluated prior to transplant. Patients received either standard donors (n=116) or lungs screened with EVLP (n=110). Results: Half of the lung grafts (110/216, 50.9%) placed on EVLP were transplanted. The incidence of primary graft dysfunction 24 hours post-transplant was higher in the EVLP group (25.5% vs 10.3%, p=0.003), but was not significantly different 48 hours (EVLP: 15.5%, control: 9.5%, p=0.49) and 72 hours (13.6% vs 6.9%, p=0.34) post-transplant. Survival was not significantly different between the 2 groups 1

year (n=226, EVLP: 86%, control: 94%, p=0.06), 3 years (n=226, EVLP: 68%, control: 76%, p=0.16, Figure), or 5 years (n=159, EVLP: 59%, control: 65%, p=0.68) post-transplant. There were also no differences in pulmonary function, the incidence of chronic lung allograft dysfunction or quality of life measures post-transplant. Conclusion: In this multicenter study, recipients of lungs that were re-evaluated on EVLP and deemed suitable for transplant had similar outcomes as a recipients of a standard lung transplants. EVLP offers the opportunity to screen donated lungs initially considered high risk and can safely increase the availability of transplantable lungs without compromising outcomes.

Surgery

Simanovski J, **Nemeh HM**, **Allenspach LL**, **Mei LL**, **Stagner LD**, **Pinto JC**, **Olexsey KM**, **Franco-Palacios DJ**, and **Alangaden GJ**. Risks and Outcomes Associated with Pleural Space Infections After Lung Transplantation. *J Heart Lung Transplant* 2022; 41(4):S394. PMID: Not assigned. Full Text

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Purpose: Pleural space infections (PSI) are a serious complication after lung transplantation (LT) however there is limited data on the associated risk factors and outcomes of PSI. We examined: 1) risk factors associated with PSI after LT; 2) effect of PSI on LT outcomes. Methods: This is a retrospective single center cohort study of 74 consecutive LT recipients (1/2018- 6/2020). Patients were divided into infected and non-infected groups, where PSI were defined as post-LT pleural effusions with pathogen(s) isolated from pleural fluid. Data were collected and compared between two groups with two-sample t-test or Fisher-exact. Multivariable logit model was performed with estimations of odds ratio (OR) and its confidence interval [CI]. Results: Among 74 LT recipients, 38 (51%) developed pleural effusions requiring drainage; of them 16 (42%) had PSI. Baseline demographics were similar in patients with and without PSI (Table). Notably, 88% of PSI group received steroids pre-LT compared to 55% in the non-infected group ($p<0.05$); 88% of the PSI group had an underlying diagnosis of interstitial lung disease versus 45% of the non-infected group ($p<0.01$). Overall post-operative complications occurred more frequently in the PSI group vs. non-infected group 77% vs. 25% ($p<0.01$) and airway complications in 86% vs. 44% ($p<0.01$). Hospital length of stay was longer in the PSI group with the median of 78 versus 31 days in the non-infected group ($p<0.01$). Results of logistical modeling showed high risk of PSI with presence of post-LT airway complications (OR =10.8 95% CI 1.7- 72.5) and presence of post operative complications (OR=10.6, 95% CI 1.8-63.5). There was no difference in the incidence of readmissions, acute cellular rejection or 1 year mortality between the two cohorts. Conclusion: PSI remain a prevalent yet under-studied complication. Airway or post-operative complications after LT were associated with PSI. One-year outcomes were similar in LT recipients with and without PSI.

Henry Ford Health Publications on COVID-19

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Gomez JMD, **Zimmerman AC**, du Fay de Lavallaz J, Wagner J, Tung L, Bouroukas A, Nguyen TTP, Canzolino J, Goldberg A, Santos Volgman A, Suboc T, and Rao AK. Echocardiographic predictors of mortality and morbidity in COVID-19 disease using focused cardiovascular ultrasound. *Int J Cardiol Heart Vasc* 2022; 39:100982. PMID: 35233442. Full Text

Cardiology/Cardiovascular Research
Jehangir Q, Lee Y, Latack K, **Poisson L**, **Wang DD**, **Song S**, Apala DR, Patel K, Halabi AR, Krishnamoorthy G, and Sule AA. Data of atrial arrhythmias in hospitalized COVID-19 and influenza patients. *Data Brief* 2022; 42:108177. PMID: 35449710. Full Text

Cardiology/Cardiovascular Research
Jehangir Q, Lee Y, **Latack K**, **Poisson L**, **Wang DD**, **Song S**, Apala DR, Patel K, Halabi AR, Krishnamoorthy G, and Sule AA. Incidence, Mortality, and Imaging Outcomes of Atrial Arrhythmias in COVID-19. *Am J Cardiol* 2022; Epub ahead of print. PMID: 35382929. Full Text

Dermatology
Prasad S, McMahon DE, Tyagi A, Ali R, Singh R, Rosenbach M, **Lim HW**, Fox LP, Blumenthal K, Hruza GJ, French LE, and Freeman EE. Cutaneous Reactions Following Booster Dose Administration of COVID-19 mRNA Vaccine: a first look from the AAD/ILDS Registry. *JAAD Int* 2022; Epub ahead of print. PMID: 35498758. Full Text

Emergency Medicine
Bruen C, Al-Saadi M, Michelson EA, Tanios M, Mendoza-Ayala R, **Miller J**, Zhang J, Stauderman K, Hebbar S, and Hou PC. Auxora vs. placebo for the treatment of patients with severe COVID-19 pneumonia: a randomized-controlled clinical trial. *Crit Care* 2022; 26(1):101. PMID: 35395943. Full Text

Emergency Medicine
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Public Health Sciences
Jehangir Q, Lee Y, **Latack K**, **Poisson L**, **Wang DD**, **Song S**, Apala DR, Patel K, Halabi AR, Krishnamoorthy G, and Sule AA. Incidence, Mortality, and Imaging Outcomes of Atrial Arrhythmias in COVID-19. *Am J Cardiol* 2022; Epub ahead of print. PMID: 35382929. Full Text