

Henry Ford Health Publication List – May 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 112 unique citations listed this month: 93 articles, 15 abstracts, and 4 book chapters, with 13 articles and 1 abstract on COVID-19.

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

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Articles

Allergy and Immunology

Eapen AA, Parameswaran S, Forney C, Edsall LE, Miller D, Donmez O, Dunn K, Lu X, Granitto M, Rowden H, Magier AZ, Pujato M, Chen X, Kaufman K, Bernstein DI, Devonshire AL, Rothenberg ME, Weirauch MT, and Kottyan LC. Epigenetic and transcriptional dysregulation in CD4+ T cells in patients with atopic dermatitis. *PLoS Genet* 2022; 18(5):e1009973. PMID: 35576187. [Full Text](#)

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Atopic dermatitis (AD) is one of the most common skin disorders among children. Disease etiology involves genetic and environmental factors, with 29 independent AD risk loci enriched for risk allele-dependent gene expression in the skin and CD4+ T cell compartments. We investigated the potential epigenetic mechanisms responsible for the genetic susceptibility of CD4+ T cells. To understand the differences in gene regulatory activity in peripheral blood T cells in AD, we measured chromatin accessibility (an assay based on transposase-accessible chromatin sequencing, ATAC-seq), nuclear factor kappa B subunit 1 (NFKB1) binding (chromatin immunoprecipitation with sequencing, ChIP-seq), and gene expression levels (RNA-seq) in stimulated CD4+ T cells from subjects with active moderate-to-severe AD, as well as in age-matched non-allergic controls. Open chromatin regions in stimulated CD4+ T cells were highly enriched for AD genetic risk variants, with almost half of the AD risk loci overlapping AD-dependent ATAC-seq peaks. AD-specific open chromatin regions were strongly enriched for NF- κ B DNA-binding motifs. ChIP-seq identified hundreds of NFKB1-occupied genomic loci that were AD- or control-specific. As expected, the AD-specific ChIP-seq peaks were strongly enriched for NF- κ B DNA-binding motifs. Surprisingly, control-specific NFKB1 ChIP-seq peaks were not enriched for NFKB1 motifs, but instead contained motifs for other classes of human transcription factors, suggesting a mechanism involving altered indirect NFKB1 binding. Using DNA sequencing data, we identified 63 instances of altered genotype-dependent chromatin accessibility at 36 AD risk variant loci (30% of AD risk loci) that might lead to genotype-dependent gene expression. Based on these findings, we propose that CD4+ T cells respond to stimulation in an AD-specific manner, resulting in disease- and genotype-dependent chromatin accessibility alterations involving NFKB1 binding.

Allergy and Immunology

Zanobetti A, Ryan PH, Coull B, Brokamp C, Datta S, Blossom J, Lothrop N, Miller RL, Beamer PI, Visness CM, Andrews H, Bacharier LB, Hartert T, **Johnson CC**, Ownby D, Khurana Hershey GK, **Joseph C**, Yiqiang S, Mendoza E, Jackson DJ, Luttmann-Gibson H, **Zoratti EM**, Wright AL, Martinez FD, Seroogy CM, **Gern JE**, and Gold DR. Childhood Asthma Incidence, Early and Persistent Wheeze, and Neighborhood Socioeconomic Factors in the ECHO/CREW Consortium. *JAMA Pediatr* 2022; Epub ahead of print. PMID: 35604671. [Full Text](#)

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Division of Allergy and Immunology, Augusta University, Augusta, Georgia.
Cincinnati Children's Hospital, Division of Asthma Research, Cincinnati, Ohio.
Indiana University School of Medicine, Bloomington.
Department of Pediatrics, Indiana University, Bloomington.
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Department of Medicine, Henry Ford Health System, Detroit, Michigan.
Division of Pulmonary and Sleep Medicine, Department of Pediatrics, College of Medicine, University of Arizona, Tucson.

IMPORTANCE: In the United States, Black and Hispanic children have higher rates of asthma and asthma-related morbidity compared with White children and disproportionately reside in communities with economic deprivation. **OBJECTIVE:** To determine the extent to which neighborhood-level socioeconomic indicators explain racial and ethnic disparities in childhood wheezing and asthma. **DESIGN, SETTING, AND PARTICIPANTS:** The study population comprised children in birth cohorts located throughout the United States that are part of the Children's Respiratory and Environmental Workgroup consortium. Cox proportional hazard models were used to estimate hazard ratios (HRs) of asthma incidence, and logistic regression was used to estimate odds ratios of early and persistent wheeze prevalence accounting for mother's education, parental asthma, smoking during pregnancy, child's race and ethnicity, sex, and region and decade of birth. **EXPOSURES:** Neighborhood-level socioeconomic indicators defined by US census tracts calculated as z scores for multiple tract-level variables relative to the US average linked to participants' birth record address and decade of birth. The parent or caregiver reported the child's race and ethnicity. **MAIN OUTCOMES AND MEASURES:** Prevalence of early and persistent childhood wheeze and asthma incidence. **RESULTS:** Of 5809 children, 46% reported wheezing before age 2 years, and 26% reported persistent wheeze through age 11 years. Asthma prevalence by age 11 years varied by cohort, with an overall median prevalence of 25%. Black children (HR, 1.47; 95% CI, 1.26-1.73) and Hispanic children (HR, 1.29; 95% CI, 1.09-1.53) were at significantly increased risk for asthma incidence compared with White children, with onset occurring earlier in childhood. Children born in tracts with a greater proportion of low-income households, population density, and poverty had increased asthma incidence. Results for early and persistent wheeze were similar. In effect modification analysis, census variables did not significantly modify the association between race and ethnicity and risk for asthma incidence; Black and Hispanic children remained at higher risk for asthma compared with White children across census tracts socioeconomic levels. **CONCLUSIONS AND RELEVANCE:** Adjusting for individual-level characteristics, we observed neighborhood socioeconomic disparities in childhood wheeze and asthma. Black and Hispanic children had more asthma in neighborhoods of all income levels. Neighborhood- and individual-level characteristics and their root causes should be considered as sources of respiratory health inequities.

Anesthesiology

Zador L, Nowak K, Sitarik A, MacLean L, Han X, Kalsi M, Yeldo N, Sibai N, Penning D, and Lewis M. The Burnout Epidemic Within A Viral Pandemic: Impact of a Wellness Initiative. *Perioper Care Oper Room Manag* 2022; 27:100251. PMID: 35382030. [Full Text](#)

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Department of Anesthesiology, Hospital for Special Surgery, Weill Medical College of Cornell University, 535 East 70th Street, New York City, New York 10021.

BACKGROUND: Anesthesiologists are at high risk of developing burnout, a condition which can lead to many deleterious effects for the physician, and far-reaching effects on their patients and hospital systems. The COVID-19 pandemic has presented new challenges that have further exacerbated the risk of burnout in anesthesiologists. It is critical to develop effective strategies to promote well-being and decrease burnout for physicians in this specialty. The purpose of this observational study was to evaluate the impact of a Physician Well-Being Initiative on distress and well-being in anesthesiologists. It was hypothesized that the wellness intervention would promote an improvement in well-being scores.

METHODS: The Physician Well-Being Initiative was launched in August 2019 in the Department of Anesthesiology, Pain Management and Perioperative Medicine at Henry Ford Hospital in Detroit, Michigan. The Physician Well-Being Initiative was designed to address several of the key factors that improve physician wellness, including 1) a sense of autonomy; 2) positive view of leadership; and 3) flexible schedule opportunities. To assess the impact of the Physician Well-Being Initiative on the well-being and distress scores of participating anesthesiologists, the physicians were emailed the validated Well-Being Index survey at baseline and 3, 6 and 12 months. The Well-Being Index evaluates multiple items of distress in the healthcare setting. The sample size was limited to the 54 anesthesiologists at Henry Ford Hospital. **RESULTS:** Forty-four of the 54 anesthesiologists completed the baseline questionnaire. A total of 44 physicians answered the questionnaire at baseline, with more male than female physicians (35 males and 7 females) and the majority (17/44) in practice for 5-10 years. Thirty-two physicians completed the survey at 3 and 6 months, and 31 physicians at 12 months after the launch of the Physician Well-Being Initiative. Twenty-one physicians completed the questionnaire at all 4 time points. Although the COVID-19 pandemic started shortly after the 6-month surveys were submitted, results indicated that there was a 0.05 decrease in the Well-Being Index sum score for every 1-month of time (coefficient -0.05, 95% CI -0.01, -0.08, P = 0.013). This study shows that, with the wellness initiative in place, the department was able to maintain and potentially even reduce physician distress despite the concurrent onset of the pandemic. **CONCLUSIONS:** Following the launch of a sustained wellness initiative, this study demonstrates that physician wellness improved with time. This suggests that it takes time for a wellness initiative to have an effect on well-being and distress in anesthesiologists.

Behavioral Health Services/Psychiatry/Neuropsychology

Abu Sneineh A, Haj Ali S, Al-Masri A, Diab A, Aldweik F, Darweesh M, Qaisi M, Alshakhatreh O, Tamimi T, Rayyan Y, Banimustafa R, and Sablaban I. Prevalence of anxiety and depressive symptoms in ulcerative colitis patients in Jordan and its relationship to patient-reported disease activity. *Sci Rep* 2022; 12(1):7682. PMID: 35538204. [Full Text](#)

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Inflammatory bowel disease is associated with higher rates of anxiety and depression compared to the general population. We aimed to determine the prevalence of anxiety and depressive symptoms among patients with ulcerative colitis and correlation to disease activity. In this cross-sectional study, we

collected data from 70 consecutive ulcerative colitis patients over one year at our inflammatory bowel disease outpatient clinic through an interview and a questionnaire containing patient demographics and disease characteristics. Anxiety and depressive symptoms were characterized using the Generalized Anxiety Disorder-7 questionnaire and Patient Health Questionnaire-9, respectively, with ulcerative colitis disease severity assessed by the Partial Mayo scoring system. The majority of our patients were females (68.6%) and the mean age was 39.3 years. Rates of anxiety and depressive symptoms among ulcerative colitis patients were 65.7% and 58.6%, respectively. Depressive symptoms were significantly associated with patient-reported disease activity ($r = 0.361$; $p = 0.010$). Significant percentages of ulcerative colitis patients were appreciated to have anxiety and depressive symptoms, and there was a correlation between patient-reported disease activity and depressive symptoms. At this high rate of prevalence, it is justified to screen patients for the presence of psychiatric comorbidities.

Behavioral Health Services/Psychiatry/Neuropsychology

Hecht LM, Braciszewski JM, Miller-Matero LR, Ahmedani BK, Kerver JM, and Loree AM. Adequacy of prenatal care utilisation and gestational weight gain among women with depression. *J Reprod Infant Psychol* 2022;1-12; Epub ahead of print. PMID: 35582731. [Full Text](#)

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BACKGROUND: Depression is common during pregnancy, can elevate risk for excessive or inadequate gestational weight gain (GWG), and is associated with both underutilisation and overutilisation of prenatal care. Whether GWG is associated with adequacy of prenatal care among women with and without depression in the United States is unknown. This study evaluated whether adequacy of prenatal care differed by depression status and GWG. **METHODS:** Data from the Pregnancy Risk Assessment Monitoring System from 1,379,870 women who were pregnant with a singleton and delivered at 37-42 weeks gestation during 2016 to 2018 were included. Depression was self-reported. The Kotelchuck index was used to evaluate adequacy of prenatal care. Maternal weight gain was compared to GWG guidelines. **RESULTS:** Approximately 13.1% of the sample experienced depression during pregnancy. Although those with depression had increased odds of both inadequate and above adequate levels of prenatal care, this association was no longer significant after accounting for demographics, medical comorbidities, and socioeconomic factors. Individuals with inadequate levels of prenatal care with a normal pre-pregnancy body mass index gained less weight during pregnancy. **CONCLUSIONS:** The association between depression and prenatal care utilisation seems driven by demographic, medical comorbidity, and socioeconomic variables. Weight outcomes were associated with inadequate prenatal care utilisation.

Behavioral Health Services/Psychiatry/Neuropsychology

Miller-Matero LR, Hecht LM, Patel S, Martens KM, Hamann A, and Carlin AM. Exploring gender, psychiatric symptoms, and eating behaviors as predictors of attrition to bariatric surgery. *Am J Surg* 2022; Epub ahead of print. PMID: 35570060. [Full Text](#)

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BACKGROUND: Only a small proportion of eligible individuals undergo bariatric surgery. The purpose was to examine attrition to surgery and whether psychiatric symptoms and eating behaviors differentially predicted attrition among men and women. **METHOD:** Data was collected from a retrospective chart review of 313 patients who underwent a pre-surgical psychosocial evaluation. **RESULTS:** The overall attrition rate was 33.5%; 42.6% of men and 31.7% of women experienced attrition. In the multivariate

analysis of the entire sample, White patients (OR = 2.33, CI: 1.33, 4.08) and those without a history of binge eating (OR = 2.71, CI: 1.23, 5.97) were more likely to undergo surgery. In a multivariate analysis of women only, race and binge eating independently predicted attrition; however, no factors significantly predicted attrition among men. **CONCLUSIONS:** Factors identified at the pre-surgical psychosocial evaluation can identify patients at risk for attrition, and these factors may differ for men and women.

Behavioral Health Services/Psychiatry/Neuropsychology

Reffi AN, Kaimbach DA, Cheng P, Jovanovic T, Norrholm SD, Sexton MB, Mahr G, Arnett L, Seymour G, and Drake CL. Sleep reactivity as a potential pathway from childhood abuse to adult insomnia. *Sleep Med* 2022; 94:70-75. PMID: 35504109. [Full Text](#)

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Neuroscience Center for Anxiety, Stress, and Trauma (NeuroCAST), Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, MI, USA.

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BACKGROUND: Survivors of childhood abuse are prone to adult insomnia, but the mechanisms for this development are poorly understood. Abuse that occurs during sensitive developmental periods might affect risk for insomnia by impacting emerging stress regulatory processes. Sleep reactivity refers to the sensitivity of the sleep system to stress and is a robust risk factor for insomnia. Recent evidence shows stress exposure itself worsens sleep reactivity, thereby increasing insomnia vulnerability. In this preliminary study, we hypothesized the association between childhood abuse experiences and adult insomnia would be mediated through greater sleep reactivity. **METHODS:** Community adults were recruited from the United States during the COVID-19 pandemic between June 2020 and June 2021 (N = 241, 88% female, M(age) = 39, SD = 13.40). Participants completed a cross-sectional survey that included the Childhood Trauma Questionnaire, Ford Insomnia Response to Stress Test, Insomnia Severity Index, and a measure of general COVID-19 stress. **RESULTS:** Reporting more frequent childhood emotional, physical, or sexual abuse was associated with more severe insomnia during the COVID-19 pandemic. Only childhood emotional and physical (but not sexual) abuse histories were associated with greater sleep reactivity, which exerted an indirect effect on the relationships between these two abuse types and insomnia symptoms. These findings were robust to the effects of gender, age, and stress about the COVID-19 pandemic. **CONCLUSIONS:** This preliminary study suggests recurrent emotional and physical abuse in childhood might promote later insomnia through heightened sleep reactivity. Stress management interventions could be important to prevent insomnia for abuse survivors by bolstering resilience of the sleep system.

Behavioral Health Services/Psychiatry/Neuropsychology

Zador L, Nowak K, Sitarik A, MacLean L, Han X, Kalsi M, Yeldo N, Sibai N, Penning D, and Lewis M. The Burnout Epidemic Within A Viral Pandemic: Impact of a Wellness Initiative. *Perioper Care Oper Room Manag* 2022; 27:100251. PMID: 35382030. [Full Text](#)

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Department of Anesthesiology, Hospital for Special Surgery, Weill Medical College of Cornell University, 535 East 70th Street, New York City, New York 10021.

BACKGROUND: Anesthesiologists are at high risk of developing burnout, a condition which can lead to many deleterious effects for the physician, and far-reaching effects on their patients and hospital systems. The COVID-19 pandemic has presented new challenges that have further exacerbated the risk of burnout

in anesthesiologists. It is critical to develop effective strategies to promote well-being and decrease burnout for physicians in this specialty. The purpose of this observational study was to evaluate the impact of a Physician Well-Being Initiative on distress and well-being in anesthesiologists. It was hypothesized that the wellness intervention would promote an improvement in well-being scores. **METHODS:** The Physician Well-Being Initiative was launched in August 2019 in the Department of Anesthesiology, Pain Management and Perioperative Medicine at Henry Ford Hospital in Detroit, Michigan. The Physician Well-Being Initiative was designed to address several of the key factors that improve physician wellness, including 1) a sense of autonomy; 2) positive view of leadership; and 3) flexible schedule opportunities. To assess the impact of the Physician Well-Being Initiative on the well-being and distress scores of participating anesthesiologists, the physicians were emailed the validated Well-Being Index survey at baseline and 3, 6 and 12 months. The Well-Being Index evaluates multiple items of distress in the healthcare setting. The sample size was limited to the 54 anesthesiologists at Henry Ford Hospital. **RESULTS:** Forty-four of the 54 anesthesiologists completed the baseline questionnaire. A total of 44 physicians answered the questionnaire at baseline, with more male than female physicians (35 males and 7 females) and the majority (17/44) in practice for 5-10 years. Thirty-two physicians completed the survey at 3 and 6 months, and 31 physicians at 12 months after the launch of the Physician Well-Being Initiative. Twenty-one physicians completed the questionnaire at all 4 time points. Although the COVID-19 pandemic started shortly after the 6-month surveys were submitted, results indicated that there was a 0.05 decrease in the Well-Being Index sum score for every 1-month of time (coefficient -0.05, 95% CI -0.01, -0.08, $P = 0.013$). This study shows that, with the wellness initiative in place, the department was able to maintain and potentially even reduce physician distress despite the concurrent onset of the pandemic. **CONCLUSIONS:** Following the launch of a sustained wellness initiative, this study demonstrates that physician wellness improved with time. This suggests that it takes time for a wellness initiative to have an effect on well-being and distress in anesthesiologists.

Cardiology/Cardiovascular Research

Brawner CA, Pack Q, **Berry R**, **Kerrigan DJ**, **Ehrman JK**, and **Keteyian SJ**. Relation of a Maximal Exercise Test to Change in Exercise Tolerance During Cardiac Rehabilitation. *Am J Cardiol* 2022; Epub ahead of print. PMID: 35570164. [Full Text](#)

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The purpose of this study was to test the hypothesis that an individualized exercise training target heart rate (HR) based on a maximal graded exercise test (GXT) is associated with greater improvements in exercise tolerance during cardiac rehabilitation (CR) compared with no GXT. In this retrospective study, we identified patients who completed 9 to 36 visits of CR between 2001 and 2016, with a length of stay ≤ 18 weeks and a visit frequency of 1 to 3 days per week. Patients were grouped based on whether their exercise was guided by a target HR determined from a GXT. To assess the relation between GXT and change in exercise training metabolic equivalents of task (METs), we used generalized linear models adjusted for age, gender, race, referral reason, CR visits, CR frequency, METs at start, CR location, and year of participation. Out of 4,455 patients (37% female, 48% White, median age = 62 years), 53% were prescribed a target HR based on a GXT. Compared with no GXT, a GXT was associated with a significantly greater increase in covariate-adjusted METs during CR and percentage change from start (+0.44 METs [95% confidence interval [CI] 0.38 to 0.51] and +17% [95% CI 14% to 19%], respectively). In a sensitivity analysis limited to patients with 24 to 36 visits at ≥ 2 days per week ($n = 1,319$), a GXT was associated with a significantly greater increase in covariate-adjusted exercise training METs (+0.51 [95% CI 0.36 to 0.66]; +19% [95% CI 13% to 24%]). In conclusion, to maximize the potential increase in exercise capacity during CR, patients should undergo a GXT to determine an individualized exercise training target HR.

Cardiology/Cardiovascular Research

Devgun JK, **Nasser T**, and **Lee J**. Pulmonary vein Doppler flow in a patient with fatigue and dyspnoea. *Heart* 2022; 108(12):931-988. PMID: 35613734. [Full Text](#)

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Cardiology/Cardiovascular Research

Ehrman JK, Salisbury D, and Treat-Jacobson D. Decision Aids for Determining Facility Versus Non-Facility-Based Exercise in Those with Symptomatic Peripheral Artery Disease. *Curr Cardiol Rep* 2022: 1-9; Epub ahead of print. PMID: 35587854. [Full Text](#)

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PURPOSE OF REVIEW: This paper sought to provide rationale for determining when a patient with symptomatic peripheral artery disease (PAD) might be referred for home-based versus facility-based exercise therapy. **RECENT FINDINGS:** Multiple randomized controlled studies have embedded supervised, structured exercise therapy as a class IA recommended therapy for those with symptomatic PAD. More recently, there is interest in non-facility-based exercise training as an alternative. The current literature is mixed on the effectiveness of non-facility-based training and is influenced by the amount of contact with clinical staff providing some supervision (e.g., occasional facility-based exercise or coaching phone calls), and the intensity (e.g., performed intermittently by inducing pain or continually and not inducing pain) and frequency (e.g., 12-week common supervised exercise program or those longer than 24 weeks) of exercise. Certainly, the data suggests non-facility-based exercise, while possibly improving walking performance, is inferior to facility-based supervised exercise training. Comprehensive data is lacking on utilization of supervised exercise therapy in those with symptomatic PAD, but is likely <2% of those eligible who participate. This suggests a possible important role for alternatives including non-facility-based (e.g., home, fitness center). Exercise training in the supervised, facility-based setting appears to be greatly underutilized. Non-facility-based exercise may help to overcome some of the most common barriers to participating in facility-based exercise including those related to motivation, transportation, and proximity. However, facility-based training is considered the gold standard so decisions about allowing a patient to exercise train at home must take into account issues including disease severity, patient motivation and available exercise resources, mobility and balance, cognitive function, and other medical concerns (e.g., symptomatic coronary artery disease or heart failure).

Cardiology/Cardiovascular Research

Gorgis S, Mawri S, **Dabbagh MF**, **Aurora L**, Ali M, **Mitchell G**, **Jacobsen G**, **Hegab S**, **Schwartz S**, **Kelly B**, **Grafton G**, **Awdish R**, **Ismail R**, and **Koenig G**. Ultrasound-assisted catheter-directed thrombolysis versus anticoagulation alone for management of submassive pulmonary embolism. *J Cardiol* 2022; Epub ahead of print. PMID: 35643741. [Full Text](#)

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BACKGROUND: Patients with submassive pulmonary embolism (PE) are vulnerable to sudden deterioration, recurrent PE, and progression to pulmonary hypertension and chronic right ventricular (RV) dysfunction. Previous studies have suggested a clinical benefit of using ultrasound-assisted catheter-

directed thrombolysis (USCDT) to invasively manage patients with submassive PE. However, there is sparse data comparing the clinical outcomes of these patients when treated with USCDT versus anticoagulation (AC) alone. We sought to compare the outcomes of USCDT versus AC alone in the management of submassive PE. **METHODS:** 192 consecutive patients who underwent USCDT for submassive PE between January 2013 and February 2019 were identified. ICD9/ICD10 codes were used to detect 2554 patients diagnosed with PE who did not undergo thrombolysis. Propensity matching identified 192 patients with acute PE treated with AC alone. Clinical outcomes were compared between the two groups. Baseline demographics, laboratory values, and pulmonary embolism severity index scores were similar between the two cohorts. **RESULTS:** There was a significant reduction in mean systolic pulmonary artery pressure (sPAP) in the USCDT group compared to the AC group ($\Delta 11$ vs $\Delta 3.9$ mmHg, $p < 0.001$). There was significant improvement in proportion of RV dysfunction in all patients, but the difference was larger in the USCDT group ($\Delta 43.3\%$ vs $\Delta 17.3\%$, $p < 0.001$). Patients who underwent USCDT had lower 30-day (4.3% vs 10.5%, $p = 0.03$), 90-day (5.5% vs 12.4%, $p = 0.03$), and 1-year mortality (6.2% vs 14.2%, $p = 0.03$). **CONCLUSIONS:** In patients with acute submassive PE, USCDT was associated with improved 30-day, 90-day, and 1 year mortality as compared to AC alone. USCDT also improved RV function and reduced sPAP to a greater degree than AC alone. Further studies are needed to verify these results in both short- and long-term outcomes.

Cardiology/Cardiovascular Research

Guduguntla V, Yaser JM, **Keteyian SJ**, Pagani FD, Likosky DS, Sukul D, and Thompson MP. Variation in Cardiac Rehabilitation Participation During Aortic Valve Replacement Episodes of Care. *Circ Cardiovasc Qual Outcomes* 2022; Epub ahead of print. PMID: 35559710. [Full Text](#)

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Background: Despite reported benefit in the setting of aortic valve replacement (AVR), cardiac rehabilitation (CR) utilization remains low, with few studies evaluating hospital and patient-level variation in CR participation. We explored determinants of CR variability during AVR episodes of care: transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR). **Methods:** A cohort of 10,124 AVR episodes of care (TAVR $n=5,121$ from 24 hospitals; SAVR $n=5,003$ from 32 hospitals) were identified from the Michigan Value Collaborative statewide multipayer registry (2015 to 2019). CR enrollment was defined as the presence of a single professional or facility claim within 90 days of discharge: 93797, 93798, G0422, G0423. Annual trends and hospital variation in CR were described for TAVR, SAVR, and all AVR. Multilevel logistic regression was used to estimate effects of predictors and hospital risk-adjusted rates of CR enrollment. **Results:** Overall, 4,027 (39.8%) patients enrolled in CR, with significant differences by treatment strategy: SAVR=50.9%, TAVR=28.9% ($p < 0.001$). CR use after SAVR was significantly higher than after TAVR and increased over time for both modalities ($p < 0.001$). There were significant differences in CR enrollment across age, gender, payer, and some comorbidities ($p < .05$). At the hospital-level, CR participation rates for all AVR varied 10-fold (4.8% to 68.7%) and were moderately correlated between SAVR and TAVR (Pearson $r=0.56$, $p < 0.01$). **Conclusions:** Substantial variation exists in CR participation during AVR episodes of care across hospitals. However, within-hospital CR participation rates were significantly correlated across treatment strategies. These findings suggest that CR participation is the product of hospital-specific practice patterns. Identifying hospital practices associated with higher CR participation can help assist future quality improvement efforts to increase CR use after AVR.

Cardiology/Cardiovascular Research

Gupta K, and **Lee JC**. Assessment of sinus of valsalva dimensions before TAVI: An independent predictor of worse outcomes? *Am Heart J* 2022; 248:165. PMID: 35491050. [Full Text](#)

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Cardiology/Cardiovascular Research

Hur DJ, **Wang DD**, and Choi AD. From a priori to evidence and advocacy: The evolving paradigm of CCT competency for structural heart disease. *J Cardiovasc Comput Tomogr* 2022; Epub ahead of print. PMID: 35618636. [Full Text](#)

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Cardiology/Cardiovascular Research

Iannaccone M, Franchin L, Hanson ID, Boccuzzi G, **Basir MB**, Truesdell AG, and **O'Neill W**. Timing of impella placement in PCI for acute myocardial infarction complicated by cardiogenic shock: An updated meta-analysis. *Int J Cardiol* 2022; Epub ahead of print. PMID: 35533755. [Full Text](#)

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INTRODUCTION: The timing of hemodynamic support in acute myocardial infarction complicated by cardiogenic shock (AMICS) has yet to be defined. The aim of this meta-analysis was to evaluate the impact of timing of Impella initiation on early and midterm mortality. **METHODS:** A systematic literature review and meta-analysis was conducted using PubMed and Cochrane databases. All studies reporting short-term mortality rates and timing of Impella placement in AMICS were included. Meta-regression analysis and sensitivity analysis were performed on the primary endpoint, short-term mortality (≤ 30 days), and secondary endpoints (midterm mortality, device-related bleeding, and limb ischemia). **RESULTS:** Of 1289 studies identified, 13 studies (6810 patients; 2970 patients identified as receiving Impella pre-PCI and 3840 patients receiving Impella during/post-PCI) were included in this analysis. Median age was 63.8 years (IQR 63-65.7); 76% of patients were male, and a high prevalence of cardiovascular risk factors was noted across the entire population. Short-term mortality was significantly reduced in those receiving pre-PCI vs. during/post-PCI Impella support (37.2% vs 53.6%, RR 0.7; CI 0.56-0.88). Midterm mortality was also lower in the pre-PCI Impella group (47.9% vs 73%, RR 0.81; CI 0.68-0.97). The rate of device-related bleeding (RR 1.05; CI 0.47-2.33) and limb ischemia (RR 1.6; CI 0.63-2.15) were similar between the two groups. **CONCLUSION:** This analysis suggests that Impella placement prior to PCI in AMICS may have a positive impact on short- and midterm mortality compared with post-PCI, with similar safety outcomes. Due to the observational nature of the included studies, further studies are needed to confirm this hypothesis (CRD42022300372).

Cardiology/Cardiovascular Research

Limkakeng AT, Jr., Hertz J, Lerebours R, Kuchibhatla M, **McCord J**, Singer AJ, Apple FS, Peacock WF, Christenson RH, and **Nowak RM**. Ideal high sensitivity troponin baseline cutoff for patients with renal dysfunction. *Am J Emerg Med* 2022; 56:323-324. PMID: 34482998. [Full Text](#)

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Cardiology/Cardiovascular Research

Mohammed M, Nona P, Abou Asala E, Chiang M, Lemor A, O'Neill B, Frisoli T, Lee J, Wang DD, O'Neill WW, Eng M, and Villablanca PA. Preclosure of large bore venous access sites in patients undergoing transcatheter mitral replacement and repair. *Catheter Cardiovasc Interv* 2022; Epub ahead of print. PMID: 35568977. [Full Text](#)

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OBJECTIVE: We aim to report on the efficacy and safety of large bore venous access (LBVA) preclosure with Perclose™ (Abbott Vascular Devices) suture-mediated device use following transcatheter edge-to-edge (TEER) and replacement (TMVR). **BACKGROUND:** Patients requiring TEER and TMVR require LBVA. Clinical outcome data on the use of suture-mediated devices for LBVA site closure are limited. **METHODS:** Between 2012 and 2019, 354 consecutive high-risk patients with mitral valvular heart disease underwent TEER (n = 287) with MitraClip and TMVR (n = 67) with Edwards Sapien Valves. Patients had LBVA with 24 or 16 French sheaths. All patients underwent preclosure of LBVA except for one that underwent manual hemostasis. **RESULTS:** There were no closure device failures. None of the cases required surgical repair of the access site following venous preclosure. Two cases had large hematomas (>6 cm) following Perclose in each group. Six cases had small hematomas (<6 cm and >2 cm) with three in each group. There was one major bleeding using Mitral Valve Academic Research Consortium 2 definition (retroperitoneal bleed from arterial puncture) unrelated to the venous closure. Transfusion related to vascular access complication was required in five cases. There were two immediate acute deep venous thromboses postprocedure; one of which occurred after preclosure. There were no arteriovenous malformations, pseudoaneurysms, or access site infections reported following Perclose. **CONCLUSION:** In this large sample size analysis, Proglide preclosure technique is a feasible and safe alternative approach to achieving hemostasis after removal of LBVA sheaths in patients undergoing TEER and TMVR. Randomized trials are needed to compare the different modalities of hemostasis.

Cardiology/Cardiovascular Research

Mohananeey D, Aljadah M, Smith AAH, Haines JF, Patel S, **Villablanca P**, and Ramakrishna H. The 2020 ACC/AHA Guidelines for Management of Patients With Valvular Heart Disease: Highlights and Perioperative Implications. *J Cardiothorac Vasc Anesth* 2022; 36(5):1467-1476. PMID: 34011447. [Full Text](#)

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Valvular heart disease contributes to a large burden of morbidity and mortality in the United States. During the last decade there has been a paradigm shift in the management of valve disease, primarily driven by the emergence of novel transcatheter technologies. In this article, the latest update of the American College of Cardiology/American Heart Association valve heart disease guidelines is reviewed.

Cardiology/Cardiovascular Research

Salerno CT, Hayward C, Hall S, Goldstein D, Saeed D, Schmitto J, Kaczorowski D, Molina E, Zimpfer D, Tsui S, Soltesz E, Pham DT, Mokadam NA, Kilic A, Davis E, Feller E, Lorts A, Silvestry S, Slaughter MS, Potapov E, Atluri P, **Cowger J**, and Pagani FD. HVAD to HeartMate 3 left ventricular assist device exchange: Best practices recommendations. *J Thorac Cardiovasc Surg* 2022; 163(6):2120-2127.e2125. PMID: 35341579. [Full Text](#)

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The HeartWare HVAD System (Medtronic) is a durable implantable left ventricular assist device that has been implanted in approximately 20,000 patients worldwide for bridge to transplant and destination therapy indications. In December 2020, Medtronic issued an Urgent Medical Device Communication informing clinicians of a critical device malfunction in which the HVAD may experience a delay or failure to restart after elective or accidental discontinuation of pump operation. Moreover, evolving retrospective comparative effectiveness studies of patients supported with the HVAD demonstrated a significantly higher risk of stroke and all-cause mortality when compared with a newer generation of a commercially available durable left ventricular assist device. Considering the totality of this new information on HVAD performance and the availability of an alternate commercially available device, Medtronic halted the sale and distribution of the HVAD System in June 2021. The decision to remove the HVAD from commercial distribution now requires the use of the HeartMate 3 left ventricular assist system (Abbott, Inc) if a patient previously implanted with an HVAD requires a pump exchange. The goal of this document is to review

important differences in the design of the HVAD and HeartMate 3 that are relevant to the medical management of patients supported with these devices, and to assess the technical aspects of an HVAD-to-HeartMate 3 exchange. This document provides the best available evidence that supports best practices.

Cardiology/Cardiovascular Research

Salerno CT, Hayward C, Hall S, Goldstein D, Saeed D, Schmitto J, Kaczorowski D, Molina E, Zimpfer D, Tsui S, Soltesz E, Pham DT, Mokadam NA, Kilic A, Davis E, Feller E, Lorts A, Silvestry S, Slaughter MS, Potapov E, Atluri P, **Cowger J**, and Pagani FD. HVAD to HeartMate 3 Left Ventricular Assist Device Exchange: Best Practices Recommendations. *Ann Thorac Surg* 2022; 113(6):1770-1777. PMID: 35341592. [Full Text](#)

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The HeartWare HVAD System (Medtronic) is a durable implantable left ventricular assist device that has been implanted in approximately 20,000 patients worldwide for bridge to transplant and destination therapy indications. In December 2020, Medtronic issued an Urgent Medical Device Communication informing clinicians of a critical device malfunction in which the HVAD may experience a delay or failure to restart after elective or accidental discontinuation of pump operation. Moreover, evolving retrospective comparative effectiveness studies of patients supported with the HVAD demonstrated a significantly higher risk of stroke and all-cause mortality when compared with a newer generation of a commercially available durable left ventricular assist device. Considering the totality of this new information on HVAD performance and the availability of an alternate commercially available device, Medtronic halted the sale and distribution of the HVAD System in June 2021. The decision to remove the HVAD from commercial distribution now requires the use of the HeartMate 3 left ventricular assist system (Abbott, Inc) if a patient previously implanted with an HVAD requires a pump exchange. The goal of this document is to review important differences in the design of the HVAD and HeartMate 3 that are relevant to the medical management of patients supported with these devices, and to assess the technical aspects of an HVAD-to-HeartMate 3 exchange. This document provides the best available evidence that supports best practices.

Cardiology/Cardiovascular Research

Sedhom R, **Megaly M**, Elbadawi A, Elgendy IY, Witzke CF, Kalra S, George JC, Omer M, Banerjee S, Jaber WA, and Shishehbor MH. Contemporary National Trends and Outcomes of Pulmonary Embolism in the United States. *Am J Cardiol* 2022; Epub ahead of print. PMID: 35637010. [Full Text](#)

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Contemporary data on the national trends in pulmonary embolism (PE) admissions and outcomes are scarce. We aimed to analyze trends in mortality and different treatment methods in acute PE. We queried the Nationwide Readmissions Database (2016 to 2019) to identify hospitalizations with acute PE using the International Classification of Diseases, Tenth Revision, Clinical Modification codes. We described the national trends in admissions, in-hospital mortality, readmissions, and different treatment methods in acute PE. We identified 1,427,491 hospitalizations with acute PE, 2.4% of them (n = 34,446) were admissions with high-risk PE. The rate of in-hospital mortality in all PE hospitalizations was 6.5%, and it remained unchanged throughout the study period. However, the rate of in-hospital mortality in high-risk PE decreased from 48.1% in the first quarter of 2016 to 38.9% in the last quarter of 2019 (p-trend <0.001). The rate of urgent 30-day readmission was 15.2% in all PE admissions and 19.1% in high-risk PE admissions. In all PE admissions, catheter-directed interventions (CDI) were used more often (2.5%) than systemic thrombolysis (ST) (2.1%). However, in admissions with high-risk PE, ST remained the most frequently used method (ST vs CDI: 11.3% vs 6.6%). In conclusion, this study showed that the rate of in-hospital mortality in high-risk PE decreased from 2016 to 2019. ST was the most frequently used method for achieving pulmonary reperfusion in high-risk PE, whereas CDI was the most frequently used method in the entire PE cohort. In-hospital death and urgent readmissions rates remain significantly high in patients with high-risk PE.

Cardiology/Cardiovascular Research

Selvaraj S, Fu Z, Jones P, Kwee LC, Windsor SL, Ilkayeva O, Newgard CB, Margulies KB, Husain M, Inzucchi SE, McGuire DK, Pitt B, Scirica BM, **Lanfear DE**, Nassif ME, Javaheri A, Mentz RJ, Kosiborod MN, and Shah SH. Metabolomic Profiling of the Effects of Dapagliflozin in Heart Failure with Reduced Ejection Fraction: DEFINE-HF. *Circulation* 2022; Epub ahead of print. PMID: 35603596. [Full Text](#)

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Background: Sodium-glucose co-transporter-2 inhibitors (SGLT2i) are foundational therapy in patients with heart failure with reduced ejection fraction (HFrEF), yet underlying mechanisms of benefit are not well defined. We sought to investigate the relationships between SGLT2i treatment, changes in metabolic pathways, and outcomes using targeted metabolomics. **Methods:** Dapagliflozin Effects on Biomarkers, Symptoms and Functional Status in Patients with HF with Reduced Ejection Fraction (DEFINE-HF) was a placebo-controlled trial of dapagliflozin in HFrEF. We performed targeted mass spectrometry-based profiling of 63 metabolites (45 acylcarnitines [markers of fatty acid oxidation], 15 amino acids, and 3 conventional metabolites) in plasma samples at randomization and 12 weeks. Using mixed models, we identified principal components analysis (PCA)-defined metabolite clusters that changed differentially with treatment, and also examined the relationship between change in metabolite clusters with change in Kansas City Cardiomyopathy Questionnaire (KCCQ) Scores and N-terminal pro-B-type natriuretic peptide (NT-proBNP). Models were adjusted for relevant clinical covariates, and nominal $p < 0.05$ with FDR-adjusted p -value < 0.10 were used to determine statistical significance. **Results:** Among the 234 DEFINE-HF participants with targeted metabolomic data, the mean age was 62.0 ± 11.1 years, 25% were women, 38% were Black, and mean ejection fraction was $27 \pm 8\%$. Dapagliflozin increased ketone-related and short/medium-chain acylcarnitine PCA metabolite clusters compared with placebo (nominal $p = 0.01$, FDR-adjusted p -value = 0.08 for both clusters). However, ketosis (B-hydroxybutyrate levels $> 500 \mu\text{M}$), was infrequently achieved (3 [2.5%] in dapagliflozin arm vs. 1 [0.9%] in placebo arm), and supraphysiologic levels were not observed. Conversely, increases in long-chain acylcarnitine, long-chain dicarboxylacylcarnitine, and aromatic amino acid metabolite clusters were associated with decreases in KCCQ scores (i.e. worse quality of life) and increases in NT-proBNP levels, without interaction by treatment group. **Conclusions:** In this study of targeted metabolomics in a placebo-controlled trial of SGLT2i in HFrEF, we observed effects of dapagliflozin on key metabolic pathways, supporting a role for altered ketone and fatty acid biology with SGLT2i in patients with HFrEF. Reassuringly, only physiologic levels of ketosis were observed. Additionally, we identified several metabolic biomarkers associated with adverse HFrEF outcomes.

Cardiology/Cardiovascular Research

Simsek B, Kostantinis S, Karacsonyi J, **Alaswad K**, Karpaliotis D, Masoumi A, Jaffer FA, Doshi D, Khatri J, Poommipanit P, Gorgulu S, Abi Rafeh N, Goktekin O, Krestyaninov O, Davies R, ElGuindy A, Haddad EV, Kerrigan J, Patel M, Chandwaney RH, Mastrodemos OC, Allana S, Rangan BV, and Brilakis ES. Predictors of success in primary retrograde strategy in chronic total occlusion percutaneous coronary intervention: insights from the PROGRESS-chronic total occlusion registry. *Catheter Cardiovasc Interv* 2022; Epub ahead of print. PMID: 35615875. [Full Text](#)

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BACKGROUND: An upfront (primary) retrograde strategy is often used in complex chronic total occlusion (CTO) percutaneous coronary intervention (PCI). **METHODS:** We examined the clinical, angiographic characteristics, and procedural outcomes of CTO PCIs that were approached with a primary retrograde strategy in the Prospective Global Registry for the Study of CTO Intervention (PROGRESS-CTO, NCT02061436). **RESULTS:** Of 10,286 CTO PCIs performed between 2012 and 2022, a primary retrograde strategy was used in 1329 (13%) with an initial technical success of 66%, and a final success of 83%. Patients who underwent successful versus unsuccessful primary retrograde cases had similar characteristics: age (65 ± 10 vs. 65 ± 9 , years, $p = 0.203$), men (83% vs. 87%, $p = 0.066$), prior PCI (71% vs. 71%, $p = 0.809$), and prior coronary artery bypass graft surgery (52% vs. 53%, $p = 0.682$). The PROGRESS-CTO score (1.3 ± 0.9 vs. 1.6 ± 0.9 , $p < 0.001$), air kerma radiation (3.9 ± 2.8 vs. 3.4 ± 2.6 , gray, $p = 0.013$), and contrast use (294 ± 148 ml vs. 248 ± 128 , ml, $p < 0.001$) were higher in the unsuccessful group, whereas the presence of interventional collaterals (95% vs. 72%, $p < 0.001$) and Werner collateral connection grade 2 (43% vs. 31%, $p < 0.001$) were higher in the successful group. On multivariable logistic regression analysis, the only variable associated with a successful primary retrograde strategy was the presence of interventional collaterals: odds ratio: 6.52 (95% confidence intervals; 3.5-12.1, $p < 0.001$). **CONCLUSION:** Presence of interventional collaterals is independently associated with higher success rates with a primary retrograde strategy in CTO PCI.

Cardiology/Cardiovascular Research

Vidula H, and **Cowger JA**. Getting to the heart of the muscle: Sarcopenia in advanced heart failure. *J Heart Lung Transplant* 2022; 41(6):763-764. PMID: 35351384. [Full Text](#)

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Center for Health Policy and Health Services Research

Hecht LM, Braciszewski JM, Miller-Matero LR, Ahmedani BK, Kerver JM, and Loree AM. Adequacy of prenatal care utilisation and gestational weight gain among women with depression. *J Reprod Infant Psychol* 2022:1-12; Epub ahead of print. PMID: 35582731. [Full Text](#)

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BACKGROUND: Depression is common during pregnancy, can elevate risk for excessive or inadequate gestational weight gain (GWG), and is associated with both underutilisation and overutilisation of prenatal care. Whether GWG is associated with adequacy of prenatal care among women with and without depression in the United States is unknown. This study evaluated whether adequacy of prenatal care differed by depression status and GWG. **METHODS:** Data from the Pregnancy Risk Assessment Monitoring System from 1,379,870 women who were pregnant with a singleton and delivered at 37-42 weeks gestation during 2016 to 2018 were included. Depression was self-reported. The Kotelchuck index was used to evaluate adequacy of prenatal care. Maternal weight gain was compared to GWG guidelines. **RESULTS:** Approximately 13.1% of the sample experienced depression during pregnancy. Although those with depression had increased odds of both inadequate and above adequate levels of prenatal care, this association was no longer significant after accounting for demographics, medical comorbidities, and socioeconomic factors. Individuals with inadequate levels of prenatal care with a normal pre-pregnancy body mass index gained less weight during pregnancy. **CONCLUSIONS:** The association between depression and prenatal care utilisation seems driven by demographic, medical comorbidity, and socioeconomic variables. Weight outcomes were associated with inadequate prenatal care utilisation.

Center for Health Policy and Health Services Research

Lim S, Bazydlo M, Macki M, Haider S, Hamilton T, Hunt R, Chaker A, Kantak P, Schultz L, Nerenz D, Schwalb JM, Abdulhak M, Park P, Aleem I, Easton R, Khalil JG, Perez-Cruet MJ, and **Chang V.**

Validation of the Benefits of Ambulation Within 8 Hours of Elective Cervical and Lumbar Surgery: A Michigan Spine Surgery Improvement Collaborative Study. *Neurosurgery* 2022; Epub ahead of print. PMID: 35550477. [Full Text](#)

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BACKGROUND: Early ambulation is considered a key element to Enhanced Recovery After Surgery protocol after spine surgery. **OBJECTIVE:** To investigate whether ambulation less than 8 hours after elective spine surgery is associated with improved outcome. **METHODS:** The Michigan Spine Surgery Improvement Collaborative database was queried to track all elective cervical and lumbar spine surgery between July 2018 and April 2021. In total, 7647 cervical and 17 616 lumbar cases were divided into 3 cohorts based on time to ambulate after surgery: (1) <8 hours, (2) 8 to 24 hours, and (3) >24 hours. **RESULTS:** For cervical cases, patients who ambulated 8 to 24 hours (adjusted odds ratio [aOR] 1.38; 95% CI 1.11-1.70; P = .003) and >24 hours (aOR 2.20; 95% CI 1.20-4.03; P = .011) after surgery had higher complication rate than those who ambulated within 8 hours of surgery. Similar findings were noted for lumbar cases with patients who ambulated 8 to 24 hours (aOR 1.31; 95% CI 1.12-1.54; P < .001) and >24 hours (aOR 1.96; 95% CI 1.50-2.56; P < .001) after surgery having significantly higher complication rate than those ambulated <8 hours after surgery. Analysis of secondary outcomes for cervical cases demonstrated that <8-hour ambulation was associated with home discharge, shorter hospital stay, lower 90-day readmission, and lower urinary retention rate. For lumbar cases, <8-hour ambulation was associated with shorter hospital stay, satisfaction with surgery, lower 30-day readmission, home discharge, and lower urinary retention rate. **CONCLUSION:** Ambulation within 8 hours after surgery is associated with significant improved outcome after elective cervical and lumbar spine surgery.

Center for Health Policy and Health Services Research

Miller-Matero LR, Hecht LM, Patel S, Martens KM, Hamann A, and Carlin AM. Exploring gender, psychiatric symptoms, and eating behaviors as predictors of attrition to bariatric surgery. *Am J Surg* 2022; Epub ahead of print. PMID: 35570060. [Full Text](#)

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Department of Surgery, Henry Ford Health System, USA.

BACKGROUND: Only a small proportion of eligible individuals undergo bariatric surgery. The purpose was to examine attrition to surgery and whether psychiatric symptoms and eating behaviors differentially predicted attrition among men and women. **METHOD:** Data was collected from a retrospective chart review of 313 patients who underwent a pre-surgical psychosocial evaluation. **RESULTS:** The overall attrition rate was 33.5%; 42.6% of men and 31.7% of women experienced attrition. In the multivariate analysis of the entire sample, White patients (OR = 2.33, CI: 1.33, 4.08) and those without a history of binge eating (OR = 2.71, CI: 1.23, 5.97) were more likely to undergo surgery. In a multivariate analysis of women only, race and binge eating independently predicted attrition; however, no factors significantly

predicted attrition among men. **CONCLUSIONS:** Factors identified at the pre-surgical psychosocial evaluation can identify patients at risk for attrition, and these factors may differ for men and women.

Center for Individualized and Genomic Medicine Research

Selvaraj S, Fu Z, Jones P, Kwee LC, Windsor SL, Ilkayeva O, Newgard CB, Margulies KB, Husain M, Inzucchi SE, McGuire DK, Pitt B, Scirica BM, **Lanfear DE**, Nassif ME, Javaheri A, Mentz RJ, Kosiborod MN, and Shah SH. Metabolomic Profiling of the Effects of Dapagliflozin in Heart Failure with Reduced Ejection Fraction: DEFINE-HF. *Circulation* 2022; Epub ahead of print. PMID: 35603596. [Full Text](#)

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Division of Cardiology, Duke University Medical Center, Durham, NC.

Background: Sodium-glucose co-transporter-2 inhibitors (SGLT2i) are foundational therapy in patients with heart failure with reduced ejection fraction (HFrEF), yet underlying mechanisms of benefit are not well defined. We sought to investigate the relationships between SGLT2i treatment, changes in metabolic pathways, and outcomes using targeted metabolomics. **Methods:** Dapagliflozin Effects on Biomarkers, Symptoms and Functional Status in Patients with HF with Reduced Ejection Fraction (DEFINE-HF) was a placebo-controlled trial of dapagliflozin in HFrEF. We performed targeted mass spectrometry-based profiling of 63 metabolites (45 acylcarnitines [markers of fatty acid oxidation], 15 amino acids, and 3 conventional metabolites) in plasma samples at randomization and 12 weeks. Using mixed models, we identified principal components analysis (PCA)-defined metabolite clusters that changed differentially with treatment, and also examined the relationship between change in metabolite clusters with change in Kansas City Cardiomyopathy Questionnaire (KCCQ) Scores and N-terminal pro-B-type natriuretic peptide (NT-proBNP). Models were adjusted for relevant clinical covariates, and nominal $p < 0.05$ with FDR-adjusted p -value < 0.10 were used to determine statistical significance. **Results:** Among the 234 DEFINE-HF participants with targeted metabolomic data, the mean age was 62.0 ± 11.1 years, 25% were women, 38% were Black, and mean ejection fraction was $27 \pm 8\%$. Dapagliflozin increased ketone-related and short/medium-chain acylcarnitine PCA metabolite clusters compared with placebo (nominal $p = 0.01$, FDR-adjusted p -value = 0.08 for both clusters). However, ketosis (B-hydroxybutyrate levels $> 500 \mu\text{M}$), was infrequently achieved (3 [2.5%] in dapagliflozin arm vs. 1 [0.9%] in placebo arm), and supraphysiologic levels were not observed. Conversely, increases in long-chain acylcarnitine, long-chain dicarboxylacylcarnitine, and aromatic amino acid metabolite clusters were associated with decreases in KCCQ scores (i.e. worse quality of life) and increases in NT-proBNP levels, without interaction by treatment group. **Conclusions:** In this study of targeted metabolomics in a placebo-controlled trial of SGLT2i in HFrEF, we observed effects of dapagliflozin on key metabolic pathways, supporting a role for altered ketone and fatty acid biology with SGLT2i in patients with HFrEF. Reassuringly, only physiologic levels of ketosis were observed. Additionally, we identified several metabolic biomarkers associated with adverse HFrEF outcomes.

Clinical Quality and Safety

Garcia R, Barnes S, Boukidjian R, Goss LK, Spencer M, Septimus EJ, Wright MO, Munro S, Reese SM, Fakhri MG, Edmiston CE, Jr., and **Levesque M**. Recommendations for Change in Infection Prevention Programs and Practice. *Am J Infect Control* 2022; Epub ahead of print. PMID: 35525498. [Full Text](#)

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Fifty years of evolution in infection prevention and control programs have involved significant accomplishments related to clinical practices, methodologies, and technology. However, regulatory mandates, and resource and research limitations, coupled with emerging infection threats such as the COVID-19 pandemic, present considerable challenges for infection preventionists. This article provides guidance and recommendations in fourteen key areas. These interventions should be considered for implementation by United States healthcare facilities in the near future.

Dermatology

Gordon KB, Langley RG, Warren RB, Okubo Y, **Stein Gold L**, Merola JF, Peterson L, Wixted K, Cross N, Deherder D, and Thaçi D. Bimekizumab Safety in Patients With Moderate to Severe Plaque Psoriasis: Pooled Results From Phase 2 and Phase 3 Randomized Clinical Trials. *JAMA Dermatol* 2022; Epub ahead of print. PMID: 35544084. [Full Text](#)

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Institute and Comprehensive Center for Inflammation Medicine, University of Lübeck, Lübeck, Germany.

IMPORTANCE: Psoriasis is a chronic disease requiring long-term management; understanding the long-term safety profiles of psoriasis treatments, such as bimekizumab, is important. **OBJECTIVE:** To evaluate the 2-year safety profile of bimekizumab in patients with moderate to severe plaque psoriasis. **DESIGN, SETTING, AND PARTICIPANTS:** Safety data were pooled from a cohort of patients from 4 phase 2 randomized clinical trials (BE ABLE 1, BE ABLE 2, PS0016, and PS0018) and 4 phase 3 randomized clinical trials (BE VIVID, BE READY, BE SURE, and BE BRIGHT) to include 2 years of study treatment. Data were obtained on adults with moderate to severe plaque psoriasis (Psoriasis Area and Severity

Index level ≥ 12 , $\geq 10\%$ body surface area affected by psoriasis, and an Investigator's Global Assessment score ≥ 3 on a 5-point scale) who were eligible for systemic psoriasis therapy and/or phototherapy. INTERVENTIONS: Included patients received 1 or more doses of bimekizumab during the phase 2 or phase 3 trials. MAIN OUTCOMES AND MEASURES: Treatment-emergent adverse events (TEAEs), serious TEAEs, and TEAEs leading to treatment discontinuation are reported using exposure-adjusted incidence rates (EAIRs) per 100 person-years. RESULTS: A total of 1789 patients (1252 [70.0%] men; mean [SD] age, 45.2 [13.5] years) were treated with 1 or more doses of bimekizumab across the phase 2/3 trials and were included in these analyses; total bimekizumab exposure was 3109.7 person-years. TEAEs occurred at an EAIR of 202.4 per 100 person-years and did not increase with longer duration of bimekizumab exposure. The 3 most frequently reported TEAEs were nasopharyngitis (19.1 per 100 person-years; 95% CI, 17.4-20.9 per 100 person-years), oral candidiasis (12.6 per 100 person-years; 95% CI, 11.3-14.0 per 100 person-years), and upper respiratory tract infection (8.9 per 100 person-years; 95% CI, 7.8-10.1 per 100 person-years). Most oral candidiasis events were mild or moderate; 3 events led to discontinuation. The EAIRs of inflammatory bowel disease (0.1 per 100 person-years; 95% CI, 0.0-0.3 per 100 person-years), adjudicated suicidal ideation and behavior (0.0 per 100 person-years; 95% CI, 0.0-0.2 per 100 person-years), and adjudicated major adverse cardiac events (0.5 per 100 person-years; 95% CI, 0.3-0.8 per 100 person-years) were low. CONCLUSIONS AND RELEVANCE: In these pooled analyses of data from a cohort of patients from 8 randomized clinical trials, bimekizumab was well tolerated aside from an increased incidence of mild to moderate oral candidiasis. No safety signals were observed compared with previous reports, and there was no increased risk of AEs with longer duration of bimekizumab exposure.

Dermatology

Jalili A, Bewley A, Sticherling M, and **Stein Gold L**. Short Term and Long-Term Efficacy of Calcipotriene/Betamethasone Dipropionate Foam Combination. *Clin Cosmet Investig Dermatol* 2022; 15:809-814. PMID: 35531463. [Full Text](#)

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Psoriasis is a well-known chronic disease characterized by the development of erythematous, indurated, scaly, pruritic plaques on the skin with cycles of remission and symptom flare-ups. The management of patients with chronic plaque psoriasis has been more challenging since the Covid-19 pandemic as health care professionals have had to adapt to remote consultations for some patients, and patients have had to adapt to the changing health landscape. The rapid resolution of psoriasis symptoms especially those with a substantial impact on quality of life can improve patient satisfaction and adherence, making it an important factor in successful treatment. Cal/BD foam contributes to improved patient adherence and treatment outcome through its rapid action and superior efficacy versus Cal or BD monotherapy, Cal/BD ointment and gel and clobetasol cream in the short-term flare treatment of psoriasis. Moreover, the benefits of proactive long-term management of psoriasis compared to reactive management and its favourable safety profile are higher efficacy and a better health-related quality of life. Cal/BD foam should be considered an effective topical treatment for short-term flare treatment and long-term control of adult psoriatic patients.

Dermatology

Kern J, Wood E, **Almukhtar R**, Angra K, Lipp M, and Goldman M. Evaluation of an SPF50 Sunscreen Containing Photolyase and Antioxidants for its Anti-Photoaging Properties and Photoprotection. *J Drugs Dermatol* 2022; 21(5):517-520. PMID: 35533024. [Full Text](#)

BACKGROUND: Background: Skin exposure to ultraviolet radiation (UVR) causes DNA damage, which can lead to mutagenesis, carcinogenesis, cellular death, and photoaging. Signs of photoaging include wrinkling, erythema, skin laxity, uneven skin texture, and hyperpigmentation. Photolyase is an exogenous DNA repair enzyme that can restore DNA integrity when applied topically to human skin. Antioxidants also play a key role in reducing UVR-associated molecular damage. OBJECTIVE: To assess the efficacy

and safety of a tinted mineral-based sunscreen containing 10.7% zinc oxide (SPF50) with the active ingredients photolyase, antioxidants (Peptide Q10), and peptides in both protecting and repairing signs of photoaging. METHODS: In an open-label, single-center, 12-week study, patients aged 35–55 years and Fitzpatrick skin phototypes II–IV applied the sunscreen daily for 84 days. VISIA photography was performed at baseline as well as 6- and 12-week follow-ups. At each visit, the investigator and subject evaluated clinical photoaging parameters including overall photodamage, fine lines/wrinkles, coarse lines/wrinkles, skin tone evenness, tactile roughness, and radiance. RESULTS: The Investigator Global Aesthetic Improvement Scale (IGAIS) found that 63% of patients showed improvement at week 6 and 81% at week 12. The Subject Global Aesthetic Improvement Scale (SGAIS) showed 58% and 62.5% of patients reported the appearance of their skin was improved at week 6 and 12, respectively. Overall, there was a statistically significant improvement in skin radiance as well as improvement in overall facial aesthetics reported by both investigators and subjects. CONCLUSION: This tinted mineral based SPF50 sunscreen containing photolyase, antioxidants, and peptides is effective at repairing some clinical signs of photoaging and is well-tolerated for daily use. *J Drugs Dermatol*. 2022;21(5):517-520. doi:10.36849/JDD.6503.

Dermatology

Konda S, Shetty N, Friedman B, and Veenstra J. Delayed drug hypersensitivity reaction to secukinumab in a patient with hidradenitis suppurativa. *BMJ Case Rep* 2022; 15(5). PMID: 35580946.

[Full Text](#)

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A woman in her 30s presented to the dermatology clinic with widespread, pruritic, red papules and plaques involving the ears, trunk and extremities. The rash developed a few days after receiving her second injection of secukinumab, which was initiated for recalcitrant Hurley stage III hidradenitis suppurativa. Investigations revealed a psoriasiform drug hypersensitivity reaction secondary to secukinumab. In this report, we describe the clinical course, histopathological correlation and treatment of this rarely documented reaction.

Dermatology

Ruvolo E, **Boothby-Shoemaker W**, Kumar N, **Hamzavi IH**, **Lim HW**, and **Kohli I**. Evaluation of efficacy of antioxidant-enriched sunscreen products against long wavelength ultraviolet A1 and visible light. *Int J Cosmet Sci* 2022; Epub ahead of print. PMID: 35587114. [Full Text](#)

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OBJECTIVE: The synergistic effects of VL and long wavelength UVA1 (VL+UVA1, 370-700 nm) on inducing pigmentation and erythema in skin have been demonstrated and linked to exacerbation of dermatologic conditions including melasma and post-inflammatory hyperpigmentation. This study aims to compare the photoprotection of organic sunscreens enriched with antioxidant (AO) combinations against VL+UVA1 induced biologic effects. The efficacy was compared to that offered by a commercially available tinted sunscreen. **METHODS:** Ten healthy adult subjects with Fitzpatrick skin phototypes IV–VI were enrolled (nine completed). VL+UVA1 dose of 380 J/cm² was utilized. Assessment methods were polarized photography, investigator global scoring, and diffuse reflectance spectroscopy (DRS). Measurements were obtained at baseline and immediately, 24 hours, and 7 days after irradiation. **RESULTS:** Sites treated with tinted sunscreen product had significantly less pigmentation compared with untreated but irradiated skin at all time points. However, DRS results demonstrated that the 5-AO sunscreen performed comparably or better than all sunscreens tested with relatively lower dyschromia, delayed erythema and pigmentation. **CONCLUSION:** These results highlight the potential of AO enriched

sunscreens to be photoprotective against VL+UVA1. The combination of efficacy and the cosmetic appearance of this product may provide wider acceptability which is crucial considering the limited available means of protection against this waveband.

Diagnostic Radiology

Ekkel E, Chandran T, Trpkovski M, and Hans S. Management of phlegmasia cerulea dolens caused by a giant leiomyoma. *J Vasc Surg Cases Innov Tech* 2022; 8(2):240-243. PMID: 35493345. [Full Text](#)

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In the present report, we describe the case of a young woman with a large uterine leiomyoma causing phlegmasia cerulea dolens with thrombosis of the left common and left external iliac veins. She underwent tissue plasminogen activator catheter thrombolysis and mechanical thrombectomy to temporize the condition until she could be evaluated by a gynecologic oncologist to remove the cause of the venous obstruction. Before the hysterectomy, a suprarenal inferior vena cava filter was placed. However, <12 hours after the hysterectomy, she developed recurrent thrombosis involving the left common and external iliac veins. She underwent repeat mechanical thrombectomy with wall stent placement in the left common iliac vein with resolution of her symptoms.

Diagnostic Radiology

Gorgis S, Mawri S, Dabbagh MF, Aurora L, Ali M, Mitchell G, Jacobsen G, Hegab S, Schwartz S, Kelly B, Grafton G, Awdish R, Ismail R, and Koenig G. Ultrasound-assisted catheter-directed thrombolysis versus anticoagulation alone for management of submassive pulmonary embolism. *J Cardiol* 2022; Epub ahead of print. PMID: 35643741. [Full Text](#)

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BACKGROUND: Patients with submassive pulmonary embolism (PE) are vulnerable to sudden deterioration, recurrent PE, and progression to pulmonary hypertension and chronic right ventricular (RV) dysfunction. Previous studies have suggested a clinical benefit of using ultrasound-assisted catheter-directed thrombolysis (USCDT) to invasively manage patients with submassive PE. However, there is sparse data comparing the clinical outcomes of these patients when treated with USCDT versus anticoagulation (AC) alone. We sought to compare the outcomes of USCDT versus AC alone in the management of submassive PE. **METHODS:** 192 consecutive patients who underwent USCDT for submassive PE between January 2013 and February 2019 were identified. ICD9/ICD10 codes were used to detect 2554 patients diagnosed with PE who did not undergo thrombolysis. Propensity matching identified 192 patients with acute PE treated with AC alone. Clinical outcomes were compared between the two groups. Baseline demographics, laboratory values, and pulmonary embolism severity index scores were similar between the two cohorts. **RESULTS:** There was a significant reduction in mean systolic pulmonary artery pressure (sPAP) in the USCDT group compared to the AC group ($\Delta 11$ vs $\Delta 3.9$ mmHg, $p < 0.001$). There was significant improvement in proportion of RV dysfunction in all patients, but the difference was larger in the USCDT group ($\Delta 43.3\%$ vs $\Delta 17.3\%$, $p < 0.001$). Patients who underwent USCDT had lower 30-day (4.3% vs 10.5%, $p = 0.03$), 90-day (5.5% vs 12.4%, $p = 0.03$), and 1-year mortality (6.2% vs 14.2%, $p = 0.03$). **CONCLUSIONS:** In patients with acute submassive PE, USCDT

was associated with improved 30-day, 90-day, and 1 year mortality as compared to AC alone. USCDT also improved RV function and reduced sPAP to a greater degree than AC alone. Further studies are needed to verify these results in both short- and long-term outcomes.

Diagnostic Radiology

Harmon QE, Patchel SA, Zhao S, Umbach DM, **Cooper TE**, and Baird DD. Depot Medroxyprogesterone Acetate Use and the Development and Progression of Uterine Leiomyoma. *Obstet Gynecol* 2022; 139(5):797-807. PMID: 35576339. [Full Text](#)

Epidemiology Branch and the Biostatistics and Computational Biology Branch, National Institute of Environmental Health Sciences, and Public Health and Epidemiology Practice, Westat, Durham, North Carolina; and the Department of Radiology, Henry Ford Health Systems, Detroit, Michigan.

OBJECTIVE: Investigate the association between use of depot medroxyprogesterone acetate (DMPA) (an injectable progestin-only contraceptive) and leiomyoma development. **METHODS:** We conducted a cohort study in the Detroit, Michigan, area that involved four clinic visits at 20-month intervals over 5 years (2010-2018) and used a standardized ultrasonography protocol to prospectively measure leiomyomas 0.5 cm or more in diameter. Participants were 1,693 self-identified Black women aged 23-35 years with no prior leiomyoma diagnosis and no hysterectomy. For this substudy, years since last use of DMPA was ascertained from questionnaire data at every visit. Leiomyoma incidence was defined as the first visit with an observed leiomyoma among women who were leiomyoma-free at enrollment. Depot medroxyprogesterone acetate associations were examined with Cox models. Leiomyoma growth was calculated as the change in log-volume for leiomyomas matched at successive visits and was modeled using linear mixed models accounting for clustered data. Leiomyoma loss, defined as a reduction in leiomyoma number in successive visits, was modeled using Poisson regression. All models used time-varying exposure and covariates. **RESULTS:** Of participants with at least one follow-up visit (N=1,610), 42.9% had ever used DMPA. Participants exposed to DMPA within the previous 2 years experienced reduced leiomyoma development during the subsequent observation interval compared with never users, including lower leiomyoma incidence (5.2% vs 10.7%), adjusted hazard ratio 0.6 (95% CI 0.4-1.0), 42.0% lower leiomyoma growth (95% CI -51.4 to -30.7) and 60% greater leiomyoma loss (adjusted risk ratio 1.6, 95% CI 1.1-2.2). Excess leiomyoma loss was also seen for those who used DMPA 2-4 years before the visit compared with never users, 2.1-fold increase (95% CI 1.4-3.1). **CONCLUSION:** Recent use of DMPA was associated with reduced leiomyoma development and increased leiomyoma loss. Such changes in early leiomyoma development in young women could delay symptom onset and reduce the need for invasive treatment.

Diagnostic Radiology

Miller CR, Morris ED, **Ghanem AI**, **Pantelic MV**, **Walker EM**, and Glide-Hurst CK. Characterizing Sensitive Cardiac Substructure Excursion Due to Respiration. *Adv Radiat Oncol* 2022; 7(3):100876. PMID: 35243181. [Full Text](#)

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PURPOSE: Whole-heart dose metrics are not as strongly linked to late cardiac morbidities as radiation doses to individual cardiac substructures. Our aim was to characterize the excursion and dosimetric variation throughout respiration of sensitive cardiac substructures for future robust safety margin design. **METHODS AND MATERIALS:** Eleven patients with cancer treatments in the thorax underwent 4-phase noncontrast 4-dimensional computed tomography (4DCT) with T2-weighted magnetic resonance imaging in end-exhale. The end-exhale phase of the 4DCT was rigidly registered with the magnetic resonance imaging and refined with an assisted alignment surrounding the heart from which 13 substructures (chambers, great vessels, coronary arteries, etc) were contoured by a radiation oncologist on the 4DCT.

Contours were deformed to the other respiratory phases via an intensity-based deformable registration for radiation oncologist verification. Measurements of centroid and volume were evaluated between phases. Mean and maximum dose to substructures were evaluated across respiratory phases for the breast (n = 8) and thoracic cancer (n = 3) cohorts. RESULTS: Paired t tests revealed reasonable maintenance of geometric and anatomic properties (P < .05 for 4/39 volume comparisons). Maximum displacements >5 mm were found for 24.8%, 8.5%, and 64.5% of the cases in the left-right, anterior-posterior, and superior-inferior axes, respectively. Vector displacements were largest for the inferior vena cava and the right coronary artery, with displacements up to 17.9 mm. In breast, the left anterior descending artery D(mean varied 3.03 ± 1.75 Gy (range, 0.53-5.18 Gy) throughout respiration whereas lung showed patient-specific results. Across all patients, whole heart metrics were insensitive to breathing phase (mean and maximum dose variations <0.5 Gy). CONCLUSIONS: This study characterized the intrafraction displacement of the cardiac substructures through the respiratory cycle and highlighted their increased dosimetric sensitivity to local dose changes not captured by whole heart metrics. Results suggest value of cardiac substructure margin generation to enable more robust cardiac sparing and to reduce the effect of respiration on overall treatment plan quality.

Diagnostic Radiology

Musa A, Afify O, Al-Hihi M, Anavim A, Holton JM, Azar S, Kumar V, Cassella KD, **Ledbetter KA**, Trivedi PS, Arnold EC, and Ter-Oganesyan R. Views of Diagnostic Radiology Residency Program Directors Regarding Methods to Increase Female and Under-Represented in Medicine Residents: A Cross-sectional Study. *Acad Radiol* 2022; Epub ahead of print. PMID: 35581054. [Full Text](#)

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RATIONALE AND OBJECTIVES: Diagnostic radiology remains one of the least diverse medical specialties. Recent reports have found that the number of female and under-represented in medicine (URiM) residents have not increased despite efforts to increase representation over the last decade. Given the critical role of residency program directors in selecting diverse applicants, this study was performed to identify which strategies were most preferred to increase the number of female and/or URiM residents by directors of diagnostic radiology residency training programs. MATERIALS AND METHODS: This was an anonymous, cross-sectional study of diagnostic radiology residency program directors that included a survey about program characteristics, demographics, and strategies to increase the number of female and/or URiM residents. RESULTS: The questionnaire was submitted to 181 potential participants with a 19.9% response rate. The most preferred strategies to increase diversity involved directly recruiting medical students, promoting mentorship, increasing the number of diverse teaching faculty, and unconscious bias training. The least supported strategies included deemphasizing exam scores, accepting more international graduates, accepting a minimum number of female and/or URiM applicants, and de-identifying applications. Female and/or URiM program directors indicated a statistically significant preference for medical student recruitment and providing an opportunity to discuss workplace issues for female and/or URiM trainees (p < 0.05). CONCLUSION: Diagnostic radiology residency program directors endorsed a wide variety of strategies to increase diversity. Recruitment of female and/or URiM medical students and promoting the number of diverse faculty members and mentorship of trainees by these faculty appear to be the most preferred strategies to increase female and/or URiM residents. Female and/or URiM program directors placed a greater importance on recruiting diverse applicants and supporting safe discussion of workplace issues faced by female and/or URiM radiology residents.

Diagnostic Radiology

Soliman SB, Davis JJ, Muh SJ, Vohra ST, Patel A, and van Holsbeeck MT. Ultrasound evaluations and guided procedures of the painful joint arthroplasty. *Skeletal Radiol* 2022; Epub ahead of print. PMID: 35624311. [Full Text](#)

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The purpose of this article is to describe the use of ultrasound for the diagnosis and treatment of painful joint arthroplasty. Ultrasound plays a crucial role in the diagnosis of the painful joint arthroplasty, especially given its unique dynamic capabilities, convenience, and high resolution. Ultrasound guidance is also instrumental for procedures in both diagnosing and in select cases, treating the painful joint arthroplasty. Topics to be discussed in this article include trends in arthroplasty placement, benefits of the use of ultrasound overall, and ultrasound evaluation of periprosthetic joint infections. We will also review the sonographic findings with dissociated/displaced components and adverse reaction to metallic debris including metallosis, trunnionosis, and metal-on-metal pseudotumors. Additionally, we will discuss ultrasound evaluation of tendon pathologies with arthroplasties, including dynamic maneuvers to evaluate for tendon impingement/snapping. Finally, we will cover ultrasound-guided joint arthroplasty injection indications and precautions. **KEY POINTS:** • Ultrasound is preferred over MRI in patients with joint arthroplasty and plays a crucial role in diagnosis, especially given its unique dynamic capabilities, convenience and high resolution. • It is especially beneficial for US-guided aspiration in periprosthetic joint infections; effectively used to evaluate periprosthetic fluid collections, facilitating differentiation between abscesses and aseptic collections, and tracking sinus tracts. • Recently, the diagnosis of periprosthetic joint infections has shifted focus to biomarkers in the periprosthetic fluid, specifically α -defensin, which has a high sensitivity and specificity for diagnosing infection. • *Cutibacterium acnes* is a major pathogen responsible for shoulder arthroplasty infections, often presenting with normal laboratory values and since slow growing, must be kept for a minimum of 14 days.

Emergency Medicine

Bunch CM, Moore EE, Moore HB, Neal MD, Thomas AV, Zackariya N, Zhao J, Zackariya S, Brenner TJ, Berquist M, Buckner H, Wiarda G, Fulkerson D, Huff W, Kwaan HC, Lankowicz G, Laubscher GJ, Lourens PJ, Pretorius E, Kotze MJ, Moolla MS, Sithole S, Maponga TG, Kell DB, Fox MD, Gillespie L, Khan RZ, Mamczak CN, March R, Macias R, Bull BS, and Walsh MM. Immuno-Thrombotic Complications of COVID-19: Implications for Timing of Surgery and Anticoagulation. *Front Surg* 2022; 9:889999. PMID: 35599794. [Full Text](#)

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Early in the coronavirus disease 2019 (COVID-19) pandemic, global governing bodies prioritized transmissibility-based precautions and hospital capacity as the foundation for delay of elective procedures. As elective surgical volumes increased, convalescent COVID-19 patients faced increased postoperative morbidity and mortality and clinicians had limited evidence for stratifying individual risk in this population. Clear evidence now demonstrates that those recovering from COVID-19 have increased postoperative morbidity and mortality. These data-in conjunction with the recent American Society of Anesthesiologists guidelines-offer the evidence necessary to expand the early pandemic guidelines and guide the surgeon's preoperative risk assessment. Here, we argue elective surgeries should still be delayed on a personalized basis to maximize postoperative outcomes. We outline a framework for stratifying the individual COVID-19 patient's fitness for surgery based on the symptoms and severity of acute or convalescent COVID-19 illness, coagulopathy assessment, and acuity of the surgical procedure. Although the most common manifestation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is COVID-19 pneumonitis, every system in the body is potentially afflicted by an endotheliitis. This endothelial derangement most often manifests as a hypercoagulable state on admission with associated occult and symptomatic venous and arterial thromboembolisms. The delicate balance between hyper and hypocoagulable states is defined by the local immune-thrombotic crosstalk that results commonly in a hemostatic derangement known as fibrinolytic shutdown. In tandem, the hemostatic derangements that occur during acute COVID-19 infection affect not only the timing of surgical procedures, but also the incidence of postoperative hemostatic complications related to COVID-19-associated coagulopathy (CAC). Traditional methods of thromboprophylaxis and treatment of thromboses after surgery require a tailored approach guided by an understanding of the pathophysiologic underpinnings of the COVID-19 patient. Likewise, a prolonged period of risk for developing hemostatic complications following hospitalization due to COVID-19 has resulted in guidelines from differing societies that recommend varying periods of delay following SARS-CoV-2 infection. In conclusion, we propose the perioperative, personalized assessment of COVID-19 patients' CAC using viscoelastic hemostatic assays and fluorescent microclot analysis.

Emergency Medicine

Limkakeng AT, Jr., Hertz J, Lerebours R, Kuchibhatla M, **McCord J**, Singer AJ, Apple FS, Peacock WF, Christenson RH, and **Nowak RM**. Ideal high sensitivity troponin baseline cutoff for patients with renal dysfunction. *Am J Emerg Med* 2022; 56:323-324. PMID: 34482998. [Full Text](#)

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Emergency Medicine

Skok H, **Jabour J**, and Betcher J. Wernicke Korsakoff syndrome in a teenage female as a complication of COVID-19. *J Am Coll Emerg Physicians Open* 2022; 3(3):e12735. PMID: 35505931. [Full Text](#)

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Wernicke encephalitis (WE) is usually associated with alcohol use disorder and caused by a deficiency in thiamine. Classic findings include confusion, ataxia, and ophthalmoplegia. This case is a unique presentation of WE in a 14-year-old female related to prior coronavirus disease infection. She had persistent dysgeusia and developed thiamine deficiency. She presented with confusion, ataxia, and changes in speech. She had a prolonged hospitalization but was discharged to an inpatient rehab facility with persistent symptoms. It is prudent to include thiamine deficiency in the differential for patients with any symptoms of WE and a history of nutritional deficiency.

Emergency Medicine

Suleyman G, Fadel R, Brar I, Kassab R, Khansa R, Sturla N, Alsaadi A, Latack K, Miller J, Tibbetts R, Samuel L, Alangaden G, and Ramesh M. Risk Factors Associated With Hospitalization and Death in COVID-19 Breakthrough Infections. *Open Forum Infect Dis* 2022; 9(5):ofac116. PMID: 35437511. [Full Text](#)

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BACKGROUND: Characterizations of coronavirus disease 2019 (COVID-19) vaccine breakthrough infections are limited. We aim to characterize breakthrough infections and identify risk factors associated with outcomes. **METHODS:** This was a retrospective case series of consecutive fully vaccinated patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a multicenter academic center in Southeast Michigan, between December 30, 2020, and September 15, 2021. **RESULTS:** A total of 982 patients were identified; the mean age was 57.9 years, 565 (59%) were female, 774 (79%) were White, and 255 (26%) were health care workers (HCWs). The median number of comorbidities was 2; 225 (23%) were immunocompromised. BNT162b2 was administered to 737 (75%) individuals. The mean time to SARS-CoV-2 detection was 135 days. The majority were asymptomatic or exhibited mild to moderate disease, 154 (16%) required hospitalization, 127 (13%) had severe-critical illness, and 19 (2%) died. Age (odds ratio [OR], 1.14; 95% CI, 1.04-1.07; $P < .001$), cardiovascular disease (OR, 3.02; 95% CI, 1.55-5.89; $P = .001$), and immunocompromised status (OR, 2.57; 95% CI, 1.70-3.90; $P < .001$) were

independent risk factors for hospitalization. Additionally, age (OR, 1.06; 95% CI, 1.02-1.11; P = .006) was significantly associated with mortality. HCWs (OR, 0.15; 95% CI, 0.05-0.50; P = .002) were less likely to be hospitalized, and prior receipt of BNT162b2 was associated with lower odds of hospitalization (OR, 0.436; 95% CI, 0.303-0.626; P < .001) and/or death (OR, 0.360; 95% CI, 0.145-0.898; P = .029).

CONCLUSIONS: COVID-19 vaccines remain effective at attenuating disease severity. However, patients with breakthrough infections necessitating hospitalization may benefit from early treatment modalities and COVID-19-mitigating strategies, especially in areas with substantial or high transmission rates.

Endocrinology and Metabolism

Deutschbein T, Reimondo G, Di Dalmazi G, Bancos I, Patrova J, Vassiliadi DA, Nekić AB, Debono M, Lardo P, Ceccato F, Petramala L, Prete A, Chiodini I, Ivović M, Pazaitou-Panayiotou K, Alexandraki KI, Hanzu FA, Loli P, Yener S, Langton K, Spyroglou A, Kocjan T, Zacharieva S, Valdés N, Ambroziak U, Suzuki M, Detomas M, Puglisi S, Tucci L, Delivanis DA, Margaritopoulos D, Dusek T, Maggio R, Scaroni C, Concistrè A, Ronchi CL, Altieri B, Mosconi C, Diamantopoulos A, Iñiguez-Ariza NM, Vicennati V, Pia A, Kroiss M, Kaltsas G, Chrisoulidou A, Marina LV, Morelli V, Arlt W, Letizia C, Boscaro M, Stigliano A, Kastelan D, Tsagarakis S, **Athimulam S**, Pagotto U, Maeder U, Falhammar H, Newell-Price J, Terzolo M, and Fassnacht M. Age-dependent and sex-dependent disparity in mortality in patients with adrenal incidentalomas and autonomous cortisol secretion: an international, retrospective, cohort study. *Lancet Diabetes Endocrinol* 2022; Epub ahead of print. PMID: 35533704. [Full Text](#)

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BACKGROUND: The association between cortisol secretion and mortality in patients with adrenal incidentalomas is controversial. We aimed to assess all-cause mortality, prevalence of comorbidities, and occurrence of cardiovascular events in uniformly stratified patients with adrenal incidentalomas and cortisol autonomy (defined as non-suppressible serum cortisol on dexamethasone suppression testing).

METHODS: We conducted an international, retrospective, cohort study (NAPACA Outcome) at 30 centres in 16 countries. Eligible patients were aged 18 years or older with an adrenal incidentaloma (diameter ≥ 1 cm) detected between Jan 1, 1996, and Dec 31, 2015, and availability of a 1 mg dexamethasone suppression test result from the time of the initial diagnosis. Patients with clinically apparent hormone excess, active malignancy, or follow-up of less than 36 months were excluded. Patients were stratified according to the 0800-0900 h serum cortisol values after an overnight 1 mg dexamethasone suppression test; less than 50 nmol/L was classed as non-functioning adenoma, 50-138 nmol/L as possible autonomous cortisol secretion, and greater than 138 nmol/L as autonomous cortisol secretion. The primary endpoint was all-cause mortality. Secondary endpoints were the prevalence of cardiometabolic comorbidities, cardiovascular events, and cause-specific mortality. The primary and secondary endpoints were assessed in all study participants.

FINDINGS: Of 4374 potentially eligible patients, 3656 (2089 [57.1%] with non-functioning adenoma, 1320 [36.1%] with possible autonomous cortisol secretion, and 247 [6.8%] with autonomous cortisol secretion) were included in the study cohort for mortality analysis

(2350 [64.3%] women and 1306 [35.7%] men; median age 61 years [IQR 53-68]; median follow-up 7.0 years [IQR 4.7-10.2]). During follow-up, 352 (9.6%) patients died. All-cause mortality (adjusted for age, sex, comorbidities, and previous cardiovascular events) was significantly increased in patients with possible autonomous cortisol secretion (HR 1.52, 95% CI 1.19-1.94) and autonomous cortisol secretion (1.77, 1.20-2.62) compared with patients with non-functioning adenoma. In women younger than 65 years, autonomous cortisol secretion was associated with higher all-cause mortality than non-functioning adenoma (HR 4.39, 95% CI 1.93-9.96), although this was not observed in men. Cardiometabolic comorbidities were significantly less frequent with non-functioning adenoma than with possible autonomous cortisol secretion and autonomous cortisol secretion (hypertension occurred in 1186 [58.6%] of 2024 patients with non-functioning adenoma, 944 [74.0%] of 1275 with possible autonomous cortisol secretion, and 179 [75.2%] of 238 with autonomous cortisol secretion; dyslipidaemia occurred in 724 [36.2%] of 1999 patients, 547 [43.8%] of 1250, and 123 [51.9%] of 237; and any diabetes occurred in 365 [18.2%] of 2002, 288 [23.0%] of 1250, and 62 [26.7%] of 232; all p values <0.001). INTERPRETATION: Cortisol autonomy is associated with increased all-cause mortality, particularly in women younger than 65 years. However, until results from randomised interventional trials are available, a conservative therapeutic approach seems to be justified in most patients with adrenal incidentaloma. FUNDING: Deutsche Forschungsgemeinschaft, Associazione Italiana per la Ricerca sul Cancro, Università di Torino.

Family Medicine

Macias D, Hand BN, Zenga J, Pipkorn P, Nilsen ML, **Williams AM**, and Graboyes EM. Association Between Observer-Rated Disfigurement and Body Image-Related Distress Among Head and Neck Cancer Survivors. *JAMA Otolaryngol Head Neck Surg* 2022; Epub ahead of print. PMID: 35554492. [Full Text](#)

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This cross-sectional study assesses the association between observer-rated disfigurement and body image-related distress among survivors of head and neck cancer.

Gastroenterology

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BACKGROUND AND AIMS: Placement of a Lumen Apposing Metal Stent (LAMS) between the gastric pouch and the excluded stomach allows for EUS Guided Transgastric Interventions (EDGI) in patients with Roux-en-Y gastric bypass (RYGB). Although EUS guided transgastric ERCP (EDGE) outcomes have been reported, there is a paucity of data on other endoscopic interventions. We aimed to evaluate the outcomes and safety of EDGI. **METHODS:** This is a retrospective study involving 9 centers (8 USA, 1 Europe) and included patients with RYGB who underwent EDGI between 06/2015 and 09/2021. The primary outcome was the technical success of EDGI. Secondary outcomes included adverse events, length of hospital stay, and fistula follow-up and management. **RESULTS:** 54 EDGI procedures were performed in 47 patients (mean age 61yr, F 72%), most commonly for the evaluation of a pancreatic mass (n=16) and management of pancreatic fluid collections (n=10). A 20mm LAMS was utilized in 26 patients and a 15mm LAMS in 21, creating a gastrogastrostomy (GG) in 37 patients and jejunogastrostomy (JG) in 10. Most patients (n=30, 64%) underwent a dual-session EDGI, with a median interval of 17d between the 2 procedures. Single-session EDGI was performed in 17 patients, of whom 10 (59%) had anchoring of the LAMS. The most common interventions were diagnostic EUS (+/-FNA/B) (n=28) and EUS-guided cystgastrostomy (n=8). The mean procedural time was 97.6 ± 78.9 mins. Technical success was achieved in 52 (96%). AEs occurred in 5 (10.6%) patients, of which only 1 (2.1%) was graded as severe. Intra-procedural LAMS migration was the most common AE, occurring in 3 patients (6.4%), while delayed spontaneous LAMS migration occurred in 2 (4.3%). 4 of the 5 LAMS migration events were managed endoscopically, and one required surgical repair. LAMS anchoring was found to be protective against LAMS migration ($p=0.001$). The median duration of hospital stay was 2.1 ± 3.7 d. Of the 17 patients who underwent objective fistula assessment endoscopically/radiologically after LAMS removal, 2 (11.7%) were found to have persistent fistulas. In one case the fistula was intentionally left open to assist with weight gain. The other fistula was successfully closed endoscopically. **CONCLUSION:** EDGI is effective and safe for the diagnosis and management of pancreatobiliary and foregut disorders in RYGB patients. It is associated with high rates of technical success and low rates of severe AEs. LAMS migration is the most common AE with evidence that anchoring can be protective against its occurrence. Persistent fistulas may occur, but endoscopic closure seems effective.

Global Health Initiative

Shallal A, Lahoud C, Merhej D, Youssef S, Verkler J, Kaljee L, Prentiss T, Joshi S, Zervos M, and Matar M. The Impact of a Post-Prescription Review and Feedback Antimicrobial Stewardship Program in Lebanon. *Antibiotics (Basel)* 2022; 11(5). PMID: 35625286. [Full Text](#)

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Antimicrobial stewardship programs (ASPs) are effective means to optimize prescribing practices. They are under-utilized in the Middle East where many challenges exist for ASP implementation. We assessed the effectiveness of infectious disease physician-driven post-prescription review and feedback as an ASP in Lebanon. This prospective cohort study was conducted over an 18-month period in the medical, surgical, and intensive care units of a tertiary care hospital. It consisted of three phases: the baseline, intervention, and follow-up. There was a washout period of two months between each phase. Patients aged ≥ 16 years receiving 48 h of antibiotics were included. During the intervention phase, the AMS team reviewed antimicrobial use within 72 h post-prescription and gave alternate recommendations based on the guidelines for use. The acceptance of the recommendations was measured at 72 h. The primary outcome of the study was days of therapy per 1000 study patient days. A total of 328 patients were recruited in the baseline phase (August-October 2020), 467 patients in the intervention phase (January-June 2021), and 301 patients in the post-intervention phase (September-December 2021). The total days of therapy decreased from 11.46 during the baseline phase to 8.64 during the intervention phase ($p < 0.001$). Intervention acceptance occurred 88.5% of the time. The infectious disease physician-driven

implementation of an ASP was successful in reducing antibiotic utilization in an acute care setting in Lebanon.

Graduate Medical Education

Zasuwa GA, Yee J, Passalacqua KD, and Frinak S. Remote Monitoring of Sustained Low-Efficiency Dialysis (SLED) Machines in Intensive Care Unit. *Kidney Med* 2022; 4(5):100452. PMID: 35518838. [Full Text](#)

Division of Nephrology and Hypertension, Henry Ford Health System, Detroit, Michigan.

The Henry Ford Health System provides patients with a safe, improved system of continuous kidney replacement therapy using a proprietary, 24-hour sustained low-efficiency dialysis (SLED). The SLED system utilizes regional citrate anticoagulation (RCA) in conventional hemodialysis machines that have been configured to provide slow dialytic therapy. Within our hospital complex, SLED-RCA systems are deployed in intensive care units distributed over 4 floors in 2 buildings. This widespread footprint represents a spatial challenge for hemodialysis technicians. Fifteen SLED-RCA machines may be running at one time, and each deployed unit may signal an alarm for multiple reasons. Previously, audible alarms prompted intensive care unit nurses to identify the alarming machine and manually notify technicians by telephone. Technicians would then travel to resolve the alarm. To improve the process of addressing SLED-RCA machine alarms, we developed a remote alert alarm system that wirelessly notifies hemodialysis technicians of specific machine alarms. A quality improvement analysis of nearly 1,000 SLED-RCA alarms over a 1-week period revealed that the average time for alarm correction with a remote alert alarm system was approximately 5 minutes. Reducing alarm resolution time may free technicians and nurses for other critical duties.

Hematology-Oncology

de la Fuente MI, Colman H, Rosenthal M, Van Tine BA, Levacic D, **Walbert T**, Gan HK, Vieito M, Milhem MM, Lipford K, Forsyth S, Guichard SM, Mikhailov Y, Sedkov A, Brevard J, Kelly PF, Mohamed H, and Monga V. Olutasidenib (FT-2102) in patients with relapsed or refractory IDH1-mutant glioma: a multicenter, open-label, phase 1b/2 trial. *Neuro Oncol* 2022; Epub ahead of print. PMID: 35639513. [Full Text](#)

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Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah, USA.

Peter MacCallum Cancer Centre Melbourne, Victoria, Australia.

Washington University in St. Louis School of Medicine, St. Louis, Missouri, USA.

Baylor and Scott White Vasicek Cancer Center, Baylor University Temple, Temple, Texas, USA.

Henry Ford Cancer Institute, Henry Ford Health System and Wayne State University, Detroit, Michigan, USA.

Olivia Newton-John Cancer Wellness and Research Centre Austin Hospital, Heidelberg, Victoria, Australia.

La Trobe University School of Cancer Medicine, Heidelberg, Victoria, Australia.

Department of Medicine, University of Melbourne, Heidelberg, Victoria, Australia.

Vall d'Hebron Institute of Oncology, Barcelona, Spain.

Holden Comprehensive Cancer Center, University of Iowa, Iowa City, Iowa, USA.

Forma Therapeutics, Inc., Watertown, Massachusetts, USA.

BACKGROUND: Olutasidenib (FT2102) is a highly potent, orally bioavailable, brain-penetrant and selective inhibitor of mutant isocitrate dehydrogenase 1 (IDH1). The aim of the study was to determine the safety and clinical activity of olutasidenib in patients with relapsed/refractory gliomas harboring an IDH1 R132X mutation. **METHODS:** This was an open-label, multicenter, non-randomized, phase 1b/2 clinical trial. Eligible patients (≥ 18 years) had histologically confirmed IDH1 R132Xmutated glioma that relapsed or progressed on or following standard therapy and had measurable disease. Patients received olutasidenib, 150 mg orally twice daily (BID) in continuous 28-day cycles. The primary endpoints were dose-limiting toxicities (DLTs) (cycle 1) and safety in phase 1 and objective response rate using the

Modified Response Assessment in Neuro-Oncology criteria in phase 2. RESULTS: Twenty-six patients were enrolled and followed for a median 15.1 months (7.3–19.4). No DLTs were observed in the single-agent glioma cohort and the pharmacokinetic relationship supported olutasidenib 150 mg BID as the recommended phase 2 dose. In the response-evaluable population, disease control rate (objective response plus stable disease) was 48%. Two (8%) patients demonstrated a best response of partial response and eight (32%) had stable disease for at least 4 months. Grade 3–4 adverse events ($\geq 10\%$) included alanine aminotransferase increased and aspartate aminotransferase increased (three [12%], each). CONCLUSIONS: Olutasidenib 150 mg BID was well tolerated in patients with relapsed/refractory gliomas harboring an IDH1 R132X mutation and demonstrated preliminary evidence of clinical activity in this heavily pretreated population.

Hematology-Oncology

Emole J, Lawal O, Lupak O, Dias A, Shune L, and Yusuf K. Demographic differences among patients treated with chimeric antigen receptor T-cell therapy in the United States. *Cancer Med* 2022; Epub ahead of print. PMID: 35527361. [Full Text](#)

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Public Health Program, Adelphi University, Garden City, New York, USA.

BACKGROUND: It is not clear if all Americans have benefitted equally from the availability of chimeric antigen receptor T-cell (CART) therapy. We aimed to evaluate if demographic differences existed among adult patients who received CART therapy and to assess predictors of CART treatment outcomes.

METHODS: Records of patients ≥ 18 years who received CART therapy for non-Hodgkin's lymphoma, acute lymphoblastic leukemia, and multiple myeloma in 2018 were evaluated in the National Inpatient Sample. Acute complications and in-hospital mortality were compared between two groups of CART recipients: Whites and non-Whites. Logistic regression analysis was used to evaluate the association between sociodemographic factors and in-hospital mortality.

RESULTS: Of 1275 CART recipients that met inclusion criteria, there were 40.4% of females, 66.9% of Whites, Blacks (4.2%), Hispanics (13.3%), Asians or Pacific Islanders (4.2%), and Native Americans (1.3%). Up to 96.8% of CART procedures were performed in urban teaching hospitals, and 85.3% of CART recipients lived in metropolitan counties. Non-Whites, compared to Whites, were younger at the time of CART therapy ($p < 0.001$). The in-hospital mortality rate was higher in non-Whites, though not statistically significant (5.4% vs. 4.4%, $p = 0.764$).

There were no differences in length of hospital stay, hospital charges, or rates of acute toxicities between the two race groups. We found no association between race and treatment outcomes. Gender, neurotoxicity, and Charlson Comorbidity Index were significant predictors of in-hospital mortality.

CONCLUSIONS: CART therapy recipients in the United States were more likely to be Whites and more likely to be residents of metropolitan areas. These observed demographic differences were not associated with treatment outcomes or in-hospital mortalities.

Hematology-Oncology

Minchom A, Viteri S, Bazhenova L, **Gadgeel SM**, Ou SI, Trigo J, Bauml JM, Backenroth D, Bhattacharya A, Li T, Mahadevia P, and Girard N. Amivantamab compared with real-world therapies in patients with advanced non-small cell lung cancer harboring EGFR exon 20 insertion mutations who progressed after platinum-based chemotherapy. *Lung Cancer* 2022; 168:74-82. PMID: 35597172. [Full Text](#)

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BACKGROUND: In the single-arm CHRYSALIS study, amivantamab showed durable responses and manageable safety in patients with advanced non-small cell lung cancer (NSCLC) harboring epidermal growth factor receptor (EGFR) exon 20 insertion mutations (ex20ins) who progressed on prior platinum-based chemotherapy. External controls can provide context for interpreting amivantamab efficacy. **METHODS:** External controls were selected from three US-based databases (ConcertAI, COTA, and Flatiron). Key inclusion criteria were diagnosis of EGFR ex20ins advanced NSCLC, prior platinum-based chemotherapy, and performance status score ≤ 1 . Duplicate external controls were identified using a tokenization procedure and removed, and adjustment for differences in baseline characteristics between amivantamab-treated and external control cohorts was achieved using propensity score weighting. **RESULTS:** Amivantamab-treated and pooled external control cohorts included 81 and 125 patients, respectively. Baseline characteristics were generally similar across cohorts, except more amivantamab-treated patients were Asian (56% vs 13%). Most common therapies received by external controls were non-platinum-based chemotherapy (25.1%), immuno-oncology therapies (24.2%), EGFR tyrosine kinase inhibitors (16.3%), and platinum-based chemotherapy (16.3%). Overall response rate was 40% among amivantamab-treated patients and 16% among external controls. Amivantamab-treated patients had longer progression-free survival (median 8.3 vs 2.9 months; hazard ratio [HR; 95% CI]: 0.47 [0.34-0.65]), time to next therapy (median 14.8 vs 4.8 months; HR [95% CI]: 0.40 [0.28-0.57]), and overall survival (median 22.8 vs 12.8 months; HR [95% CI]: 0.49 [0.31-0.77]) than external controls. Results were consistent in sensitivity analyses comparing each external control dataset against the amivantamab-treated group separately. **CONCLUSION:** Among post-platinum patients with EGFR ex20ins advanced NSCLC, those treated with amivantamab had improved outcomes, including 10-month longer overall survival, versus external controls.

Hospital Medicine

Barnes GD, Burnett A, Allen A, Ansell J, Blumenstein M, Clark NP, Crowther M, Dager WE, Deitelzweig SB, **Ellsworth S**, Garcia D, **Kaatz S**, Raffini L, Rajasekhar A, Beek AV, and Minichiello T. Thromboembolic prevention and anticoagulant therapy during the COVID-19 pandemic: updated clinical guidance from the anticoagulation forum. *J Thromb Thrombolysis* 2022; 1-14; Epub ahead of print. PMID: 35579732. [Full Text](#)

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McMaster University, Hamilton, ON, Canada.
UC Davis Medical Center, Sacramento, CA, USA.
Ochsner Health System, New Orleans, LA, USA.
Henry Ford Hospital, Detroit, MI, USA.
University of Washington, Seattle, WA, USA.

University of Pennsylvania Children's Hospital of Philadelphia, Philadelphia, PA, USA.
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Thromboembolism is a common and deadly consequence of COVID-19 infection for hospitalized patients. Based on clinical evidence pre-dating the COVID-19 pandemic and early observational reports, expert consensus and guidance documents have strongly encouraged the use of prophylactic anticoagulation for patients hospitalized for COVID-19 infection. More recently, multiple clinical trials and larger observational studies have provided evidence for tailoring the approach to thromboprophylaxis for patients with COVID-19. This document provides updated guidance for the use of anticoagulant therapies in patients with COVID-19 from the Anticoagulation Forum, the leading North American organization of anticoagulation providers. We discuss ambulatory, in-hospital, and post-hospital thromboprophylaxis strategies as well as provide guidance for patients with thrombotic conditions who are considering COVID-19 vaccination.

Hospital Medicine

Gupta K, Obeidat L, Kakar TS, Fadel RA, Al Rifai M, Abushamat LA, and Virani SS. Trends in Undiagnosed Diabetes Mellitus Among United States Adults: Cross-Sectional Analyses from NHANES 2011-2020. *Am J Cardiol* 2022; Epub ahead of print. PMID: 35613950. [Full Text](#)

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Section of Cardiology and Cardiovascular Research, Department of Medicine, Baylor College of Medicine, Houston, Texas; Health Policy, Quality & Informatics Program, Health Services Research and Development Center for Innovations in Quality, Effectiveness, and Safety (IQuEST), Michael E. DeBakey Veterans Affairs Medical Center, Houston, Texas; Section of Cardiology, Michael E. DeBakey Veterans Affairs Medical Center, Houston, Texas.

Hypertension and Vascular Research

Pan G, Roy B, Harding P, Lanigan T, Hilgarth R, Thandavarayan RA, and **Palaniyandi SS**. Effects of intracardiac delivery of aldehyde dehydrogenase 2 gene in myocardial salvage. *Gene Ther* 2022; Epub ahead of print. PMID: 35606494. [Full Text](#)

Division of Hypertension and Vascular Research, Department of Internal Medicine, Henry Ford Health System, Detroit, MI, 48202, USA.
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Intrinsic activity of aldehyde dehydrogenase (ALDH)2, a cardiac mitochondrial enzyme, is vital in detoxifying 4-hydroxy-2-nonenal (4HNE) like cellular reactive carbonyl species (RCS) and thereby conferring cardiac protection against pathological stress. It was also known that a single point mutation (E487K) in ALDH2 (prevalent in East Asians) known as ALDH2*2 reduces its activity intrinsically and was associated with increased cardiovascular diseases. We and others have shown that ALDH2 activity is reduced in several pathologies in WT animals as well. Thus, exogenous augmentation of ALDH2 activity is a good strategy to protect the myocardium from pathologies. In this study, we will test the efficacy of intracardiac injections of the ALDH2 gene in mice. We injected both wild type (WT) and ALDH2*2 knock-in mutant mice with ALDH2 constructs, AAV9-cTNT-hALDH2-HA tag-P2A-eGFP or their control constructs, AAV9-cTNT-eGFP. We found that intracardiac ALDH2 gene transfer increased myocardial

levels of ALDH2 compared to GFP alone after 1 and 3 weeks. When we subjected the hearts of these mice to 30 min global ischemia and 90 min reperfusion (I-R) using the Langendorff perfusion system, we found reduced infarct size in the hearts of mice with ALDH2 gene vs GFP alone. A single time injection has shown increased myocardial ALDH2 activity for at least 3 weeks and reduced myocardial 4HNE adducts and infarct size along with increased contractile function of the hearts while subjected to I-R. Thus, ALDH2 overexpression protected the myocardium from I-R injury by reducing 4HNE protein adducts implicating increased 4HNE detoxification by ALDH2. In conclusion, intracardiac ALDH2 gene transfer is an effective strategy to protect the myocardium from pathological insults.

Infectious Diseases

Gudipati S, Lee M, Scott M, Yaphe S, Huisting J, Yared N, Brar I, and Markowitz N. The seroprevalence of COVID-19 in patients living with HIV in metropolitan Detroit. *Int J STD AIDS* 2022; 33(6):554-558. PMID: 35333100. [Full Text](#)

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BACKGROUND: COVID-19, a novel respiratory illness caused by SARS-CoV-2, has become a global pandemic. As of December 2020, 4.8% of the 941 people living with HIV in our Ryan White clinic have tested polymerase chain reaction positive for SARS-CoV-2. The aim of our study was to estimate the seroprevalence of COVID-19 in our Ryan White people living with HIV, irrespective of known past infection. **METHODS:** We conducted a cross-sectional study that recruited people living with HIV in the Ryan White program at Henry Ford Hospital in Detroit, Michigan, from September 2020 through May 2021. All Ryan White patients were offered participation during clinic visits. After informed consent, patients completed a survey, and had blood sampled for SARS-CoV-2 antibody testing. **RESULTS:** Of the 529 individuals who completed the written survey, 504 participants were tested for SARS-CoV-2 antibody and 52 people living with HIV were COVID-19 immunoglobulin (Ig) G positive resulting in a seroprevalence of 10.3%. Among 36 persons with PCR-confirmed COVID-19, 52.8% were IgG negative. Inclusion of PCR positive but IgG-negative people living with HIV yields a COVID-19 infection prevalence of 14.1%. **CONCLUSIONS:** These findings suggest that passive public health-based antibody surveillance in people living with HIV significantly underestimates past infection.

Infectious Diseases

Mercuro NJ, Medler CJ, Kenney RM, MacDonald NC, Neuhauser MM, Hicks LA, Srinivasan A, Divine G, Beaulac A, Eriksson E, Kendall R, Martinez M, Weinmann A, Zervos M, and Davis SL. Pharmacist-Driven Transitions of Care Practice Model for Prescribing Oral Antimicrobials at Hospital Discharge. *JAMA Netw Open* 2022; 5(5):e2211331. PMID: 35536577. [Full Text](#)

Department of Pharmacy, Henry Ford Health System, Detroit, Michigan.

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Division of Infectious Diseases, Henry Ford Health System, Detroit, Michigan.

IMPORTANCE: Although prescribers face numerous patient-centered challenges during transitions of care (TOC) at hospital discharge, prolonged duration of antimicrobial therapy for common infections remains problematic, and resources are needed for antimicrobial stewardship throughout this period. **OBJECTIVE:** To evaluate a pharmacist-driven intervention designed to improve selection and duration of oral antimicrobial therapy prescribed at hospital discharge for common infections. **DESIGN, SETTING, AND PARTICIPANTS:** This quality improvement study used a nonrandomized stepped-wedge design with 3 study phases from September 1, 2018, to August 31, 2019. Seventeen distinct medicine, surgery, and specialty units from a health system in Southeast Michigan participated, including 1 academic tertiary hospital and 4 community hospitals. Hospitalized adults who had urinary, respiratory, skin and/or soft tissue, and intra-abdominal infections and were prescribed antimicrobials at discharge were included in the analysis. Data were analyzed from February 18, 2020, to February 28, 2022. **INTERVENTIONS:**

Clinical pharmacists engaged in a new standard of care for antimicrobial stewardship practices during TOC by identifying patients to be discharged with a prescription for oral antimicrobials and collaborating with primary teams to prescribe optimal therapy. Academic and community hospitals used both antimicrobial stewardship and clinical pharmacists in a multidisciplinary rounding model to discuss, document, and facilitate order entry of the antimicrobial prescription at discharge. MAIN OUTCOMES AND MEASURES: The primary end point was frequency of optimized antimicrobial prescription at discharge. Health system guidelines developed from national guidelines and best practices for short-course therapies were used to evaluate optimal therapy. RESULTS: A total of 800 patients prescribed oral antimicrobials at hospital discharge were included in the analysis (441 women [55.1%]; mean [SD] age, 66.8 [17.3] years): 400 in the preintervention period and 400 in the postintervention period. The most common diagnoses were pneumonia (264 [33.0%]), upper respiratory tract infection and/or acute exacerbation of chronic obstructive pulmonary disease (214 [26.8%]), and urinary tract infection (203 [25.4%]). Patients in the postintervention group were more likely to have an optimal antimicrobial prescription (time-adjusted generalized estimating equation odds ratio, 5.63 [95% CI, 3.69-8.60]). The absolute increase in optimal prescribing in the postintervention group was consistent in both academic (37.4% [95% CI, 27.5%-46.7%]) and community (43.2% [95% CI, 32.4%-52.8%]) TOC models. There were no differences in clinical resolution or mortality. Fewer severe antimicrobial-related adverse effects (time-adjusted generalized estimating equation odds ratio, 0.40 [95% CI, 0.18-0.88]) were identified in the postintervention (13 [3.2%]) compared with the preintervention (36 [9.0%]) groups. CONCLUSIONS AND RELEVANCE: The findings of this quality improvement study suggest that targeted antimicrobial stewardship interventions during TOC were associated with increased optimal, guideline-concordant antimicrobial prescriptions at discharge.

Infectious Diseases

Monday LM, Brar I, Alangaden G, and Ramesh MS. SARS-CoV-2 neutralizing antibodies for COVID-19: Outcomes for bamlanivimab versus bamlanivimab-etesevimab combination in a racially diverse cohort of patients with significant comorbidities. *J Clin Pharm Ther* 2022; Epub ahead of print. PMID: 35633095.

[Full Text](#)

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WHAT IS KNOWN AND OBJECTIVE: Anti-spike monoclonal antibodies (MAB) including bamlanivimab (BAM) and bamlanivimab/etesevimab (BAM/E) have shown reduced hospitalization rates for non-severe coronavirus disease 2019 (COVID-19) in clinical trials. Recent data have provided real-world hospitalization rates for high-risk patients treated with BAM, however, data on a similar cohort treated with BAM/E are lacking. METHODS: This retrospective cohort study evaluated outpatients ≥ 18 years with laboratory-confirmed mild/moderate COVID-19 who received MAB from 1 December 2020 to 19 April 2021. Use of BAM monotherapy changed to BAM/E combination on 27 March 2021. Primary outcome was overall rate of COVID-19 related-hospitalization, including comparison of hospitalization rates between MAB-formulation groups. Secondary outcomes were 30-day mortality and length of stay (LOS). RESULTS AND DISCUSSION: The population included 643 patients (BAM and BAM/E); median age was 58 years, 43% were male, median BMI was 33 kg/m², and 24% self-identified as Black. Patients in the BAM/E combination group were significantly younger with higher median BMI and a longer time from symptom onset to infusion. The incidence of 30-day COVID-19 related hospitalization was similar between patients receiving either BAM or BAM/E combination (7.8% and 7.2%, respectively). WHAT IS NEW AND CONCLUSION: This study represents the first such publication of real-world BAM/E hospitalization outcomes. Hospitalization rates utilizing BAM/E were comparable to BAM in our real-world study.

Infectious Diseases

Shallal A, Lahoud C, Merhej D, Youssef S, Verkler J, Kaljee L, Prentiss T, Joshi S, Zervos M, and Matar M. The Impact of a Post-Prescription Review and Feedback Antimicrobial Stewardship Program in Lebanon. *Antibiotics (Basel)* 2022; 11(5). PMID: 35625286. [Full Text](#)

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Antimicrobial stewardship programs (ASPs) are effective means to optimize prescribing practices. They are under-utilized in the Middle East where many challenges exist for ASP implementation. We assessed the effectiveness of infectious disease physician-driven post-prescription review and feedback as an ASP in Lebanon. This prospective cohort study was conducted over an 18-month period in the medical, surgical, and intensive care units of a tertiary care hospital. It consisted of three phases: the baseline, intervention, and follow-up. There was a washout period of two months between each phase. Patients aged ≥ 16 years receiving 48 h of antibiotics were included. During the intervention phase, the AMS team reviewed antimicrobial use within 72 h post-prescription and gave alternate recommendations based on the guidelines for use. The acceptance of the recommendations was measured at 72 h. The primary outcome of the study was days of therapy per 1000 study patient days. A total of 328 patients were recruited in the baseline phase (August-October 2020), 467 patients in the intervention phase (January-June 2021), and 301 patients in the post-intervention phase (September-December 2021). The total days of therapy decreased from 11.46 during the baseline phase to 8.64 during the intervention phase ($p < 0.001$). Intervention acceptance occurred 88.5% of the time. The infectious disease physician-driven implementation of an ASP was successful in reducing antibiotic utilization in an acute care setting in Lebanon.

Infectious Diseases

Shallal A, Lahoud C, **Zervos M**, and Matar M. Antibiotic Stewardship in Disaster Situations: Lessons Learned in Lebanon. *Antibiotics (Basel)* 2022; 11(5). PMID: 35625204. [Full Text](#)

Division of Infectious Diseases, Henry Ford Hospital, Detroit, MI 48202, USA.
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A post-prescription review and feedback program was implemented as an antimicrobial stewardship intervention in Lebanon as the country grappled with complete economic collapse, the COVID-19 pandemic, and a large blast in Beirut. We describe the implications of antimicrobial use in disaster preparedness and crisis situations, the sequelae related to increasing antimicrobial resistance, and our lessons learned in Lebanon. We explore opportunities and potential solutions for future disaster preparedness.

Infectious Diseases

Suleyman G, **Fadel R**, **Brar I**, **Kassab R**, **Khansa R**, **Sturla N**, **Alsaadi A**, **Latack K**, **Miller J**, **Tibbetts R**, **Samuel L**, **Alangaden G**, and **Ramesh M**. Risk Factors Associated With Hospitalization and Death in COVID-19 Breakthrough Infections. *Open Forum Infect Dis* 2022; 9(5):ofac116. PMID: 35437511. [Full Text](#)

Division of Infectious Disease, Henry Ford Health System, Detroit, Michigan, USA.
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BACKGROUND: Characterizations of coronavirus disease 2019 (COVID-19) vaccine breakthrough infections are limited. We aim to characterize breakthrough infections and identify risk factors associated with outcomes. **METHODS:** This was a retrospective case series of consecutive fully vaccinated patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a multicenter academic center in Southeast Michigan, between December 30, 2020, and September 15, 2021. **RESULTS:** A total of 982 patients were identified; the mean age was 57.9 years, 565 (59%) were female, 774 (79%) were White, and 255 (26%) were health care workers (HCWs). The median number of comorbidities was 2; 225 (23%) were immunocompromised. BNT162b2 was administered to 737 (75%) individuals. The mean time to SARS-CoV-2 detection was 135 days. The majority were asymptomatic or exhibited mild to moderate disease, 154 (16%) required hospitalization, 127 (13%) had severe-critical illness, and 19 (2%) died. Age (odds ratio [OR], 1.14; 95% CI, 1.04-1.07; $P < .001$), cardiovascular disease (OR, 3.02; 95% CI, 1.55-5.89; $P = .001$), and immunocompromised status (OR, 2.57; 95% CI, 1.70-3.90; $P < .001$) were independent risk factors for hospitalization. Additionally, age (OR, 1.06; 95% CI, 1.02-1.11; $P = .006$) was significantly associated with mortality. HCWs (OR, 0.15; 95% CI, 0.05-0.50; $P = .002$) were less likely to be hospitalized, and prior receipt of BNT162b2 was associated with lower odds of hospitalization (OR, 0.436; 95% CI, 0.303-0.626; $P < .001$) and/or death (OR, 0.360; 95% CI, 0.145-0.898; $P = .029$). **CONCLUSIONS:** COVID-19 vaccines remain effective at attenuating disease severity. However, patients with breakthrough infections necessitating hospitalization may benefit from early treatment modalities and COVID-19-mitigating strategies, especially in areas with substantial or high transmission rates.

Internal Medicine

Barnes GD, Burnett A, Allen A, Ansell J, Blumenstein M, Clark NP, Crowther M, Dager WE, Deitelzweig SB, **Ellsworth S**, Garcia D, **Kaatz S**, Raffini L, Rajasekhar A, Beek AV, and Minichiello T. Thromboembolic prevention and anticoagulant therapy during the COVID-19 pandemic: updated clinical guidance from the anticoagulation forum. *J Thromb Thrombolysis* 2022:1-14; Epub ahead of print. PMID: 35579732. [Full Text](#)

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Thromboembolism is a common and deadly consequence of COVID-19 infection for hospitalized patients. Based on clinical evidence pre-dating the COVID-19 pandemic and early observational reports, expert consensus and guidance documents have strongly encouraged the use of prophylactic anticoagulation for patients hospitalized for COVID-19 infection. More recently, multiple clinical trials and larger observational studies have provided evidence for tailoring the approach to thromboprophylaxis for patients with COVID-19. This document provides updated guidance for the use of anticoagulant therapies in patients with COVID-19 from the Anticoagulation Forum, the leading North American organization of anticoagulation providers. We discuss ambulatory, in-hospital, and post-hospital thromboprophylaxis strategies as well as provide guidance for patients with thrombotic conditions who are considering COVID-19 vaccination.

Internal Medicine

Ghandour B, Shinn B, Dawod QM, Fansa S, El Chafic AH, Irani SS, Pawa R, Gutta A, **Ichkhanian Y**, Paranandi B, Pawa S, Al-Haddad MA, **Zuchelli T**, Huggett MT, Bejjani M, Sharaiha RZ, Kowalski TE, and Khashab MA. EUS-directed transgastric interventions in Roux-En-Y Gastric Bypass anatomy: a multicenter experience. *Gastrointest Endosc* 2022; Epub ahead of print. PMID: 35623383. [Full Text](#)

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BACKGROUND AND AIMS: Placement of a Lumen Apposing Metal Stent (LAMS) between the gastric pouch and the excluded stomach allows for EUS Guided Transgastric Interventions (EDGI) in patients with Roux-en-Y gastric bypass (RYGB). Although EUS guided transgastric ERCP (EDGE) outcomes have been reported, there is a paucity of data on other endoscopic interventions. We aimed to evaluate the outcomes and safety of EDGI. **METHODS:** This is a retrospective study involving 9 centers (8 USA, 1 Europe) and included patients with RYGB who underwent EDGI between 06/2015 and 09/2021. The primary outcome was the technical success of EDGI. Secondary outcomes included adverse events, length of hospital stay, and fistula follow-up and management. **RESULTS:** 54 EDGI procedures were performed in 47 patients (mean age 61yr, F 72%), most commonly for the evaluation of a pancreatic mass (n=16) and management of pancreatic fluid collections (n=10). A 20mm LAMS was utilized in 26 patients and a 15mm LAMS in 21, creating a gastrogastrostomy (GG) in 37 patients and jejunogastrostomy (JG) in 10. Most patients (n=30, 64%) underwent a dual-session EDGI, with a median interval of 17d between the 2 procedures. Single-session EDGI was performed in 17 patients, of whom 10 (59%) had anchoring of the LAMS. The most common interventions were diagnostic EUS (+/-FNA/B) (n=28) and EUS-guided cystgastrostomy (n=8). The mean procedural time was 97.6 ± 78.9 mins. Technical success was achieved in 52 (96%). AEs occurred in 5 (10.6%) patients, of which only 1 (2.1%) was graded as severe. Intraprocedural LAMS migration was the most common AE, occurring in 3 patients (6.4%), while delayed spontaneous LAMS migration occurred in 2 (4.3%). 4 of the 5 LAMS migration events were managed endoscopically, and one required surgical repair. LAMS anchoring was found to be protective against LAMS migration (p=0.001). The median duration of hospital stay was 2.1 ± 3.7d. Of the 17 patients who underwent objective fistula assessment endoscopically/radiologically after LAMS removal, 2 (11.7%) were found to have persistent fistulas. In one case the fistula was intentionally left open to assist with weight gain. The other fistula was successfully closed endoscopically. **CONCLUSION:** EDGI is effective and safe for the diagnosis and management of pancreatobiliary and foregut disorders in RYGB patients. It is associated with high rates of technical success and low rates of severe AEs. LAMS migration is the most common AE with evidence that anchoring can be protective against its occurrence. Persistent fistulas may occur, but endoscopic closure seems effective.

Internal Medicine

Gupta K, and **Lee JC**. Assessment of sinus of valsalva dimensions before TAVI: An independent predictor of worse outcomes? *Am Heart J* 2022; 248:165. PMID: 35491050. [Full Text](#)

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Internal Medicine

Gupta K, Obeidat L, Kakar TS, Fadel RA, Al Rifai M, Abushamat LA, and Virani SS. Trends in Undiagnosed Diabetes Mellitus Among United States Adults: Cross-Sectional Analyses from NHANES 2011-2020. *Am J Cardiol* 2022; Epub ahead of print. PMID: 35613950. [Full Text](#)

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Internal Medicine

Mohammed M, Nona P, Abou Asala E, Chiang M, Lemor A, O'Neill B, Frisoli T, Lee J, Wang DD, O'Neill WW, Eng M, and Villablanca PA. Preclosure of large bore venous access sites in patients undergoing transcatheter mitral replacement and repair. *Catheter Cardiovasc Interv* 2022; Epub ahead of print. PMID: 35568977. [Full Text](#)

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OBJECTIVE: We aim to report on the efficacy and safety of large bore venous access (LBVA) preclosure with Perclose™ (Abbott Vascular Devices) suture-mediated device use following transcatheter edge-to-edge (TEER) and replacement (TMVR). **BACKGROUND:** Patients requiring TEER and TMVR require LBVA. Clinical outcome data on the use of suture-mediated devices for LBVA site closure are limited. **METHODS:** Between 2012 and 2019, 354 consecutive high-risk patients with mitral valvular heart disease underwent TEER (n = 287) with MitraClip and TMVR (n = 67) with Edwards Sapien Valves. Patients had LBVA with 24 or 16 French sheaths. All patients underwent preclosure of LBVA except for one that underwent manual hemostasis. **RESULTS:** There were no closure device failures. None of the cases required surgical repair of the access site following venous preclosure. Two cases had large hematomas (>6 cm) following Perclose in each group. Six cases had small hematomas (<6 cm and >2 cm) with three in each group. There was one major bleeding using Mitral Valve Academic Research Consortium 2 definition (retroperitoneal bleed from arterial puncture) unrelated to the venous closure. Transfusion related to vascular access complication was required in five cases. There were two immediate acute deep venous thromboses postprocedure; one of which occurred after preclosure. There were no arteriovenous malformations, pseudoaneurysms, or access site infections reported following Perclose. **CONCLUSION:** In this large sample size analysis, Proglide preclosure technique is a feasible and safe alternative approach to achieving hemostasis after removal of LBVA sheaths in patients undergoing TEER and TMVR. Randomized trials are needed to compare the different modalities of hemostasis.

Internal Medicine

Nimri FM, Muhanna A, Almomani Z, Khazaaleh S, Alomari M, Almomani L, and Likhitsup A. The association between microscopic colitis and celiac disease: a systematic review and meta-analysis. *Ann Gastroenterol* 2022; 35(3):281-289. PMID: 35599929. [Full Text](#)

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BACKGROUND: Multiple studies suggested that celiac disease (CD) may be associated with microscopic colitis (MC); however, most were limited by a small sample size or the main scope of interest. We aimed to analyze previously published literature on this association to determine its extent and significance. **METHODS:** A systematic review was conducted in PubMed, Embase, PubMed Central, Cochrane, and ScienceDirect databases from inception through January 2022. The PRISMA guideline was followed for data extraction. Effect estimates were extracted and combined using random effect, the generic inverse variance method of DerSimonian and Laird and pooled odds ratio (OR), and event rates (ER) were calculated. The Newcastle-Ottawa scale was used to evaluate the risk of bias. Forest plots were generated and publication bias assessed via conventional techniques. **RESULTS:** Twenty-six studies with a total of 22,802 patients with MC were included in this analysis. CD was significantly associated with MC (odds ratio [OR] 8.276, 95% confidence interval [CI] 5.888-11.632; $P < 0.001$). The ER for MC in CD patients was 6.2% (95%CI 4.1-9.2%; $P < 0.001$), while the ER for CD in MC patients was 6.1% (95%CI 3.9-9.5%; $P < 0.001$). CD was prevalent in both types of MC: 5.2% (95%CI 2.2-12.1%; $P < 0.001$) in collagenous colitis and 6.3% (95%CI 3.4-11.5%; $P < 0.001$) in lymphocytic colitis. We found no publication bias, according to funnel plots and Egger's regression asymmetry testing. **CONCLUSIONS:** Our meta-analysis confirms a statistically significant association between CD and MC, with a high prevalence of CD in both types of MC. Gastroenterologists should be wary of this association when evaluating patients with either disease, particularly patients with a suboptimal response to first-line therapy.

Internal Medicine

Rehana RW, Moad JC, and Jiwani RA. Diagnosis of acute myeloid leukemia made by skin biopsy. *Am J Med Sci* 2022; 363(6):e51-e52. PMID: 33546879. [Full Text](#)

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Internal Medicine

Suleyman G, Fadel R, Brar I, Kassab R, Khansa R, Sturla N, Alsaadi A, Latack K, Miller J, Tibbetts R, Samuel L, Alangaden G, and Ramesh M. Risk Factors Associated With Hospitalization and Death in COVID-19 Breakthrough Infections. *Open Forum Infect Dis* 2022; 9(5):ofac116. PMID: 35437511. [Full Text](#)

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BACKGROUND: Characterizations of coronavirus disease 2019 (COVID-19) vaccine breakthrough infections are limited. We aim to characterize breakthrough infections and identify risk factors associated with outcomes. **METHODS:** This was a retrospective case series of consecutive fully vaccinated patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a multicenter academic center in Southeast Michigan, between December 30, 2020, and September 15, 2021. **RESULTS:** A total of 982 patients were identified; the mean age was 57.9 years, 565 (59%) were female, 774 (79%) were White, and 255 (26%) were health care workers (HCWs). The median number of comorbidities was 2; 225 (23%) were immunocompromised. BNT162b2 was administered to 737 (75%) individuals. The mean time to SARS-CoV-2 detection was 135 days. The majority were asymptomatic or exhibited mild to moderate

disease, 154 (16%) required hospitalization, 127 (13%) had severe-critical illness, and 19 (2%) died. Age (odds ratio [OR], 1.14; 95% CI, 1.04-1.07; $P < .001$), cardiovascular disease (OR, 3.02; 95% CI, 1.55-5.89; $P = .001$), and immunocompromised status (OR, 2.57; 95% CI, 1.70-3.90; $P < .001$) were independent risk factors for hospitalization. Additionally, age (OR, 1.06; 95% CI, 1.02-1.11; $P = .006$) was significantly associated with mortality. HCWs (OR, 0.15; 95% CI, 0.05-0.50; $P = .002$) were less likely to be hospitalized, and prior receipt of BNT162b2 was associated with lower odds of hospitalization (OR, 0.436; 95% CI, 0.303-0.626; $P < .001$) and/or death (OR, 0.360; 95% CI, 0.145-0.898; $P = .029$). CONCLUSIONS: COVID-19 vaccines remain effective at attenuating disease severity. However, patients with breakthrough infections necessitating hospitalization may benefit from early treatment modalities and COVID-19-mitigating strategies, especially in areas with substantial or high transmission rates.

Nephrology

Thongprayoon C, Vaitla P, Jadlowiec CC, Leeaphorn N, Mao SA, Mao MA, Pattharanitima P, Bruminhent J, **Khoury NJ**, Garovic VD, Cooper M, and Cheungpasitporn W. Use of Machine Learning Consensus Clustering to Identify Distinct Subtypes of Black Kidney Transplant Recipients and Associated Outcomes. *JAMA Surg* 2022:e221286; Epub ahead of print. PMID: 35507356. [Full Text](#)

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IMPORTANCE: Among kidney transplant recipients, Black patients continue to have worse graft function and reduced patient and graft survival. Better understanding of different phenotypes and subgroups of Black kidney transplant recipients may help the transplant community to identify individualized strategies to improve outcomes among these vulnerable groups. OBJECTIVE: To cluster Black kidney transplant recipients in the US using an unsupervised machine learning approach. DESIGN, SETTING, AND PARTICIPANTS: This cohort study performed consensus cluster analysis based on recipient-, donor-, and transplant-related characteristics in Black kidney transplant recipients in the US from January 1, 2015, to December 31, 2019, in the Organ Procurement and Transplantation Network/United Network for Organ Sharing database. Each cluster's key characteristics were identified using the standardized mean difference, and subsequently the posttransplant outcomes were compared among the clusters. Data were analyzed from June 9 to July 17, 2021. EXPOSURE: Machine learning consensus clustering approach. MAIN OUTCOMES AND MEASURES: Death-censored graft failure, patient death within 3 years after kidney transplant, and allograft rejection within 1 year after kidney transplant. RESULTS: Consensus cluster analysis was performed for 22 687 Black kidney transplant recipients (mean [SD] age, 51.4 [12.6] years; 13 635 men [60%]), and 4 distinct clusters that best represented their clinical characteristics were identified. Cluster 1 was characterized by highly sensitized recipients of deceased donor kidney retransplants; cluster 2, by recipients of living donor kidney transplants with no or short prior dialysis; cluster 3, by young recipients with hypertension and without diabetes who received young deceased donor transplants with low kidney donor profile index scores; and cluster 4, by older recipients with diabetes who received kidneys from older donors with high kidney donor profile index scores and extended criteria donors. Cluster 2 had the most favorable outcomes in terms of death-censored graft failure, patient death, and allograft rejection. Compared with cluster 2, all other clusters had a higher risk of death-censored graft failure and death. Higher risk for rejection was found in clusters 1 and 3, but not cluster 4. CONCLUSIONS AND RELEVANCE: In this cohort study using an unsupervised machine

learning approach, the identification of clinically distinct clusters among Black kidney transplant recipients underscores the need for individualized care strategies to improve outcomes among vulnerable patient groups.

Nephrology

Zasuwa GA, Yee J, Passalacqua KD, and Frinak S. Remote Monitoring of Sustained Low-Efficiency Dialysis (SLED) Machines in Intensive Care Unit. *Kidney Med* 2022; 4(5):100452. PMID: 35518838. [Full Text](#)

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The Henry Ford Health System provides patients with a safe, improved system of continuous kidney replacement therapy using a proprietary, 24-hour sustained low-efficiency dialysis (SLED). The SLED system utilizes regional citrate anticoagulation (RCA) in conventional hemodialysis machines that have been configured to provide slow dialytic therapy. Within our hospital complex, SLED-RCA systems are deployed in intensive care units distributed over 4 floors in 2 buildings. This widespread footprint represents a spatial challenge for hemodialysis technicians. Fifteen SLED-RCA machines may be running at one time, and each deployed unit may signal an alarm for multiple reasons. Previously, audible alarms prompted intensive care unit nurses to identify the alarming machine and manually notify technicians by telephone. Technicians would then travel to resolve the alarm. To improve the process of addressing SLED-RCA machine alarms, we developed a remote alert alarm system that wirelessly notifies hemodialysis technicians of specific machine alarms. A quality improvement analysis of nearly 1,000 SLED-RCA alarms over a 1-week period revealed that the average time for alarm correction with a remote alert alarm system was approximately 5 minutes. Reducing alarm resolution time may free technicians and nurses for other critical duties.

Neurology

Bergquist JR, Shariq OA, **Li AY**, Worth PJ, Chatzizacharias N, Soonawalla Z, Athanasopoulos P, Toumpanakis C, Hansen P, Parks RW, Connor S, Parker K, Koea J, Srinivasa S, Ielpo B, Lopez EV, Norton JA, Lawrence B, and Visser BC. Clinical features and postoperative survival in patients with sporadic versus multiple endocrine neoplasia type 1-related pancreatic neuroendocrine tumors: An international cohort study. *Surgery* 2022; Epub ahead of print. PMID: 35577612. [Full Text](#)

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BACKGROUND: The optimal surgical management of pancreatic neuroendocrine tumors in patients with multiple endocrine neoplasia type 1 is controversial. This study sought to compare clinicopathologic characteristics and outcomes of multiple endocrine neoplasia type 1-associated and sporadic pancreatic neuroendocrine tumors from a large multi-national database. **METHODS:** A multi-institutional, international database of patients with surgically resected pancreatic neuroendocrine tumors was analyzed. The cohort was divided into 2 groups: those with multiple endocrine neoplasia type 1 versus those with sporadic disease. Clinicopathologic comparisons were made. Overall and disease-free survival

were analyzed. Propensity score matching was used to reduce bias. RESULTS: Of 651 patients included, 45 (6.9%) had multiple endocrine neoplasia type 1 and 606 sporadic pancreatic neuroendocrine tumors. Multiple endocrine neoplasia type 1-associated pancreatic neuroendocrine tumors were more common in younger patients and associated with multifocal disease at the time of surgery and higher T-stage. Lymph node involvement and the presence of metastasis were similar. Total pancreatectomy rate was 5-fold higher in the multiple endocrine neoplasia type 1 cohort. Median survival did not differ (disease-free survival 126 months multiple endocrine neoplasia type 1 vs 198 months sporadic, $P > .5$). After matching, survival remained similar (overall survival not reached in either cohort, disease-free survival 126 months multiple endocrine neoplasia type 1 vs 198 months sporadic, $P > .5$). Equivalence in overall survival and disease-free survival persisted even when patients who underwent subtotal and total pancreatectomy were excluded. CONCLUSION: Multiple endocrine neoplasia type 1-associated pancreatic neuroendocrine tumors are more common in younger patients and are associated with multifocality and higher T-stage. Survival for patients with multiple endocrine neoplasia type 1-associated pancreatic neuroendocrine tumors is comparable to those with sporadic pancreatic neuroendocrine tumors, even in the absence of radical pancreatectomy. Consideration should be given to parenchymal-sparing surgery to preserve pancreatic function.

Neurology

Brang D, Plass J, Sherman A, Stacey WC, **Wasade VS**, Grabowecy M, Ahn E, Towle VL, Tao JX, Wu S, Issa NP, and Suzuki S. Visual cortex responds to sound onset and offset during passive listening. *J Neurophysiol* 2022; Epub ahead of print. PMID: 35507478. [Full Text](#)

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Sounds enhance our ability to detect, localize, and respond to co-occurring visual targets. Research suggests that sounds improve visual processing by resetting the phase of ongoing oscillations in visual cortex. However, it remains unclear what information is relayed from the auditory system to visual areas and if sounds modulate visual activity even in the absence of visual stimuli (e.g., during passive listening). Using intracranial electroencephalography (iEEG) in humans, we examined the sensitivity of visual cortex to three forms of auditory information during a passive listening task: auditory onset responses, auditory offset responses, and rhythmic entrainment to sounds. Because some auditory neurons respond to both sound onsets and offsets, visual timing and duration processing may benefit from each. Additionally, if auditory entrainment information is relayed to visual cortex, it could support the processing of complex stimulus dynamics that are aligned between auditory and visual stimuli. Results demonstrate that in visual cortex, amplitude-modulated sounds elicited transient onset and offset responses in multiple areas, but no entrainment to sound modulation frequencies. These findings suggest that activity in visual cortex (as measured with iEEG in response to auditory stimuli) may not be affected by temporally fine-grained auditory stimulus dynamics during passive listening (though it remains possible that this signal may be observable with simultaneous auditory-visual stimuli). Moreover, auditory responses were maximal in low-level visual cortex, potentially implicating a direct pathway for rapid interactions between auditory and visual cortices. This mechanism may facilitate perception by time-locking visual computations to environmental events marked by auditory discontinuities.

Neurology

Culmone L, Powell B, Landschoot-Ward J, Zacharek A, Gao H, Findeis EL, Malik A, Lu M, Chopp M, and Venkat P. Treatment With an Angiopoietin-1 Mimetic Peptide Improves Cognitive Outcome in Rats With Vascular Dementia. *Front Cell Neurosci* 2022; 16:869710. PMID: 35602559. [Full Text](#)

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BACKGROUND AND PURPOSE: Vascular dementia (VaD) is a complex neurodegenerative disease affecting cognition and memory. There is a lack of approved pharmacological treatments specifically for VaD. In this study, we investigate the therapeutic effects of AV-001, a Tie2 receptor agonist, in middle-aged rats subjected to a multiple microinfarct (MMI) model of VaD. **METHODS:** Male, 10-12 month-old, Wistar rats were employed. The following experimental groups were used: Sham, MMI, MMI+1 µg/Kg AV-001, MMI+3 µg/Kg AV-001, MMI+6 µg/Kg AV-001. AV-001 treatment was initiated at 1 day after MMI and administered once daily via intraperitoneal injection. An investigator blinded to the experimental groups conducted a battery of neuro-cognitive tests including modified neurological severity score (mNSS) test, novel object recognition test, novel odor recognition test, three chamber social interaction test, and Morris water maze test. Rats were sacrificed at 6 weeks after MMI. **RESULTS:** There was no mortality observed after 1, 3, or 6 µg/Kg AV-001 treatment in middle-aged rats subjected to MMI. AV-001 treatment (1, 3, or 6 µg/Kg) does not significantly alter blood pressure or heart rate at 6 weeks after MMI compared to baseline values or the MMI control group. Treatment of MMI with 1 or 3 µg/Kg AV-001 treatment does not significantly alter body weight compared to Sham or MMI control group. While 6 µg/Kg AV-001 treated group exhibit significantly lower body weight compared to Sham and MMI control group, the weight loss is evident starting at 1 day after MMI when treatment was initiated and is not significantly different compared to its baseline values at day 0 or day 1 after MMI. AV-001 treatment significantly decreases serum alanine aminotransferase, serum creatinine, and serum troponin I levels compared to the MMI control group; however, all values are within normal range. MMI induces mild neurological deficits in middle-aged rats indicated by low mNSS scores (<6 on a scale of 0-18). Compared to control MMI group, 1 µg/Kg AV-001 treatment group did not exhibit significantly different mNSS scores, while 3 and 6 µg/Kg AV-001 treatment induced significantly worse mNSS scores on days 21-42 and 14-42 after MMI, respectively. MMI in middle-aged rats induces significant cognitive impairment including short-term memory loss, long-term memory loss, reduced preference for social novelty and impaired spatial learning and memory compared to sham control rats. Rats treated with 1 µg/Kg AV-001 exhibit significantly improved short-term and long-term memory, increased preference for social novelty, and improved spatial learning and memory compared to MMI rats. Treatment with 3 µg/Kg AV-001 improves short-term memory and preference for social novelty but does not improve long-term memory or spatial learning and memory compared to MMI rats. Treatment with 6 µg/Kg AV-001 improves only long-term memory compared to MMI rats. Thus, 1 µg/Kg AV-001 treatment was selected as an optimal dose. Treatment of middle-aged rats subjected to MMI with 1 µg/Kg AV-001 significantly increases axon density, myelin density and myelin thickness in the corpus callosum, as well as increases synaptic protein expression, neuronal branching and dendritic spine density in the cortex, oligodendrocytes and oligodendrocyte progenitor cell number in the cortex and striatum and promotes neurogenesis in the subventricular zone compared to control MMI rats. **CONCLUSIONS:** In this study, we present AV-001 as a novel therapeutic agent to improve cognitive function and reduce white matter injury in middle aged-rats subjected to a MMI model of VaD. Treatment of MMI with 1 µg/Kg AV-001 significantly improves cognitive function, and increases axon density, remyelination and neuroplasticity in the brain of middle-aged rats.

Neurology

Monternier PA, **Singh J, Parasar P**, Theurey P, DeWitt S, Jacques V, Klett E, **Kaur N, Nagaraja TN**, Moller DE, and Hallakou-Bozec S. Therapeutic potential of deuterium-stabilized (R)-pioglitazone-PXL065- for X-linked adrenoleukodystrophy. *J Inherit Metab Dis* 2022; Epub ahead of print. PMID: 35510808. [Full Text](#)

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X-linked adrenoleukodystrophy (ALD) results from ABCD1 gene mutations which impair Very Long Chain Fatty Acids (VLCFA; C26:0 and C24:0) peroxisomal import and β-oxidation, leading to accumulation in plasma and tissues. Excess VLCFA drives impaired cellular functions (e.g. disrupted mitochondrial

function), inflammation, and neurodegeneration. Major disease phenotypes include: adrenomyeloneuropathy (AMN), progressive spinal cord axonal degeneration, and cerebral ALD (C-ALD), inflammatory white matter demyelination and degeneration. No pharmacological treatment is available to-date for ALD. Pioglitazone, an anti-diabetic thiazolidinedione, exerts potential benefits in ALD models. Its mechanisms are genomic (PPAR γ agonism) and nongenomic (mitochondrial pyruvate carrier-MPC, long-chain acyl-CoA synthetase 4-ACSL4, inhibition). However, its use is limited by PPAR γ -driven side effects (e.g. weight gain, edema). PXL065 is a clinical-stage deuterium-stabilized (R)-enantiomer of pioglitazone which lacks PPAR γ agonism but retains MPC activity. Here, we show that incubation of ALD patient-derived cells (both AMN and C-ALD) and glial cells from *Abcd1*-null mice with PXL065 resulted in: normalization of elevated VLCFA, improved mitochondrial function, and attenuated indices of inflammation. Compensatory peroxisomal transporter gene expression was also induced. Additionally, chronic treatment of *Abcd1*-null mice lowered VLCFA in plasma, brain and spinal cord and improved both neural histology (sciatic nerve) and neurobehavioral test performance. Several *in vivo* effects of PXL065 exceeded those achieved with pioglitazone. PXL065 was confirmed to lack PPAR γ agonism but retained ACSL4 activity of pioglitazone. PXL065 has novel actions and mechanisms and exhibits a range of potential benefits in ALD models; further testing of this molecule in ALD patients is warranted.

Neurology

Park BY, Larivière S, Rodríguez-Cruces R, Royer J, Tavakol S, Wang Y, Caciagli L, Caligiuri ME, Gambardella A, Concha L, Keller SS, Cendes F, Alvim MKM, Yasuda C, Bonilha L, Gleichgerrcht E, Focke NK, Kreilkamp BAK, Domin M, von Podewils F, Langner S, Rummel C, Rebsamen M, Wiest R, Martin P, Kotikalapudi R, Bender B, O'Brien TJ, Law M, Sinclair B, Vivash L, Kwan P, Desmond PM, Malpas CB, Lui E, Alhusaini S, Doherty CP, Cavalleri GL, Delanty N, Kälviäinen R, Jackson GD, Kowalczyk M, Mascalchi M, Semmelroch M, Thomas RH, **Soltanian-Zadeh H, Davoodi-Bojd E**, Zhang J, Lenge M, Guerrini R, Bartolini E, Hamandi K, Foley S, Weber B, Depondt C, Absil J, Carr SJA, Abela E, Richardson MP, Devinsky O, Severino M, Striano P, Parodi C, Tortora D, Hatton SN, Vos SB, Duncan JS, Galovic M, Whelan CD, Bargalló N, Pariente J, Conde-Blanco E, Vaudano AE, Tondelli M, Meletti S, Kong XZ, Francks C, Fisher SE, Caldairou B, Ryten M, Labate A, Sisodiya SM, Thompson PM, McDonald CR, Bernasconi A, Bernasconi N, and Bernhardt BC. Topographic divergence of atypical cortical asymmetry and atrophy patterns in temporal lobe epilepsy. *Brain* 2022; 145(4):1285-1298. PMID: 35333312. [Full Text](#)

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Temporal lobe epilepsy, a common drug-resistant epilepsy in adults, is primarily a limbic network disorder associated with predominant unilateral hippocampal pathology. Structural MRI has provided an *in vivo* window into whole-brain grey matter structural alterations in temporal lobe epilepsy relative to controls, by either mapping (i) atypical inter-hemispheric asymmetry; or (ii) regional atrophy. However, similarities and differences of both atypical asymmetry and regional atrophy measures have not been systematically investigated. Here, we addressed this gap using the multisite ENIGMA-Epilepsy dataset comprising MRI brain morphological measures in 732 temporal lobe epilepsy patients and 1418 healthy controls. We compared spatial distributions of grey matter asymmetry and atrophy in temporal lobe epilepsy, contextualized their topographies relative to spatial gradients in cortical microstructure and functional connectivity calculated using 207 healthy controls obtained from Human Connectome Project and an independent dataset containing 23 temporal lobe epilepsy patients and 53 healthy controls and examined clinical associations using machine learning. We identified a marked divergence in the spatial distribution of atypical inter-hemispheric asymmetry and regional atrophy mapping. The former revealed a temporo-limbic disease signature while the latter showed diffuse and bilateral patterns. Our findings were robust across individual sites and patients. Cortical atrophy was significantly correlated with disease duration and age at seizure onset, while degrees of asymmetry did not show a significant relationship to these clinical variables. Our findings highlight that the mapping of atypical inter-hemispheric asymmetry and regional atrophy tap into two complementary aspects of temporal lobe epilepsy-related pathology, with the former revealing primary substrates in ipsilateral limbic circuits and the latter capturing bilateral disease effects. These findings refine our notion of the neuropathology of temporal lobe epilepsy and may inform future discovery and validation of complementary MRI biomarkers in temporal lobe epilepsy.

Neurosurgery

Kabir MH, Marquez E, Djokoto G, Parker M, Weinstein T, Ghann W, Uddin J, **Ali MM**, Alam MM, Thompson M, Poyraz AS, Msimanga HZ, Rahman MM, Rulison M, and Cramer J. Energy Harvesting by Mesoporous Reduced Graphene Oxide Enhanced the Mediator-Free Glucose-Powered Enzymatic Biofuel Cell for Biomedical Applications. *ACS Appl Mater Interfaces* 2022; 14(21):24229-24244. PMID: 35594363. [Full Text](#)

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Harnessing electrochemical energy in an engineered electrical circuit from biochemical substrates in the human body using biofuel cells is gaining increasing research attention in the current decade due to the wide range of biomedical possibilities it creates for electronic devices. In this report, we describe and characterize the construction of just such an enzymatic biofuel cell (EBFC). It is simple, mediator-free, and glucose-powered, employing only biocompatible materials. A novel feature is the two-dimensional mesoporous thermally reduced graphene oxide (rGO) host electrode. An additional novelty is that we explored the potential of using biocompatible, low-cost filter paper (FP) instead of carbon paper, a conductive polymer, or gold as support for the host electrode. Using glucose (C(6)H(12)O(6)) and molecular oxygen (O(2)) as the power-generating fuel, the cell consists of a pair of bioelectrodes incorporating immobilized enzymes, the bioanode modified by rGO-glucose oxidase (GOx/rGO), and the biocathode modified by rGO-laccase (Lac/rGO). Scanning electron microscopy/energy-dispersive X-ray spectroscopy (SEM/EDX), transmission electron microscopy, and Raman spectroscopy techniques have been employed to investigate the surface morphology, defects, and chemical structure of rGO, GOx/rGO, and Lac/rGO. N(2) sorption, SEM/EDX, and powder X-ray diffraction revealed a high Brunauer-Emmett-Teller surface area (179 m(2) g(-1)) mesoporous rGO structure with the high C/O ratio of 80:1 as well. Results from the Fourier transform infrared spectroscopy, UV-visible spectroscopy, and electrochemical impedance spectroscopy studies indicated that GOx remained in its native biochemical functional form upon being embedded onto the rGO matrix. Cyclic voltammetry studies showed that the presence of mesoporous rGO greatly enhanced the direct electrochemistry and electrocatalytic properties of the GOx/rGO and Lac/rGO nanocomposites. The electron transfer rate constant between GOx and rGO was estimated to be 2.14 s(-1). The fabricated EBFC (GOx/rGO/FP-Lac/rGO/FP) using a single GOx/rGO/FP bioanode and a single Lac/rGO/FP biocathode provides a maximum power density (P(max)) of 4.0 nW cm(-2) with an open-circuit voltage (V(OC)) of 0.04 V and remains stable for more than 15 days with a power output of ~9.0 nW cm(-2) at a pH of 7.4 under ambient conditions.

Neurosurgery

Lim S, Bazydlo M, Macki M, Haider S, Hamilton T, Hunt R, Chaker A, Kantak P, Schultz L, Nerenz D, Schwalb JM, Abdulhak M, Park P, Aleem I, Easton R, Khalil JG, Perez-Cruet MJ, and **Chang V.**

Validation of the Benefits of Ambulation Within 8 Hours of Elective Cervical and Lumbar Surgery: A Michigan Spine Surgery Improvement Collaborative Study. *Neurosurgery* 2022; Epub ahead of print. PMID: 35550477. [Full Text](#)

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BACKGROUND: Early ambulation is considered a key element to Enhanced Recovery After Surgery protocol after spine surgery. **OBJECTIVE:** To investigate whether ambulation less than 8 hours after elective spine surgery is associated with improved outcome. **METHODS:** The Michigan Spine Surgery Improvement Collaborative database was queried to track all elective cervical and lumbar spine surgery between July 2018 and April 2021. In total, 7647 cervical and 17 616 lumbar cases were divided into 3 cohorts based on time to ambulate after surgery: (1) <8 hours, (2) 8 to 24 hours, and (3) >24 hours. **RESULTS:** For cervical cases, patients who ambulated 8 to 24 hours (adjusted odds ratio [aOR] 1.38;

95% CI 1.11-1.70; P = .003) and >24 hours (aOR 2.20; 95% CI 1.20-4.03; P = .011) after surgery had higher complication rate than those who ambulated within 8 hours of surgery. Similar findings were noted for lumbar cases with patients who ambulated 8 to 24 hours (aOR 1.31; 95% CI 1.12-1.54; P < .001) and >24 hours (aOR 1.96; 95% CI 1.50-2.56; P < .001) after surgery having significantly higher complication rate than those ambulated <8 hours after surgery. Analysis of secondary outcomes for cervical cases demonstrated that <8-hour ambulation was associated with home discharge, shorter hospital stay, lower 90-day readmission, and lower urinary retention rate. For lumbar cases, <8-hour ambulation was associated with shorter hospital stay, satisfaction with surgery, lower 30-day readmission, home discharge, and lower urinary retention rate. **CONCLUSION:** Ambulation within 8 hours after surgery is associated with significant improved outcome after elective cervical and lumbar spine surgery.

Neurosurgery

Monternier PA, **Singh J, Parasar P**, Theurey P, DeWitt S, Jacques V, Klett E, **Kaur N, Nagaraja TN**, Moller DE, and Hallakou-Bozec S. Therapeutic potential of deuterium-stabilized (R)-pioglitazone-PXL065 for X-linked adrenoleukodystrophy. *J Inherit Metab Dis* 2022; Epub ahead of print. PMID: 35510808. [Full Text](#)

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X-linked adrenoleukodystrophy (ALD) results from ABCD1 gene mutations which impair Very Long Chain Fatty Acids (VLCFA; C26:0 and C24:0) peroxisomal import and β -oxidation, leading to accumulation in plasma and tissues. Excess VLCFA drives impaired cellular functions (e.g. disrupted mitochondrial function), inflammation, and neurodegeneration. Major disease phenotypes include: adrenomyeloneuropathy (AMN), progressive spinal cord axonal degeneration, and cerebral ALD (C-ALD), inflammatory white matter demyelination and degeneration. No pharmacological treatment is available to-date for ALD. Pioglitazone, an anti-diabetic thiazolidinedione, exerts potential benefits in ALD models. Its mechanisms are genomic (PPAR γ agonism) and nongenomic (mitochondrial pyruvate carrier-MPC, long-chain acyl-CoA synthetase 4-ACSL4, inhibition). However, its use is limited by PPAR γ -driven side effects (e.g. weight gain, edema). PXL065 is a clinical-stage deuterium-stabilized (R)-enantiomer of pioglitazone which lacks PPAR γ agonism but retains MPC activity. Here, we show that incubation of ALD patient-derived cells (both AMN and C-ALD) and glial cells from *Abcd1*-null mice with PXL065 resulted in: normalization of elevated VLCFA, improved mitochondrial function, and attenuated indices of inflammation. Compensatory peroxisomal transporter gene expression was also induced. Additionally, chronic treatment of *Abcd1*-null mice lowered VLCFA in plasma, brain and spinal cord and improved both neural histology (sciatic nerve) and neurobehavioral test performance. Several in vivo effects of PXL065 exceeded those achieved with pioglitazone. PXL065 was confirmed to lack PPAR γ agonism but retained ACSL4 activity of pioglitazone. PXL065 has novel actions and mechanisms and exhibits a range of potential benefits in ALD models; further testing of this molecule in ALD patients is warranted.

Obstetrics, Gynecology and Women's Health Services

Vadlamudi GD, Keerthy M, and Goyert G. Postpartum bilateral lung transplantation in COVID-19 associated respiratory failure. *BMJ Case Rep* 2022; 15(5). PMID: 35580959. [Full Text](#)

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In critically ill patients with COVID-19, established therapies in the setting of respiratory failure include invasive mechanical ventilation and extracorporeal membrane oxygenation (ECMO). This case report describes a pregnant woman in her 30s who was hospitalised at 35 weeks gestation with moderate

COVID-19 disease. Her condition worsened following delivery, and she required intubation, maximum ventilatory support and ECMO. Because of the severe and irreversible nature of her lung disease, she ultimately underwent bilateral lung transplantation. This case showcases lung transplantation as an alternative life-saving option for patients with severe COVID-19 associated respiratory failure refractory to ECMO and mechanical ventilation. Further studies are needed to develop a multidisciplinary approach for patient selection for transplantation within the context of COVID-19 and to assess long-term outcomes.

Ophthalmology and Eye Care Services

Patel N, Alabiad CR, Wick MR, Elgart GW, Tang VD, Abou Khzam RA, and Dubovy SR. Squamoid Eccrine Ductal Carcinoma of the Eyelid: Clinicopathologic Correlation of a Case. *Ophthalmic Plast Reconstr Surg* 2022; 38(3):e80-e82. PMID: 35561118. [Full Text](#)

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Squamoid eccrine ductal carcinoma (SEDC) is a rare cutaneous neoplasm that often manifests as a plaque or nodule in sun-exposed areas of older patients. Herein, the authors report the first case of SEDC in the eyelid. A 76-year-old man presented with a 2.5 × 1.5 mm area of left upper eyelid erythema, thickening, ulceration, and scaling with madarosis superotemporally just above the lash line. Full-thickness wedge biopsy demonstrated irregular epithelial tubules with nuclear atypia and focal squamous differentiation, consistent with SEDC. The patient underwent Mohs resection and has had no recurrence approximately 27 months after surgical removal. The authors present this case to raise awareness of SEDC to ophthalmologists as all previous cases have been described in the nonophthalmic literature. A full-thickness biopsy is recommended to avoid misdiagnosing SEDC as squamous cell carcinoma (SCC), a less aggressive tumor. With greater awareness, there may be increased recognition of this likely underreported, more malignant entity.

Orthopedics/Bone and Joint Center

Aliaj K, **Lawrence RL**, Bo Foreman K, Chalmers PN, and Henninger HB. Kinematic coupling of the glenohumeral and scapulothoracic joints generates humeral axial rotation. *J Biomech* 2022; 136:111059. PMID: 35367838. [Full Text](#)

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Glenohumeral and scapulothoracic motion combine to generate humerothoracic motion, but their discrete contributions towards humerothoracic axial rotation have not been investigated. Understanding their contributions to axial rotation is important to judge the effects of pathology, surgical intervention, and physiotherapy. Therefore, the purpose of this study was to investigate the kinematic coupling between glenohumeral and scapulothoracic motion and determine their relative contributions towards axial rotation. Twenty healthy subjects (10 M/10F, ages 22-66) were previously recorded using biplane

fluoroscopy while performing arm elevation in the coronal, scapular, and sagittal planes, and external rotation in 0° and 90° of abduction. Glenohumeral and scapulothoracic contributions towards axial rotation were computed by integrating the projection of glenohumeral and scapulothoracic angular velocity onto the humeral longitudinal axis, and analyzed using one dimensional statistical parametric mapping and linear regression. During arm elevation, scapulothoracic motion supplied 13-20° (76-94%) of axial rotation, mainly via scapulothoracic upward rotation. The contribution of scapulothoracic motion towards axial rotation was strongly correlated with glenohumeral plane of elevation during arm elevation. During external rotation, scapulothoracic motion contributed 10° (8%) towards axial rotation in 0° of abduction and 15° (15%) in 90° of abduction. The contribution of scapulothoracic motion towards humerothoracic axial rotation could explain the simultaneous changes in glenohumeral plane of elevation and axial rotation associated with some pathologies and surgeries. Understanding how humerothoracic motion results from the functional coupling of scapulothoracic and glenohumeral motions may inform diagnostic and treatment strategies by targeting the source of movement impairments in clinical populations.

Orthopedics/Bone and Joint Center

Gaudiani MA, Samuel LT, Diana JN, DeBattista JL, Coon TM, Moore RE, and Kamath AF. 5-Year Survivorship and Outcomes of Robotic-Arm-Assisted Medial Unicompartmental Knee Arthroplasty. *Appl Bionics Biomech* 2022; 2022:8995358. PMID: 35572062. [Full Text](#)

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PURPOSE: While unicompartmental knee arthroplasty (UKA) has demonstrated benefits over total knee arthroplasty (TKA) in selected populations, component placement continues to be challenging with conventional surgical instruments, resulting in higher early failure rates. Robotic-arm-assisted UKA (RA-UKA) has shown to be successful in component positioning through preop planning and intraop adjustability. The purpose of this study is to assess the 5-year clinical outcomes of medial RA-UKA.

METHODS: This study was a retrospective review of a single-center prospectively maintained cohort of 133 patients (146 knees) indicated for medial UKA from 2009 to 2013. Perioperative data and 2- and 5-year Knee injury Osteoarthritis Outcome Score (KOOS), Western Ontario and McMaster Universities Osteoarthritis Score (WOMAC), and Forgotten Joint Score (FJS) outcome measures were collected. Five-year follow-up was recorded in 119 patients (131 knees). **RESULTS:** Mean follow-up was 5.1 ± 0.2 years. Mean age and BMI were 68.0 ± 8.1 years and 29.3 ± 4.7 kg/m², respectively. At 2-year follow-up, mean KOOS, WOMAC, and FJS were 71.5 ± 15.3, 14.3 ± 7.9, and 79.1 ± 25.8, respectively. At 5-year follow-up, mean KOOS, WOMAC, and FJS were 71.6 ± 15.2, 14.2 ± 7.9, and 80.9 ± 25.1, respectively. Mean change in KOOS and WOMAC was 34.6 ± 21.4 and 11.0 ± 13.6, respectively (p < 0.001 and p < 0.001). For patient satisfaction at last follow-up, 89% of patients were very satisfied/satisfied and 5% were dissatisfied. For patient activity expectations at last follow-up, 85% met activity expectations, 52% were more active than before, 25% have the same level of activity, 23% were less active than before, and 89% were walking without support. All patients returned to driving after surgery at a mean 15.2 ± 9.4 days. Survivorship was 95% (95% CI 0.91-0.98) at 5 years. One knee (1%) had a patellofemoral revision, two knees (1.3%) were revised to different partial knee replacements, and five knees (3.4%) were converted to TKA. **CONCLUSION:** Overall, medial RA-UKA demonstrated improved patient-recorded outcomes, high patient satisfaction, met expectations, and excellent functional recovery. Midterm survivorship was excellent. Longitudinal follow-up is needed to evaluate long-term outcomes of robotic-arm-assisted UKA procedures.

Orthopedics/Bone and Joint Center

Soliman SB, Davis JJ, Muh SJ, Vohra ST, Patel A, and van Holsbeek MT. Ultrasound evaluations and guided procedures of the painful joint arthroplasty. *Skeletal Radiol* 2022; Epub ahead of print. PMID: 35624311. [Full Text](#)

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The purpose of this article is to describe the use of ultrasound for the diagnosis and treatment of painful joint arthroplasty. Ultrasound plays a crucial role in the diagnosis of the painful joint arthroplasty, especially given its unique dynamic capabilities, convenience, and high resolution. Ultrasound guidance is also instrumental for procedures in both diagnosing and in select cases, treating the painful joint arthroplasty. Topics to be discussed in this article include trends in arthroplasty placement, benefits of the use of ultrasound overall, and ultrasound evaluation of periprosthetic joint infections. We will also review the sonographic findings with dissociated/displaced components and adverse reaction to metallic debris including metallosis, trunnionosis, and metal-on-metal pseudotumors. Additionally, we will discuss ultrasound evaluation of tendon pathologies with arthroplasties, including dynamic maneuvers to evaluate for tendon impingement/snapping. Finally, we will cover ultrasound-guided joint arthroplasty injection indications and precautions. **KEY POINTS:** • Ultrasound is preferred over MRI in patients with joint arthroplasty and plays a crucial role in diagnosis, especially given its unique dynamic capabilities, convenience and high resolution. • It is especially beneficial for US-guided aspiration in periprosthetic joint infections; effectively used to evaluate periprosthetic fluid collections, facilitating differentiation between abscesses and aseptic collections, and tracking sinus tracts. • Recently, the diagnosis of periprosthetic joint infections has shifted focus to biomarkers in the periprosthetic fluid, specifically α -defensin, which has a high sensitivity and specificity for diagnosing infection. • *Cutibacterium acnes* is a major pathogen responsible for shoulder arthroplasty infections, often presenting with normal laboratory values and since slow growing, must be kept for a minimum of 14 days.

Otolaryngology – Head and Neck Surgery

Marget MJ, Dunn R, and Morgan CL. Association of APACHE-II Scores With 30-Day Mortality After Tracheostomy: A Retrospective Study. *Laryngoscope* 2022; Epub ahead of print. PMID: 35548918. [Full Text](#)

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OBJECTIVE: The objective of this study was to assess whether the Acute Physiology, Age, Chronic Health Evaluation II (APACHE-II) score is a reliable predictor of 30-day mortality in the setting of adult patients with ventilator-dependent respiratory failure (VDRF) who undergo tracheostomy. **METHODS:** This is a retrospective, single-institution study. Potential subjects were identified using the current procedural terminology codes for the tracheostomy procedure and International Classification of Diseases, 10th Revision, codes for VDRF. APACHE-II scores were retrospectively calculated. Tracheostomies were performed in our population over an 18-month period (November 2018 through April 2020). Our study population did not include patients with novel coronavirus. The primary outcome was mortality at 30 days after tracheostomy. **RESULTS:** A total of 238 patients with VDRF who had a tracheostomy were included in this study. Twenty-eight (11.8%) patients died within 30 days of tracheostomy. The mean (standard deviation) APACHE-II score was 22.5 (10.2) for patients who died within 30 days of tracheostomy and 19.8 (7.4) for patients living within 30 days of tracheostomy ($p = 0.30$). Patients with APACHE-II scores greater than or equal to 30 showed higher odds of death within 30 days of tracheostomy (odds ratio, 3.0; 95% CI, 1.14-7.89, $p = 0.03$). **CONCLUSION:** An APACHE-II score of 30 and above is associated with mortality within 30 days of tracheostomy in patients with VDRF. APACHE-II scores may be a promising tool for assessing risk of mortality in patients with VDRF after tracheostomy. **LEVEL OF EVIDENCE:** 3 *Laryngoscope*, 2022.

Pathology and Laboratory Medicine

Hengy M, Veenstra J, **Perry K**, Ozog DM, and **Friedman BJ.** ETS-related Gene (ERG) is Differentially Expressed in Dermatofibroma (Fibrous Histiocytoma) as Compared With Dermatofibrosarcoma Protuberans and Hypertrophic Scars: A Pilot Immunohistochemical Study. *Appl Immunohistochem Mol Morphol* 2022; Epub ahead of print. PMID: 35510745. [Full Text](#)

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Immunohistochemical staining can be of great utility in differentiating various cutaneous spindle cell neoplasms, particularly when the histomorphologic appearance of the lesions is inconclusive. Nuclear staining for ETS-related gene (ERG), a highly sensitive endothelial cell marker, has seldom been studied in the context of cutaneous spindle cell neoplasms. Little is known about its specificity for vascular differentiation. In this pilot study, immunohistochemical analysis for ERG was performed on 15 dermatofibromas (DF), 10 keloids, and 9 dermatofibrosarcoma protuberans (DFSP) tumors. Consistent nuclear expression of ERG was found in DF [100% (15/15) of the lesions demonstrated >50% labeling of tumor cells with moderate to strong intensity]. However, ERG expression was largely absent in DFSP [89% (8/9) of the lesions demonstrating <50% labeling staining, generally of mild intensity] and hypertrophic scars-keloids [80% (8/10) without expression]. On the basis of the results of this pilot study, immunohistochemical staining for ERG may prove useful in helping to differentiate DF from DFSP and hypertrophic scars in the context of partial biopsy sampling. If replicated in a larger number of samples, this finding could mitigate the use of costly sequencing panels and potentially avoid unnecessary reexcisions in certain contexts.

Pathology and Laboratory Medicine

Suleyman G, Fadel R, Brar I, Kassab R, Khansa R, Sturla N, Alsaadi A, Latack K, Miller J, Tibbetts R, Samuel L, Alangaden G, and Ramesh M. Risk Factors Associated With Hospitalization and Death in COVID-19 Breakthrough Infections. *Open Forum Infect Dis* 2022; 9(5):ofac116. PMID: 35437511. [Full Text](#)

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BACKGROUND: Characterizations of coronavirus disease 2019 (COVID-19) vaccine breakthrough infections are limited. We aim to characterize breakthrough infections and identify risk factors associated with outcomes. **METHODS:** This was a retrospective case series of consecutive fully vaccinated patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a multicenter academic center in Southeast Michigan, between December 30, 2020, and September 15, 2021. **RESULTS:** A total of 982 patients were identified; the mean age was 57.9 years, 565 (59%) were female, 774 (79%) were White, and 255 (26%) were health care workers (HCWs). The median number of comorbidities was 2; 225 (23%) were immunocompromised. BNT162b2 was administered to 737 (75%) individuals. The mean time to SARS-CoV-2 detection was 135 days. The majority were asymptomatic or exhibited mild to moderate disease, 154 (16%) required hospitalization, 127 (13%) had severe-critical illness, and 19 (2%) died. Age (odds ratio [OR], 1.14; 95% CI, 1.04-1.07; $P < .001$), cardiovascular disease (OR, 3.02; 95% CI, 1.55-5.89; $P = .001$), and immunocompromised status (OR, 2.57; 95% CI, 1.70-3.90; $P < .001$) were independent risk factors for hospitalization. Additionally, age (OR, 1.06; 95% CI, 1.02-1.11; $P = .006$) was significantly associated with mortality. HCWs (OR, 0.15; 95% CI, 0.05-0.50; $P = .002$) were less likely to be hospitalized, and prior receipt of BNT162b2 was associated with lower odds of hospitalization (OR, 0.436; 95% CI, 0.303-0.626; $P < .001$) and/or death (OR, 0.360; 95% CI, 0.145-0.898; $P = .029$). **CONCLUSIONS:** COVID-19 vaccines remain effective at attenuating disease severity. However, patients with breakthrough infections necessitating hospitalization may benefit from early treatment modalities and COVID-19-mitigating strategies, especially in areas with substantial or high transmission rates.

Pathology and Laboratory Medicine

Tibbetts R, George S, Burwell R, Rajeev L, Rhodes PA, Singh P, and **Samuel L**. Performance of the Reveal Rapid Antibiotic Susceptibility Testing System on Gram-Negative Blood Cultures at a Large Urban Hospital. *J Clin Microbiol* 2022:e0009822; Epub ahead of print. PMID: 35607972. [Full Text](#)

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Timely and effective antibiotic treatment is vital for sepsis, with increasing incidence of antimicrobial-resistant bacteremia driving interest in rapid phenotypic susceptibility testing. To enable the widespread adoption needed to make an impact, antibiotic susceptibility testing (AST) systems need to be accurate, enable rapid intervention, have a broad antimicrobial menu and be easy to use and affordable. We evaluated the Specific Reveal (Specific Diagnostics, San Jose, CA) rapid AST system on positive blood cultures with Gram-negative organisms in a relatively resistant population in a large urban hospital to assess its potential for routine clinical use. One hundred four randomly selected positive blood cultures (Virtuo; bioMérieux) were Gram stained, diluted 1:1,000 in Pluronic water, inoculated into 96-well antibiotic plates, sealed with the Reveal sensor panel, and placed in the Reveal instrument for incubation and reading. The MIC and susceptible/intermediate/resistant category was determined and compared to results from Vitek 2 (bioMérieux) for the 17 antimicrobials available and to Sensititre (Thermo Fisher) for 24 antimicrobials. Performance was also assessed with contrived blood cultures with 33 highly resistant strains. Reveal was in 98.0% essential agreement (EA) and 96.3% categorical agreement (CA) with Sensititre, with just 1.3% very major error (VME) and 97.0%/96.2%/1.3% EA/CA/VME versus Vitek 2. Reveal results for contrived highly resistant strains were equivalent, with EA/CA/VME of 97.7%/95.2%/1.0% with CDC/FDA Antibiotic Resistance Isolate Bank references. Average time to result (TTR) for Reveal was 4.6 h. Sample preparation was relatively low skill and averaged 3 min. We conclude that the Reveal system enables accurate and rapid susceptibility testing of Gram-negative blood cultures.

Pharmacy

Mercuro NJ, Medler CJ, Kenney RM, MacDonald NC, Neuhauser MM, Hicks LA, Srinivasan A, **Divine G, Beaulac A, Eriksson E, Kendall R, Martinez M, Weinmann A, Zervos M**, and **Davis SL**.

Pharmacist-Driven Transitions of Care Practice Model for Prescribing Oral Antimicrobials at Hospital Discharge. *JAMA Netw Open* 2022; 5(5):e2211331. PMID: 35536577. [Full Text](#)

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IMPORTANCE: Although prescribers face numerous patient-centered challenges during transitions of care (TOC) at hospital discharge, prolonged duration of antimicrobial therapy for common infections remains problematic, and resources are needed for antimicrobial stewardship throughout this period.

OBJECTIVE: To evaluate a pharmacist-driven intervention designed to improve selection and duration of oral antimicrobial therapy prescribed at hospital discharge for common infections.

DESIGN, SETTING, AND PARTICIPANTS: This quality improvement study used a nonrandomized stepped-wedge design with 3 study phases from September 1, 2018, to August 31, 2019. Seventeen distinct medicine, surgery, and specialty units from a health system in Southeast Michigan participated, including 1 academic tertiary hospital and 4 community hospitals. Hospitalized adults who had urinary, respiratory, skin and/or soft tissue, and intra-abdominal infections and were prescribed antimicrobials at discharge were included in the analysis. Data were analyzed from February 18, 2020, to February 28, 2022. **INTERVENTIONS:** Clinical pharmacists engaged in a new standard of care for antimicrobial stewardship practices during TOC by identifying patients to be discharged with a prescription for oral antimicrobials and collaborating with primary teams to prescribe optimal therapy. Academic and community hospitals used both antimicrobial stewardship and clinical pharmacists in a multidisciplinary rounding model to discuss,

document, and facilitate order entry of the antimicrobial prescription at discharge. **MAIN OUTCOMES AND MEASURES:** The primary end point was frequency of optimized antimicrobial prescription at discharge. Health system guidelines developed from national guidelines and best practices for short-course therapies were used to evaluate optimal therapy. **RESULTS:** A total of 800 patients prescribed oral antimicrobials at hospital discharge were included in the analysis (441 women [55.1%]; mean [SD] age, 66.8 [17.3] years): 400 in the preintervention period and 400 in the postintervention period. The most common diagnoses were pneumonia (264 [33.0%]), upper respiratory tract infection and/or acute exacerbation of chronic obstructive pulmonary disease (214 [26.8%]), and urinary tract infection (203 [25.4%]). Patients in the postintervention group were more likely to have an optimal antimicrobial prescription (time-adjusted generalized estimating equation odds ratio, 5.63 [95% CI, 3.69-8.60]). The absolute increase in optimal prescribing in the postintervention group was consistent in both academic (37.4% [95% CI, 27.5%-46.7%]) and community (43.2% [95% CI, 32.4%-52.8%]) TOC models. There were no differences in clinical resolution or mortality. Fewer severe antimicrobial-related adverse effects (time-adjusted generalized estimating equation odds ratio, 0.40 [95% CI, 0.18-0.88]) were identified in the postintervention (13 [3.2%]) compared with the preintervention (36 [9.0%]) groups. **CONCLUSIONS AND RELEVANCE:** The findings of this quality improvement study suggest that targeted antimicrobial stewardship interventions during TOC were associated with increased optimal, guideline-concordant antimicrobial prescriptions at discharge.

Pharmacy

Rebold N, Alosaimy S, Morrisette T, Holger D, Lagnf AM, Ansari I, Belza AC, Cheaney L, Hussain H, **Herbin SR**, Abdul-Mutakabbir J, Carron C, Sandhu A, Chopra T, and Rybak MJ. Clinical Characteristics Associated with Bacterial Bloodstream Coinfection in COVID-19. *Infect Dis Ther* 2022; 11(3):1281-1296. PMID: 35538335. [Full Text](#)

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INTRODUCTION: Inappropriate antibiotic use in COVID-19 is often due to treatment of presumed bacterial coinfection. Predictive factors to distinguish COVID-19 from COVID-19 with bacterial coinfection or bloodstream infection are limited. **METHODS:** We conducted a retrospective cohort study of 595 COVID-19 patients admitted between March 8, 2020, and April 4, 2020, to describe factors associated with a bacterial bloodstream coinfection (BSI). The primary outcome was any characteristic associated with BSI in COVID-19, with secondary outcomes including 30-day mortality and days of antibiotic therapy

(DOT) by antibiotic consumption (DOT/1000 patient-days). Variables of interest were compared between true BSI (n = 25) and all other COVID-19 cases (n = 570). A secondary comparison was performed between positive blood cultures with true BSI (n = 25) and contaminants (n = 33) on antibiotic use. RESULTS: Fever (> 38 °C) (as a COVID-19 symptom) was not different between true BSI (n = 25) and all other COVID-19 patients (n = 570) (p = 0.93), although it was different as a reason for emergency department (ED) admission (p = 0.01). Neurological symptoms (ED reason or COVID-19 symptom) were significantly higher in the true BSI group (p < 0.01, p < 0.01) and were independently associated with true BSI (ED reason: OR = 3.27, p < 0.01; COVID-19 symptom: OR = 2.69, p = 0.03) on multivariate logistic regression. High (15-19.9 × 10⁹/L) white blood cell (WBC) count at admission was also higher in the true BSI group (p < 0.01) and was independently associated with true BSI (OR = 2.56, p = 0.06) though was not statistically significant. Thirty-day mortality was higher among true BSI (p < 0.01). Antibiotic consumption (DOT/1000 patient-days) between true BSI and contaminants was not different (p = 0.34). True bloodstream coinfection was 4.2% (25/595) over the 28-day period. CONCLUSION: True BSI in COVID-19 was associated with neurological symptoms and nonsignificant higher WBC, and led to overall higher 30-day mortality and worse patient outcomes.

Public Health Sciences

Culmone L, Powell B, Landschoot-Ward J, Zacharek A, Gao H, Findeis EL, Malik A, Lu M, Chopp M, and Venkat P. Treatment With an Angiopoietin-1 Mimetic Peptide Improves Cognitive Outcome in Rats With Vascular Dementia. *Front Cell Neurosci* 2022; 16:869710. PMID: 35602559. [Full Text](#)

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BACKGROUND AND PURPOSE: Vascular dementia (VaD) is a complex neurodegenerative disease affecting cognition and memory. There is a lack of approved pharmacological treatments specifically for VaD. In this study, we investigate the therapeutic effects of AV-001, a Tie2 receptor agonist, in middle-aged rats subjected to a multiple microinfarct (MMI) model of VaD. **METHODS:** Male, 10-12 month-old, Wistar rats were employed. The following experimental groups were used: Sham, MMI, MMI+1 µg/Kg AV-001, MMI+3 µg/Kg AV-001, MMI+6 µg/Kg AV-001. AV-001 treatment was initiated at 1 day after MMI and administered once daily via intraperitoneal injection. An investigator blinded to the experimental groups conducted a battery of neuro-cognitive tests including modified neurological severity score (mNSS) test, novel object recognition test, novel odor recognition test, three chamber social interaction test, and Morris water maze test. Rats were sacrificed at 6 weeks after MMI. **RESULTS:** There was no mortality observed after 1, 3, or 6 µg/Kg AV-001 treatment in middle-aged rats subjected to MMI. AV-001 treatment (1, 3, or 6 µg/Kg) does not significantly alter blood pressure or heart rate at 6 weeks after MMI compared to baseline values or the MMI control group. Treatment of MMI with 1 or 3 µg/Kg AV-001 treatment does not significantly alter body weight compared to Sham or MMI control group. While 6 µg/Kg AV-001 treated group exhibit significantly lower body weight compared to Sham and MMI control group, the weight loss is evident starting at 1 day after MMI when treatment was initiated and is not significantly different compared to its baseline values at day 0 or day 1 after MMI. AV-001 treatment significantly decreases serum alanine aminotransferase, serum creatinine, and serum troponin I levels compared to the MMI control group; however, all values are within normal range. MMI induces mild neurological deficits in middle-aged rats indicated by low mNSS scores (<6 on a scale of 0-18). Compared to control MMI group, 1 µg/Kg AV-001 treatment group did not exhibit significantly different mNSS scores, while 3 and 6 µg/Kg AV-001 treatment induced significantly worse mNSS scores on days 21-42 and 14-42 after MMI, respectively. MMI in middle-aged rats induces significant cognitive impairment including short-term memory loss, long-term memory loss, reduced preference for social novelty and impaired spatial learning and memory compared to sham control rats. Rats treated with 1 µg/Kg AV-001 exhibit significantly improved short-term and long-term memory, increased preference for social novelty, and improved spatial learning and memory compared to MMI rats. Treatment with 3 µg/Kg AV-001 improves short-term memory and preference for social novelty but does not improve long-term memory or spatial learning and memory compared to MMI rats. Treatment with 6 µg/Kg AV-001 improves only long-term memory compared to MMI rats. Thus, 1 µg/Kg AV-001 treatment was selected as an optimal dose. Treatment of middle-aged rats subjected to MMI with 1 µg/Kg AV-001 significantly increases axon density, myelin density and

myelin thickness in the corpus callosum, as well as increases synaptic protein expression, neuronal branching and dendritic spine density in the cortex, oligodendrocytes and oligodendrocyte progenitor cell number in the cortex and striatum and promotes neurogenesis in the subventricular zone compared to control MMI rats. **CONCLUSIONS:** In this study, we present AV-001 as a novel therapeutic agent to improve cognitive function and reduce white matter injury in middle aged-rats subjected to a MMI model of VaD. Treatment of MMI with 1 µg/Kg AV-001 significantly improves cognitive function, and increases axon density, remyelination and neuroplasticity in the brain of middle-aged rats.

Public Health Sciences

Gorgis S, Mawri S, Dabbagh MF, Aurora L, Ali M, Mitchell G, Jacobsen G, Hegab S, Schwartz S, Kelly B, Grafton G, Awdish R, Ismail R, and Koenig G. Ultrasound-assisted catheter-directed thrombolysis versus anticoagulation alone for management of submassive pulmonary embolism. *J Cardiol* 2022; Epub ahead of print. PMID: 35643741. [Full Text](#)

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BACKGROUND: Patients with submassive pulmonary embolism (PE) are vulnerable to sudden deterioration, recurrent PE, and progression to pulmonary hypertension and chronic right ventricular (RV) dysfunction. Previous studies have suggested a clinical benefit of using ultrasound-assisted catheter-directed thrombolysis (USCDT) to invasively manage patients with submassive PE. However, there is sparse data comparing the clinical outcomes of these patients when treated with USCDT versus anticoagulation (AC) alone. We sought to compare the outcomes of USCDT versus AC alone in the management of submassive PE. **METHODS:** 192 consecutive patients who underwent USCDT for submassive PE between January 2013 and February 2019 were identified. ICD9/ICD10 codes were used to detect 2554 patients diagnosed with PE who did not undergo thrombolysis. Propensity matching identified 192 patients with acute PE treated with AC alone. Clinical outcomes were compared between the two groups. Baseline demographics, laboratory values, and pulmonary embolism severity index scores were similar between the two cohorts. **RESULTS:** There was a significant reduction in mean systolic pulmonary artery pressure (sPAP) in the USCDT group compared to the AC group ($\Delta 11$ vs $\Delta 3.9$ mmHg, $p < 0.001$). There was significant improvement in proportion of RV dysfunction in all patients, but the difference was larger in the USCDT group ($\Delta 43.3\%$ vs $\Delta 17.3\%$, $p < 0.001$). Patients who underwent USCDT had lower 30-day (4.3% vs 10.5%, $p = 0.03$), 90-day (5.5% vs 12.4%, $p = 0.03$), and 1-year mortality (6.2% vs 14.2%, $p = 0.03$). **CONCLUSIONS:** In patients with acute submassive PE, USCDT was associated with improved 30-day, 90-day, and 1 year mortality as compared to AC alone. USCDT also improved RV function and reduced sPAP to a greater degree than AC alone. Further studies are needed to verify these results in both short- and long-term outcomes.

Public Health Sciences

Lee Y, Jehangir Q, **Li P**, Gudimella D, Mahale P, **Lin CH**, Apala DR, Krishnamoorthy G, Halabi AR, Patel K, **Poisson L**, Balijepally V, Sule AA, and Nair GB. Venous thromboembolism in COVID-19 patients and prediction model: a multicenter cohort study. *BMC Infect Dis* 2022; 22(1):462. PMID: 35562677. [Full Text](#)

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BACKGROUND: Patients with COVID-19 infection are commonly reported to have an increased risk of venous thrombosis. The choice of anti-thrombotic agents and doses are currently being studied in randomized controlled trials and retrospective studies. There exists a need for individualized risk stratification of venous thromboembolism (VTE) to assist clinicians in decision-making on anticoagulation. We sought to identify the risk factors of VTE in COVID-19 patients, which could help physicians in the prevention, early identification, and management of VTE in hospitalized COVID-19 patients and improve clinical outcomes in these patients. **METHOD:** This is a multicenter, retrospective database of four main health systems in Southeast Michigan, United States. We compiled comprehensive data for adult COVID-19 patients who were admitted between 1st March 2020 and 31st December 2020. Four models, including the random forest, multiple logistic regression, multilinear regression, and decision trees, were built on the primary outcome of in-hospital acute deep vein thrombosis (DVT) and pulmonary embolism (PE) and tested for performance. The study also reported hospital length of stay (LOS) and intensive care unit (ICU) LOS in the VTE and the non-VTE patients. Four models were assessed using the area under the receiver operating characteristic curve and confusion matrix. **RESULTS:** The cohort included 3531 admissions, 3526 had discharge diagnoses, and 6.68% of patients developed acute VTE (N = 236). VTE group had a longer hospital and ICU LOS than the non-VTE group (hospital LOS 12.2 days vs. 8.8 days, $p < 0.001$; ICU LOS 3.8 days vs. 1.9 days, $p < 0.001$). 9.8% of patients in the VTE group required more advanced oxygen support, compared to 2.7% of patients in the non-VTE group ($p < 0.001$). Among all four models, the random forest model had the best performance. The model suggested that blood pressure, electrolytes, renal function, hepatic enzymes, and inflammatory markers were predictors for in-hospital VTE in COVID-19 patients. **CONCLUSIONS:** Patients with COVID-19 have a high risk for VTE, and patients who developed VTE had a prolonged hospital and ICU stay. This random forest prediction model for VTE in COVID-19 patients identifies predictors which could aid physicians in making a clinical judgment on empirical dosages of anticoagulation.

Public Health Sciences

Lim S, Bazydlo M, Macki M, Haider S, Hamilton T, Hunt R, Chaker A, Kantak P, Schultz L, Nerenz D, Schwalb JM, Abdulhak M, Park P, Aleem I, Easton R, Khalil JG, Perez-Cruet MJ, and **Chang V.**

Validation of the Benefits of Ambulation Within 8 Hours of Elective Cervical and Lumbar Surgery: A Michigan Spine Surgery Improvement Collaborative Study. *Neurosurgery* 2022; Epub ahead of print.

PMID: 35550477. [Full Text](#)

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BACKGROUND: Early ambulation is considered a key element to Enhanced Recovery After Surgery protocol after spine surgery. **OBJECTIVE:** To investigate whether ambulation less than 8 hours after elective spine surgery is associated with improved outcome. **METHODS:** The Michigan Spine Surgery Improvement Collaborative database was queried to track all elective cervical and lumbar spine surgery between July 2018 and April 2021. In total, 7647 cervical and 17 616 lumbar cases were divided into 3 cohorts based on time to ambulate after surgery: (1) <8 hours, (2) 8 to 24 hours, and (3) >24 hours.

RESULTS: For cervical cases, patients who ambulated 8 to 24 hours (adjusted odds ratio [aOR] 1.38; 95% CI 1.11-1.70; P = .003) and >24 hours (aOR 2.20; 95% CI 1.20-4.03; P = .011) after surgery had higher complication rate than those who ambulated within 8 hours of surgery. Similar findings were noted for lumbar cases with patients who ambulated 8 to 24 hours (aOR 1.31; 95% CI 1.12-1.54; P < .001) and >24 hours (aOR 1.96; 95% CI 1.50-2.56; P < .001) after surgery having significantly higher complication rate than those ambulated <8 hours after surgery. Analysis of secondary outcomes for cervical cases demonstrated that <8-hour ambulation was associated with home discharge, shorter hospital stay, lower 90-day readmission, and lower urinary retention rate. For lumbar cases, <8-hour ambulation was associated with shorter hospital stay, satisfaction with surgery, lower 30-day readmission, home discharge, and lower urinary retention rate. **CONCLUSION:** Ambulation within 8 hours after surgery is associated with significant improved outcome after elective cervical and lumbar spine surgery.

Public Health Sciences

Mercuro NJ, Medler CJ, Kenney RM, MacDonald NC, Neuhauser MM, Hicks LA, Srinivasan A, Divine G, Beaulac A, Eriksson E, Kendall R, Martinez M, Weinmann A, Zervos M, and Davis SL.

Pharmacist-Driven Transitions of Care Practice Model for Prescribing Oral Antimicrobials at Hospital Discharge. *JAMA Netw Open* 2022; 5(5):e2211331. PMID: 35536577. [Full Text](#)

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IMPORTANCE: Although prescribers face numerous patient-centered challenges during transitions of care (TOC) at hospital discharge, prolonged duration of antimicrobial therapy for common infections remains problematic, and resources are needed for antimicrobial stewardship throughout this period. **OBJECTIVE:** To evaluate a pharmacist-driven intervention designed to improve selection and duration of oral antimicrobial therapy prescribed at hospital discharge for common infections. **DESIGN, SETTING, AND PARTICIPANTS:** This quality improvement study used a nonrandomized stepped-wedge design with 3 study phases from September 1, 2018, to August 31, 2019. Seventeen distinct medicine, surgery, and specialty units from a health system in Southeast Michigan participated, including 1 academic tertiary hospital and 4 community hospitals. Hospitalized adults who had urinary, respiratory, skin and/or soft tissue, and intra-abdominal infections and were prescribed antimicrobials at discharge were included in the analysis. Data were analyzed from February 18, 2020, to February 28, 2022. **INTERVENTIONS:** Clinical pharmacists engaged in a new standard of care for antimicrobial stewardship practices during TOC by identifying patients to be discharged with a prescription for oral antimicrobials and collaborating with primary teams to prescribe optimal therapy. Academic and community hospitals used both antimicrobial stewardship and clinical pharmacists in a multidisciplinary rounding model to discuss, document, and facilitate order entry of the antimicrobial prescription at discharge. **MAIN OUTCOMES AND MEASURES:** The primary end point was frequency of optimized antimicrobial prescription at discharge. Health system guidelines developed from national guidelines and best practices for short-course therapies were used to evaluate optimal therapy. **RESULTS:** A total of 800 patients prescribed oral antimicrobials at hospital discharge were included in the analysis (441 women [55.1%]; mean [SD] age, 66.8 [17.3] years): 400 in the preintervention period and 400 in the postintervention period. The most common diagnoses were pneumonia (264 [33.0%]), upper respiratory tract infection and/or acute exacerbation of chronic obstructive pulmonary disease (214 [26.8%]), and urinary tract infection (203 [25.4%]). Patients in the postintervention group were more likely to have an optimal antimicrobial prescription (time-adjusted generalized estimating equation odds ratio, 5.63 [95% CI, 3.69-8.60]). The absolute increase in optimal prescribing in the postintervention group was consistent in both academic (37.4% [95% CI, 27.5%-46.7%]) and community (43.2% [95% CI, 32.4%-52.8%]) TOC models. There were no differences in clinical resolution or mortality. Fewer severe antimicrobial-related adverse effects (time-adjusted generalized estimating equation odds ratio, 0.40 [95% CI, 0.18-0.88]) were identified in the postintervention (13 [3.2%]) compared with the preintervention (36 [9.0%]) groups. **CONCLUSIONS AND**

RELEVANCE: The findings of this quality improvement study suggest that targeted antimicrobial stewardship interventions during TOC were associated with increased optimal, guideline-concordant antimicrobial prescriptions at discharge.

Public Health Sciences

Mesa-Frias M, Rossi C, Emond B, Bookhart B, Anderson D, Drummond S, Wang J, Lefebvre P, **Lamerato LE**, and Lafeuille MH. Incidence and economic burden of respiratory syncytial virus among adults in the United States: A retrospective analysis using 2 insurance claims databases. *J Manag Care Spec Pharm* 2022;1-13; Epub ahead of print. PMID: 35503888. [Full Text](#)

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BACKGROUND: Respiratory syncytial virus (RSV) is a common, contagious, and seasonal pathogen causing 64 million acute respiratory infections annually in adults and children worldwide. High-risk adults, including older adults and those with cardiopulmonary conditions or weakened immune systems, are more likely to be infected. However, limited information exists on RSV incidence and associated costs among adults, including high-risk patients. OBJECTIVE: To evaluate the annual incidence of medically attended, International Classification of Diseases (ICD)-coded RSV among commercially insured adults and assess health care costs among adults with ICD-coded RSV in the United States. METHODS: Optum's deidentified Clinformatics Data Mart Database (January 01, 2007, to June 30, 2020) and IBM's MarketScan Databases (January 01, 2000, to July 31, 2020) were used. Medically attended, ICD-coded RSV incidence among adults was assessed from July 1 of a given year to June 30 of the next year and reported per 100,000 population. Trends in all-cause mean weekly costs pre-RSV and post-RSV diagnosis were reported. Results were reported overall and among patients aged 60-64 years, 65 years or older, 85 years or older, and 18-59 years at high risk of severe RSV (defined as having cardiopulmonary conditions or a weakened immune system). RESULTS: Annual incidence of medically attended, ICD-coded RSV in adults overall was 22.0-52.9 in Optum and 23.4-63.6 in MarketScan. Incidence rates were higher among patients aged 60-64 years (Optum: 25.2-66.1; MarketScan: 31.9-82.1), 65 years or older (Optum: 37.3-75.5; MarketScan: 54.1-97.3), 85 years or older (Optum: 92.4-140.6; MarketScan: 79.4-234.7), and 18-59 years at high risk of severe RSV (Optum: 41.3-135.9; MarketScan: 46.3-112.4). Mean weekly costs increased during the week before (Optum: \$2,325; MarketScan: \$2,080) and post-RSV diagnosis (Optum: \$9,523; MarketScan: \$3,551), compared with those in weeks 2-8 pre-RSV diagnosis (Optum: \$1,350; MarketScan: \$872). The increases in mean weekly costs during the week before and the week following RSV diagnosis were higher among patients aged 60-64 years (mean weekly costs in weeks 2-8 pre-RSV, week 1 pre-RSV, week 1 post-RSV; Optum: \$1,623, \$2,690, \$10,823; MarketScan: \$1,259, \$2,992, \$5,069), 65 years or older (Optum: \$1,731, \$3,067, \$12,866; MarketScan: \$1,517, \$3,571, \$5,268), 85 years or older (Optum: \$1,563, \$2,430, \$18,134; MarketScan: \$1,613, \$4,113, \$6,231), and 18-59 years at high risk of severe RSV (only for MarketScan: \$1,237, \$3,294, \$5,531; costs were similar for Optum). CONCLUSIONS: Incidence of medically attended, ICD-coded RSV in adults was 22.0-63.6 per 100,000 population, a likely underestimation since RSV was not systematically tested and only RSV-coded cases were observed. Incremental costs associated with RSV were substantial. Incidence rates and costs were higher among patients aged 60 years or older and patients at high risk of severe RSV. DISCLOSURES: This study was sponsored by Janssen Scientific Affairs, LLC. The sponsor was involved in the study design, interpretation of results, manuscript preparation, and publication decisions. B. Bookhart and D. Anderson are employees of Janssen Scientific Affairs, LLC, and are stockholders of Johnson & Johnson. C. Rossi, B. Emond, J. Wang, P. Lefebvre, and M.-H. Lafeuille are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Janssen Scientific Affairs, LLC, which funded the development and conduct of this study and manuscript. M. Mesa-Frias. and S. Drummond are former employees of Janssen Scientific Affairs, LLC. L. Lamerato is an employee of Henry Ford Health System and received research funding from Janssen Scientific Affairs, LLC.

Public Health Sciences

Suleyman G, Fadel R, Brar I, Kassab R, Khansa R, Sturla N, Alsaadi A, Latack K, Miller J, Tibbetts R, Samuel L, Alangaden G, and Ramesh M. Risk Factors Associated With Hospitalization and Death in COVID-19 Breakthrough Infections. *Open Forum Infect Dis* 2022; 9(5):ofac116. PMID: 35437511. [Full Text](#)

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BACKGROUND: Characterizations of coronavirus disease 2019 (COVID-19) vaccine breakthrough infections are limited. We aim to characterize breakthrough infections and identify risk factors associated with outcomes. **METHODS:** This was a retrospective case series of consecutive fully vaccinated patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a multicenter academic center in Southeast Michigan, between December 30, 2020, and September 15, 2021. **RESULTS:** A total of 982 patients were identified; the mean age was 57.9 years, 565 (59%) were female, 774 (79%) were White, and 255 (26%) were health care workers (HCWs). The median number of comorbidities was 2; 225 (23%) were immunocompromised. BNT162b2 was administered to 737 (75%) individuals. The mean time to SARS-CoV-2 detection was 135 days. The majority were asymptomatic or exhibited mild to moderate disease, 154 (16%) required hospitalization, 127 (13%) had severe-critical illness, and 19 (2%) died. Age (odds ratio [OR], 1.14; 95% CI, 1.04-1.07; $P < .001$), cardiovascular disease (OR, 3.02; 95% CI, 1.55-5.89; $P = .001$), and immunocompromised status (OR, 2.57; 95% CI, 1.70-3.90; $P < .001$) were independent risk factors for hospitalization. Additionally, age (OR, 1.06; 95% CI, 1.02-1.11; $P = .006$) was significantly associated with mortality. HCWs (OR, 0.15; 95% CI, 0.05-0.50; $P = .002$) were less likely to be hospitalized, and prior receipt of BNT162b2 was associated with lower odds of hospitalization (OR, 0.436; 95% CI, 0.303-0.626; $P < .001$) and/or death (OR, 0.360; 95% CI, 0.145-0.898; $P = .029$). **CONCLUSIONS:** COVID-19 vaccines remain effective at attenuating disease severity. However, patients with breakthrough infections necessitating hospitalization may benefit from early treatment modalities and COVID-19-mitigating strategies, especially in areas with substantial or high transmission rates.

Public Health Sciences

Tecson KM, Kluger AY, Cassidy-Bushrow AE, Liu B, Coleman CM, Jones LK, Jefferson CR, VanWormer JJ, and McCullough PA. Usefulness of Statins as Secondary Prevention Against Recurrent and Terminal Major Adverse Cardiovascular Events. *Am J Cardiol* 2022; Epub ahead of print. PMID: 35606173. [Full Text](#)

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Clinical guidelines recommend statins for patients with atherosclerotic cardiovascular disease (ASCVD), but many remain untreated. The goal of this study was to assess the impact of statin use on recurrent major adverse cardiovascular events (MACE). This study used medical records and insurance claims from 4 health care systems in the United States. Eligible adults who survived an ASCVD hospitalization from September 2013 to September 2014 were followed for 1 year. A multivariable extended Cox model examined the outcome of time-to-first MACE, then a multivariable joint marginal model investigated the association between post-index statin use and nonfatal and fatal MACE. There were 8,168 subjects in this study; 3,866 filled a statin prescription ≤ 90 days before the index ASCVD event (47.33%) and 4,152

filled a statin prescription after the index ASCVD event (50.83%). These post-index statin users were younger, with more co-morbidities. There were 763 events (315/763, 41.3% terminal) experienced by 686 (8.4%) patients. The adjusted overall MACE risk reduction was 18% (HR 0.82, 95% CI 0.70 to 0.95, $p = 0.007$) and was more substantial in the first 180 days (HR 0.72, 95% CI 0.60 to 0.86, $p < 0.001$). There was a nonsignificant 19% reduction in the number of nonfatal MACE (rate ratio 0.81, 95% CI 0.49 to 1.32, $p = 0.394$) and a 65% reduction in the risk of all-cause death (HR 0.35, 95% CI 0.22 to 0.56, $p < 0.001$). In conclusion, we found a modest increase in statin use after an ASCVD event, with nearly half of the patients untreated. The primary benefit of statin use was protection against early death. Statin use had the greatest impact in the first 6 months after an ASCVD event; therefore, it is crucial for patients to quickly adhere to this therapy.

Public Health Sciences

Zador L, Nowak K, Sitarik A, MacLean L, Han X, Kalsi M, Yeldo N, Sibai N, Penning D, and Lewis M. The Burnout Epidemic Within A Viral Pandemic: Impact of a Wellness Initiative. *Perioper Care Oper Room Manag* 2022; 27:100251. PMID: 35382030. [Full Text](#)

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BACKGROUND: Anesthesiologists are at high risk of developing burnout, a condition which can lead to many deleterious effects for the physician, and far-reaching effects on their patients and hospital systems. The COVID-19 pandemic has presented new challenges that have further exacerbated the risk of burnout in anesthesiologists. It is critical to develop effective strategies to promote well-being and decrease burnout for physicians in this specialty. The purpose of this observational study was to evaluate the impact of a Physician Well-Being Initiative on distress and well-being in anesthesiologists. It was hypothesized that the wellness intervention would promote an improvement in well-being scores. **METHODS:** The Physician Well-Being Initiative was launched in August 2019 in the Department of Anesthesiology, Pain Management and Perioperative Medicine at Henry Ford Hospital in Detroit, Michigan. The Physician Well-Being Initiative was designed to address several of the key factors that improve physician wellness, including 1) a sense of autonomy; 2) positive view of leadership; and 3) flexible schedule opportunities. To assess the impact of the Physician Well-Being Initiative on the well-being and distress scores of participating anesthesiologists, the physicians were emailed the validated Well-Being Index survey at baseline and 3, 6 and 12 months. The Well-Being Index evaluates multiple items of distress in the healthcare setting. The sample size was limited to the 54 anesthesiologists at Henry Ford Hospital. **RESULTS:** Forty-four of the 54 anesthesiologists completed the baseline questionnaire. A total of 44 physicians answered the questionnaire at baseline, with more male than female physicians (35 males and 7 females) and the majority (17/44) in practice for 5-10 years. Thirty-two physicians completed the survey at 3 and 6 months, and 31 physicians at 12 months after the launch of the Physician Well-Being Initiative. Twenty-one physicians completed the questionnaire at all 4 time points. Although the COVID-19 pandemic started shortly after the 6-month surveys were submitted, results indicated that there was a 0.05 decrease in the Well-Being Index sum score for every 1-month of time (coefficient -0.05, 95% CI -0.01, -0.08, $P = 0.013$). This study shows that, with the wellness initiative in place, the department was able to maintain and potentially even reduce physician distress despite the concurrent onset of the pandemic. **CONCLUSIONS:** Following the launch of a sustained wellness initiative, this study demonstrates that physician wellness improved with time. This suggests that it takes time for a wellness initiative to have an effect on well-being and distress in anesthesiologists.

Public Health Sciences

Zanobetti A, Ryan PH, Coull B, Brokamp C, Datta S, Blossom J, Lothrop N, Miller RL, Beamer PI, Visness CM, Andrews H, Bacharier LB, Hartert T, **Johnson CC**, Ownby D, Khurana Hershey GK, **Joseph C**, Yiqiang S, Mendoza E, Jackson DJ, Luttmann-Gibson H, **Zoratti EM**, Wright AL, Martinez FD, Seroogy CM, **Gern JE**, and Gold DR. Childhood Asthma Incidence, Early and Persistent Wheeze, and

Neighborhood Socioeconomic Factors in the ECHO/CREW Consortium. *JAMA Pediatr* 2022; Epub ahead of print. PMID: 35604671. [Full Text](#)

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IMPORTANCE: In the United States, Black and Hispanic children have higher rates of asthma and asthma-related morbidity compared with White children and disproportionately reside in communities with economic deprivation. **OBJECTIVE:** To determine the extent to which neighborhood-level socioeconomic indicators explain racial and ethnic disparities in childhood wheezing and asthma. **DESIGN, SETTING, AND PARTICIPANTS:** The study population comprised children in birth cohorts located throughout the United States that are part of the Children's Respiratory and Environmental Workgroup consortium. Cox proportional hazard models were used to estimate hazard ratios (HRs) of asthma incidence, and logistic regression was used to estimate odds ratios of early and persistent wheeze prevalence accounting for mother's education, parental asthma, smoking during pregnancy, child's race and ethnicity, sex, and region and decade of birth. **EXPOSURES:** Neighborhood-level socioeconomic indicators defined by US census tracts calculated as z scores for multiple tract-level variables relative to the US average linked to participants' birth record address and decade of birth. The parent or caregiver reported the child's race and ethnicity. **MAIN OUTCOMES AND MEASURES:** Prevalence of early and persistent childhood wheeze and asthma incidence. **RESULTS:** Of 5809 children, 46% reported wheezing before age 2 years, and 26% reported persistent wheeze through age 11 years. Asthma prevalence by age 11 years varied by cohort, with an overall median prevalence of 25%. Black children (HR, 1.47; 95% CI, 1.26-1.73) and Hispanic children (HR, 1.29; 95% CI, 1.09-1.53) were at significantly increased risk for asthma incidence compared with White children, with onset occurring earlier in childhood. Children born in tracts with a greater proportion of low-income households, population density, and poverty had increased asthma incidence. Results for early and persistent wheeze were similar. In effect modification analysis, census variables did not significantly modify the association between race and ethnicity and risk for asthma incidence; Black and Hispanic children remained at higher risk for asthma compared with White children across census tracts socioeconomic levels. **CONCLUSIONS AND RELEVANCE:** Adjusting for individual-level characteristics, we observed neighborhood socioeconomic disparities in childhood wheeze and

asthma. Black and Hispanic children had more asthma in neighborhoods of all income levels. Neighborhood- and individual-level characteristics and their root causes should be considered as sources of respiratory health inequities.

Pulmonary and Critical Care Medicine

Gorgis S, Mawri S, Dabbagh MF, Aurora L, Ali M, Mitchell G, Jacobsen G, Hegab S, Schwartz S, Kelly B, Grafton G, Awdish R, Ismail R, and Koenig G. Ultrasound-assisted catheter-directed thrombolysis versus anticoagulation alone for management of submassive pulmonary embolism. *J Cardiol* 2022; Epub ahead of print. PMID: 35643741. [Full Text](#)

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BACKGROUND: Patients with submassive pulmonary embolism (PE) are vulnerable to sudden deterioration, recurrent PE, and progression to pulmonary hypertension and chronic right ventricular (RV) dysfunction. Previous studies have suggested a clinical benefit of using ultrasound-assisted catheter-directed thrombolysis (USCDT) to invasively manage patients with submassive PE. However, there is sparse data comparing the clinical outcomes of these patients when treated with USCDT versus anticoagulation (AC) alone. We sought to compare the outcomes of USCDT versus AC alone in the management of submassive PE. **METHODS:** 192 consecutive patients who underwent USCDT for submassive PE between January 2013 and February 2019 were identified. ICD9/ICD10 codes were used to detect 2554 patients diagnosed with PE who did not undergo thrombolysis. Propensity matching identified 192 patients with acute PE treated with AC alone. Clinical outcomes were compared between the two groups. Baseline demographics, laboratory values, and pulmonary embolism severity index scores were similar between the two cohorts. **RESULTS:** There was a significant reduction in mean systolic pulmonary artery pressure (sPAP) in the USCDT group compared to the AC group ($\Delta 11$ vs $\Delta 3.9$ mmHg, $p < 0.001$). There was significant improvement in proportion of RV dysfunction in all patients, but the difference was larger in the USCDT group ($\Delta 43.3\%$ vs $\Delta 17.3\%$, $p < 0.001$). Patients who underwent USCDT had lower 30-day (4.3% vs 10.5%, $p = 0.03$), 90-day (5.5% vs 12.4%, $p = 0.03$), and 1-year mortality (6.2% vs 14.2%, $p = 0.03$). **CONCLUSIONS:** In patients with acute submassive PE, USCDT was associated with improved 30-day, 90-day, and 1 year mortality as compared to AC alone. USCDT also improved RV function and reduced sPAP to a greater degree than AC alone. Further studies are needed to verify these results in both short- and long-term outcomes.

Pulmonary and Critical Care Medicine

Kim RY, Oke JL, Pickup LC, Munden RF, Dotson TL, Bellinger CR, **Cohen A, Simoff MJ**, Massion PP, Filippini C, Gleeson FV, and Vachani A. Artificial Intelligence Tool for Assessment of Indeterminate Pulmonary Nodules Detected with CT. *Radiology* 2022;212182; Epub ahead of print. PMID: 35608444.

[Full Text](#)

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Salem, NC (T.L.D., C.R.B.); Division of Pulmonary and Critical Care Medicine, Department of Medicine, Henry Ford Health System, Detroit, Mich (A.C., M.J.S.); Division of Allergy, Pulmonary and Critical Care Medicine, Vanderbilt Ingram Cancer Center, Nashville, Tenn (P.P.M.); and Department of Oncology, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom (C.F., F.V.G.).

Background Limited data are available regarding whether computer-aided diagnosis (CAD) improves assessment of malignancy risk in indeterminate pulmonary nodules (IPNs). **Purpose** To evaluate the effect of an artificial intelligence-based CAD tool on clinician IPN diagnostic performance and agreement for both malignancy risk categories and management recommendations. **Materials and Methods** This was a retrospective multireader multicase study performed in June and July 2020 on chest CT studies of IPNs. Readers used only CT imaging data and provided an estimate of malignancy risk and a management recommendation for each case without and with CAD. The effect of CAD on average reader diagnostic performance was assessed using the Obuchowski-Rockette and Dorfman-Berbaum-Metz method to calculate estimates of area under the receiver operating characteristic curve (AUC), sensitivity, and specificity. Multirater Fleiss κ statistics were used to measure interobserver agreement for malignancy risk and management recommendations. **Results** A total of 300 chest CT scans of IPNs with maximal diameters of 5-30 mm (50.0% malignant) were reviewed by 12 readers (six radiologists, six pulmonologists) (patient median age, 65 years; IQR, 59-71 years; 164 [55%] men). Readers' average AUC improved from 0.82 to 0.89 with CAD ($P < .001$). At malignancy risk thresholds of 5% and 65%, use of CAD improved average sensitivity from 94.1% to 97.9% ($P = .01$) and from 52.6% to 63.1% ($P < .001$), respectively. Average reader specificity improved from 37.4% to 42.3% ($P = .03$) and from 87.3% to 89.9% ($P = .05$), respectively. Reader interobserver agreement improved with CAD for both the less than 5% (Fleiss κ , 0.50 vs 0.71; $P < .001$) and more than 65% (Fleiss κ , 0.54 vs 0.71; $P < .001$) malignancy risk categories. Overall reader interobserver agreement for management recommendation categories (no action, CT surveillance, diagnostic procedure) also improved with CAD (Fleiss κ , 0.44 vs 0.52; $P = .001$). **Conclusion** Use of computer-aided diagnosis improved estimation of indeterminate pulmonary nodule malignancy risk on chest CT scans and improved interobserver agreement for both risk stratification and management recommendations. © RSNA, 2022 Online supplemental material is available for this article. See also the editorial by Yanagawa.

Pulmonary and Critical Care Medicine

Liang E, Dolan JL, Morris ED, Vono J, Bazan LF, Lu M, and Glide-Hurst CK. Application of Continuous Positive Airway Pressure for Thoracic Respiratory Motion Management: An Assessment in a Magnetic Resonance Imaging-Guided Radiation Therapy Environment. *Adv Radiat Oncol* 2022; 7(3):100889. PMID: 35198838. [Full Text](#)

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PURPOSE: Patient tolerability of magnetic resonance (MR)-guided radiation treatment delivery is limited by the need for repeated deep inspiratory breath holds (DIBHs). This volunteer study assessed the feasibility of continuous positive airway pressure (CPAP) with and without DIBH for respiratory motion management during radiation treatment with an MR-linear accelerator (MR-linac). **METHODS AND MATERIALS:** MR imaging safety was first addressed by placing the CPAP device in an MR-safe closet and configuring a tube circuit via waveguide to the magnet bore. Reproducibility and linearity of the final configuration were assessed. Six healthy volunteers underwent thoracic imaging in a 0.35T MR-linac, with one free breathing (FB) and 2 DIBH acquisitions being obtained at 5 pressures from 0 to 15 cm-H₂O. Lung and heart volumes and positions were recorded; repeatability was assessed by comparing 2 consecutive DIBH scans. Blinded reviewers graded images for motion artifact using a 3-point grading scale. Participants completed comfort and perception surveys before and after imaging sessions. **RESULTS:** Compared with FB alone, FB-10, FB-12, and FB-15 cm H₂O significantly increased lung volumes (+23%, +34%, +44%; all $P < .05$) and inferiorly displaced the heart (0.86 cm, 0.96 cm, 1.18 cm; all $P < .05$). Lung volumes were significantly greater with DIBH-0 cm H₂O compared with FB-15 cm H₂O (+105% vs +44%, $P = .01$), and DIBH-15 cm H₂O yielded additional volume increase (+131% vs

+105%, $P = .01$). Adding CPAP to DIBH decreased lung volume differences between consecutive breath holds (correlation coefficient 0.97 at 15 cm H₂O vs 0.00 at 0 cm H₂O). The addition of 15 cm H₂O CPAP reduced artifact scores ($P = .03$) compared with FB; all DIBH images (0-15 cm H₂O) had less artifact ($P < .01$). **CONCLUSIONS:** This work demonstrates the feasibility of integrating CPAP in an MR-linac environment in healthy volunteers. Extending this work to a larger patient cohort is warranted to further establish the role of CPAP as an alternative and concurrent approach to DIBH in MR-guided radiation therapy.

Pulmonary and Critical Care Medicine

Munroe E, Claar D, Tamae-Kakazu M, **Tatem G**, Blamoun J, McSparron JI, and Prescott HC. Hospital Policies on Intravenous Vasopressor Administration and Monitoring: A Survey of Michigan Hospitals. *Ann Am Thorac Soc* 2022; Epub ahead of print. PMID: 35608405. [Full Text](#)

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Radiation Oncology

Liang E, Dolan JL, Morris ED, Vono J, Bazan LF, Lu M, and Glide-Hurst CK. Application of Continuous Positive Airway Pressure for Thoracic Respiratory Motion Management: An Assessment in a Magnetic Resonance Imaging-Guided Radiation Therapy Environment. *Adv Radiat Oncol* 2022; 7(3):100889. PMID: 35198838. [Full Text](#)

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PURPOSE: Patient tolerability of magnetic resonance (MR)-guided radiation treatment delivery is limited by the need for repeated deep inspiratory breath holds (DIBHs). This volunteer study assessed the feasibility of continuous positive airway pressure (CPAP) with and without DIBH for respiratory motion management during radiation treatment with an MR-linear accelerator (MR-linac). **METHODS AND MATERIALS:** MR imaging safety was first addressed by placing the CPAP device in an MR-safe closet and configuring a tube circuit via waveguide to the magnet bore. Reproducibility and linearity of the final configuration were assessed. Six healthy volunteers underwent thoracic imaging in a 0.35T MR-linac, with one free breathing (FB) and 2 DIBH acquisitions being obtained at 5 pressures from 0 to 15 cm-H₂O. Lung and heart volumes and positions were recorded; repeatability was assessed by comparing 2 consecutive DIBH scans. Blinded reviewers graded images for motion artifact using a 3-point grading scale. Participants completed comfort and perception surveys before and after imaging sessions.

RESULTS: Compared with FB alone, FB-10, FB-12, and FB-15 cm H₂O significantly increased lung volumes (+23%, +34%, +44%; all $P < .05$) and inferiorly displaced the heart (0.86 cm, 0.96 cm, 1.18 cm; all $P < .05$). Lung volumes were significantly greater with DIBH-0 cm H₂O compared with FB-15 cm H₂O (+105% vs +44%, $P = .01$), and DIBH-15 cm H₂O yielded additional volume increase (+131% vs +105%, $P = .01$). Adding CPAP to DIBH decreased lung volume differences between consecutive breath holds (correlation coefficient 0.97 at 15 cm H₂O vs 0.00 at 0 cm H₂O). The addition of 15 cm H₂O CPAP reduced artifact scores ($P = .03$) compared with FB; all DIBH images (0-15 cm H₂O) had less artifact ($P < .01$). **CONCLUSIONS:** This work demonstrates the feasibility of integrating CPAP in an MR-linac environment in healthy volunteers. Extending this work to a larger patient cohort is warranted to further establish the role of CPAP as an alternative and concurrent approach to DIBH in MR-guided radiation therapy.

Radiation Oncology

Miller CR, Morris ED, **Ghanem AI, Pantelic MV, Walker EM**, and Glide-Hurst CK. Characterizing Sensitive Cardiac Substructure Excursion Due to Respiration. *Adv Radiat Oncol* 2022; 7(3):100876. PMID: 35243181. [Full Text](#)

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PURPOSE: Whole-heart dose metrics are not as strongly linked to late cardiac morbidities as radiation doses to individual cardiac substructures. Our aim was to characterize the excursion and dosimetric variation throughout respiration of sensitive cardiac substructures for future robust safety margin design. **METHODS AND MATERIALS:** Eleven patients with cancer treatments in the thorax underwent 4-phase noncontrast 4-dimensional computed tomography (4DCT) with T2-weighted magnetic resonance imaging in end-exhale. The end-exhale phase of the 4DCT was rigidly registered with the magnetic resonance imaging and refined with an assisted alignment surrounding the heart from which 13 substructures (chambers, great vessels, coronary arteries, etc) were contoured by a radiation oncologist on the 4DCT. Contours were deformed to the other respiratory phases via an intensity-based deformable registration for radiation oncologist verification. Measurements of centroid and volume were evaluated between phases. Mean and maximum dose to substructures were evaluated across respiratory phases for the breast (n = 8) and thoracic cancer (n = 3) cohorts. **RESULTS:** Paired t tests revealed reasonable maintenance of geometric and anatomic properties (P < .05 for 4/39 volume comparisons). Maximum displacements >5 mm were found for 24.8%, 8.5%, and 64.5% of the cases in the left-right, anterior-posterior, and superior-inferior axes, respectively. Vector displacements were largest for the inferior vena cava and the right coronary artery, with displacements up to 17.9 mm. In breast, the left anterior descending artery D(mean) varied 3.03 ± 1.75 Gy (range, 0.53-5.18 Gy) throughout respiration whereas lung showed patient-specific results. Across all patients, whole heart metrics were insensitive to breathing phase (mean and maximum dose variations <0.5 Gy). **CONCLUSIONS:** This study characterized the intrafraction displacement of the cardiac substructures through the respiratory cycle and highlighted their increased dosimetric sensitivity to local dose changes not captured by whole heart metrics. Results suggest value of cardiac substructure margin generation to enable more robust cardiac sparing and to reduce the effect of respiration on overall treatment plan quality.

Research Administration

Park BY, Larivière S, Rodríguez-Cruces R, Royer J, Tavakol S, Wang Y, Caciagli L, Caligiuri ME, Gambardella A, Concha L, Keller SS, Cendes F, Alvim MKM, Yasuda C, Bonilha L, Gleichgerrcht E, Focke NK, Kreilkamp BAK, Domin M, von Podewils F, Langner S, Rummel C, Rebsamen M, Wiest R, Martin P, Kotikalapudi R, Bender B, O'Brien TJ, Law M, Sinclair B, Vivash L, Kwan P, Desmond PM, Malpas CB, Lui E, Alhusaini S, Doherty CP, Cavalleri GL, Delanty N, Kälviäinen R, Jackson GD, Kowalczyk M, Mascialchi M, Semmelroch M, Thomas RH, **Soltanian-Zadeh H, Davoodi-Bojd E**, Zhang J, Lenge M, Guerrini R, Bartolini E, Hamandi K, Foley S, Weber B, Depondt C, Absil J, Carr SJA, Abela E, Richardson MP, Devinsky O, Severino M, Striano P, Parodi C, Tortora D, Hatton SN, Vos SB, Duncan JS, Galovic M, Whelan CD, Bargalló N, Pariente J, Conde-Blanco E, Vaudano AE, Tondelli M, Meletti S, Kong XZ, Francks C, Fisher SE, Caldairou B, Ryten M, Labate A, Sisodiya SM, Thompson PM, McDonald CR, Bernasconi A, Bernasconi N, and Bernhardt BC. Topographic divergence of atypical cortical asymmetry and atrophy patterns in temporal lobe epilepsy. *Brain* 2022; 145(4):1285-1298. PMID: 35333312. [Full Text](#)

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Temporal lobe epilepsy, a common drug-resistant epilepsy in adults, is primarily a limbic network disorder associated with predominant unilateral hippocampal pathology. Structural MRI has provided an in vivo window into whole-brain grey matter structural alterations in temporal lobe epilepsy relative to controls, by either mapping (i) atypical inter-hemispheric asymmetry; or (ii) regional atrophy. However, similarities and differences of both atypical asymmetry and regional atrophy measures have not been systematically investigated. Here, we addressed this gap using the multisite ENIGMA-Epilepsy dataset comprising MRI brain morphological measures in 732 temporal lobe epilepsy patients and 1418 healthy controls. We compared spatial distributions of grey matter asymmetry and atrophy in temporal lobe epilepsy, contextualized their topographies relative to spatial gradients in cortical microstructure and functional connectivity calculated using 207 healthy controls obtained from Human Connectome Project and an independent dataset containing 23 temporal lobe epilepsy patients and 53 healthy controls and examined clinical associations using machine learning. We identified a marked divergence in the spatial distribution of atypical inter-hemispheric asymmetry and regional atrophy mapping. The former revealed a temporo- limbic disease signature while the latter showed diffuse and bilateral patterns. Our findings were robust

across individual sites and patients. Cortical atrophy was significantly correlated with disease duration and age at seizure onset, while degrees of asymmetry did not show a significant relationship to these clinical variables. Our findings highlight that the mapping of atypical inter-hemispheric asymmetry and regional atrophy tap into two complementary aspects of temporal lobe epilepsy-related pathology, with the former revealing primary substrates in ipsilateral limbic circuits and the latter capturing bilateral disease effects. These findings refine our notion of the neuropathology of temporal lobe epilepsy and may inform future discovery and validation of complementary MRI biomarkers in temporal lobe epilepsy.

Sleep Medicine

Kalmbach DA. The emerging role of prenatal insomnia therapy in the prevention of perinatal depression and anxiety. *Sleep* 2022; 45(5). PMID: 35554574. [Full Text](#)

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Sleep Medicine

Liang E, Dolan JL, Morris ED, Vono J, Bazan LF, Lu M, and Glide-Hurst CK. Application of Continuous Positive Airway Pressure for Thoracic Respiratory Motion Management: An Assessment in a Magnetic Resonance Imaging-Guided Radiation Therapy Environment. *Adv Radiat Oncol* 2022; 7(3):100889. PMID: 35198838. [Full Text](#)

Department of Radiation Oncology, Henry Ford Health System, Detroit, Michigan.
Department of Radiation Oncology, University of California, Los Angeles, California.
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PURPOSE: Patient tolerability of magnetic resonance (MR)-guided radiation treatment delivery is limited by the need for repeated deep inspiratory breath holds (DIBHs). This volunteer study assessed the feasibility of continuous positive airway pressure (CPAP) with and without DIBH for respiratory motion management during radiation treatment with an MR-linear accelerator (MR-linac). **METHODS AND MATERIALS:** MR imaging safety was first addressed by placing the CPAP device in an MR-safe closet and configuring a tube circuit via waveguide to the magnet bore. Reproducibility and linearity of the final configuration were assessed. Six healthy volunteers underwent thoracic imaging in a 0.35T MR-linac, with one free breathing (FB) and 2 DIBH acquisitions being obtained at 5 pressures from 0 to 15 cm-H₂O. Lung and heart volumes and positions were recorded; repeatability was assessed by comparing 2 consecutive DIBH scans. Blinded reviewers graded images for motion artifact using a 3-point grading scale. Participants completed comfort and perception surveys before and after imaging sessions. **RESULTS:** Compared with FB alone, FB-10, FB-12, and FB-15 cm H₂O significantly increased lung volumes (+23%, +34%, +44%; all P < .05) and inferiorly displaced the heart (0.86 cm, 0.96 cm, 1.18 cm; all P < .05). Lung volumes were significantly greater with DIBH-0 cm H₂O compared with FB-15 cm H₂O (+105% vs +44%, P = .01), and DIBH-15 cm H₂O yielded additional volume increase (+131% vs +105%, P = .01). Adding CPAP to DIBH decreased lung volume differences between consecutive breath holds (correlation coefficient 0.97 at 15 cm H₂O vs 0.00 at 0 cm H₂O). The addition of 15 cm H₂O CPAP reduced artifact scores (P = .03) compared with FB; all DIBH images (0-15 cm H₂O) had less artifact (P < .01). **CONCLUSIONS:** This work demonstrates the feasibility of integrating CPAP in an MR-linac environment in healthy volunteers. Extending this work to a larger patient cohort is warranted to further establish the role of CPAP as an alternative and concurrent approach to DIBH in MR-guided radiation therapy.

Sleep Medicine

Reffi AN, Kalmbach DA, Cheng P, Jovanovic T, Norrholm SD, Sexton MB, Mahr G, Arnett L, Seymour G, and Drake CL. Sleep reactivity as a potential pathway from childhood abuse to adult insomnia. *Sleep Med* 2022; 94:70-75. PMID: 35504109. [Full Text](#)

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BACKGROUND: Survivors of childhood abuse are prone to adult insomnia, but the mechanisms for this development are poorly understood. Abuse that occurs during sensitive developmental periods might affect risk for insomnia by impacting emerging stress regulatory processes. Sleep reactivity refers to the sensitivity of the sleep system to stress and is a robust risk factor for insomnia. Recent evidence shows stress exposure itself worsens sleep reactivity, thereby increasing insomnia vulnerability. In this preliminary study, we hypothesized the association between childhood abuse experiences and adult insomnia would be mediated through greater sleep reactivity. **METHODS:** Community adults were recruited from the United States during the COVID-19 pandemic between June 2020 and June 2021 (N = 241, 88% female, M(age) = 39, SD = 13.40). Participants completed a cross-sectional survey that included the Childhood Trauma Questionnaire, Ford Insomnia Response to Stress Test, Insomnia Severity Index, and a measure of general COVID-19 stress. **RESULTS:** Reporting more frequent childhood emotional, physical, or sexual abuse was associated with more severe insomnia during the COVID-19 pandemic. Only childhood emotional and physical (but not sexual) abuse histories were associated with greater sleep reactivity, which exerted an indirect effect on the relationships between these two abuse types and insomnia symptoms. These findings were robust to the effects of gender, age, and stress about the COVID-19 pandemic. **CONCLUSIONS:** This preliminary study suggests recurrent emotional and physical abuse in childhood might promote later insomnia through heightened sleep reactivity. Stress management interventions could be important to prevent insomnia for abuse survivors by bolstering resilience of the sleep system.

Sleep Medicine

Skiba V, and McLellan B. Safe use of donated positive airway pressure devices to increase access to treatment for obstructive sleep apnea: a clinical outreach program. *J Clin Sleep Med* 2022; 18(5):1455-1457. PMID: 35484640. [Full Text](#)

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Coverage to provide positive airway pressure (PAP) therapy for patients with obstructive sleep apnea (OSA) by the Centers for Medicare and Medicaid Services (CMS) and most private insurers is limited to those patients who meet diagnostic criteria for OSA based on a sleep study. Despite PAP therapy being a covered benefit by most insurers, many patients have high out-of-pocket costs due to copays and deductibles. Also, a subset of patients may be diagnosed per the American Academy of Sleep Medicine (AASM) recommended rule (H3A), while not meeting the diagnosis using the acceptable rule (H4) that their insurer requires.(1) To help patients such as these, our sleep medicine program envisioned and developed a PAP device donation program for patients with diagnosed or suspected OSA. Through our novel initiative, we were able to safely provide patients with donated and refurbished PAP devices at no cost to them. Here we outline the complexity involved in the provision of PAP therapy for patients with OSA and describe our PAP device donation program. **CITATION:** Skiba V, McLellan B. Safe use of donated positive airway pressure devices to increase access to treatment for obstructive sleep apnea: a clinical outreach program. *J Clin Sleep Med.* 2022;18(5):1455-1457.

Surgery

Davidson GH, Monsell SE, Evans H, Voldal EC, Fannon E, Lawrence SO, Krishnadasan A, Talan DA, Bizzell B, Heagerty PJ, Comstock BA, Lavalley DC, Villegas C, Winchell R, Thompson CM, Self WH, Kao LS, Dodwad SJ, Sabbatini AK, Drouillard D, Machado-Aranda D, Gibbons MM, Kaji AH, DeUgarte DA, Ferrigno L, Salzberg M, Mandell KA, Siparsky N, Price TP, Raman A, Corsa J, Wisler J, Ayoung-Chee P,

Victory J, Jones A, Kutcher M, McGrane K, Holihan J, Liang MK, Cuschieri J, **Johnson J**, Fischkoff K, Drake FT, Sanchez SE, Odom SR, Kessler LG, and Flum DR. Self-selection vs Randomized Assignment of Treatment for Appendicitis. *JAMA Surg* 2022; Epub ahead of print. PMID: 35612859. [Full Text](#)

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Bellevue Hospital Center NYU School of Medicine, New York, New York.
University of Mississippi Medical Center, Jackson, Mississippi.
Madigan Army Medical Center, Tacoma, Washington.
Mason General Hospital, Shelton, Washington.
University of Texas Lyndon B. Johnson General Hospital, Houston, Texas.
University of Houston, HCA Healthcare, Kingwood, Texas.
University of California, San Francisco, San Francisco, California.
Henry Ford Health System, Detroit, Michigan.
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IMPORTANCE: For adults with appendicitis, several randomized clinical trials have demonstrated that antibiotics are an effective alternative to appendectomy. However, it remains unknown how the characteristics of patients in such trials compare with those of patients who select their treatment and whether outcomes differ. **OBJECTIVE:** To compare participants in the Comparison of Outcomes of Antibiotic Drugs and Appendectomy (CODA) randomized clinical trial (RCT) with a parallel cohort study of participants who declined randomization and self-selected treatment. **DESIGN, SETTING, AND PARTICIPANTS:** The CODA trial was conducted in 25 US medical centers. Participants were enrolled between May 3, 2016, and February 5, 2020; all participants were eligible for at least 1 year of follow-up, with all follow-up ending in 2021. The randomized cohort included 1094 adults with appendicitis; the self-selection cohort included patients who declined participation in the randomized group, of whom 253 selected appendectomy and 257 selected antibiotics. In this secondary analysis, characteristics and outcomes in both self-selection and randomized cohorts are described with an exploratory analysis of cohort status and receipt of appendectomy. **INTERVENTIONS:** Appendectomy vs antibiotics. **MAIN OUTCOMES AND MEASURES:** Characteristics among participants randomized to either appendectomy or antibiotics were compared with those of participants who selected their own treatment. **RESULTS:** Clinical characteristics were similar across the self-selection cohort (510 patients; mean age, 35.8 years [95% CI, 34.5-37.1]; 218 female [43%; 95% CI, 39%-47%]) and the randomized group (1094 patients; mean age, 38.2 years [95% CI, 37.4-39.0]; 386 female [35%; 95% CI, 33%-38%]). Compared with the randomized group, those in the self-selection cohort were less often Spanish speaking (n = 99 [19%; 95%

CI, 16%-23%] vs n = 336 [31%; 95% CI, 28%-34%]), reported more formal education (some college or more, n = 355 [72%; 95% CI, 68%-76%] vs n = 674 [63%; 95% CI, 60%-65%]), and more often had commercial insurance (n = 259 [53%; 95% CI, 48%-57%] vs n = 486 [45%; 95% CI, 42%-48%]). Most outcomes were similar between the self-selection and randomized cohorts. The number of patients undergoing appendectomy by 30 days was 38 (15.3%; 95% CI, 10.7%-19.7%) among those selecting antibiotics and 155 (19.2%; 95% CI, 15.9%-22.5%) in those who were randomized to antibiotics (difference, 3.9%; 95% CI, -1.7% to 9.5%). Differences in the rate of appendectomy were primarily observed in the non-appendicolith subgroup. **CONCLUSIONS AND RELEVANCE:** This secondary analysis of the CODA RCT found substantially similar outcomes across the randomized and self-selection cohorts, suggesting that the randomized trial results are generalizable to the community at large. **TRIAL REGISTRATION:** ClinicalTrials.gov Identifier: NCT02800785.

Surgery

Ekkel E, Chandran T, Trpkovski M, and Hans S. Management of phlegmasia cerulea dolens caused by a giant leiomyoma. *J Vasc Surg Cases Innov Tech* 2022; 8(2):240-243. PMID: 35493345. [Full Text](#)

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In the present report, we describe the case of a young woman with a large uterine leiomyoma causing phlegmasia cerulea dolens with thrombosis of the left common and left external iliac veins. She underwent tissue plasminogen activator catheter thrombolysis and mechanical thrombectomy to temporize the condition until she could be evaluated by a gynecologic oncologist to remove the cause of the venous obstruction. Before the hysterectomy, a suprarenal inferior vena cava filter was placed. However, <12 hours after the hysterectomy, she developed recurrent thrombosis involving the left common and external iliac veins. She underwent repeat mechanical thrombectomy with wall stent placement in the left common iliac vein with resolution of her symptoms.

Surgery

Fasano GA, Bayard S, Tamimi R, Bea V, Malik M, Davis M, Simmons R, Swistel A, Marti J, Drotman M, Katzen J, Formenti S, Ng J, Astrow A, Taiwo E, Balogun O, Siegel B, Radzio A, Elreda L, **Chen Y**, and Newman L. Impact of the COVID-19 breast cancer screening hiatus on clinical stage and racial disparities in New York City. *Am J Surg* 2022; Epub ahead of print. PMID: 35641320. [Full Text](#)

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BACKGROUND: The impact of the COVID-19 mammography screening hiatus as well as of post-hiatus efforts promoting restoration of elective healthcare on breast cancer detection patterns and stage distribution is unknown. **METHODS:** Newly diagnosed breast cancer patients (2019-2021) at the New York Presbyterian (NYP) Hospital Network were analyzed. Chi-square and student's t-test compared characteristics of patients presenting before and after the screening hiatus. **RESULTS:** A total of 2137 patients were analyzed. Frequency of screen-detected and early-stage breast cancer declined post-hiatus (59.7%), but returned to baseline (69.3%). Frequency of screen-detected breast cancer was lowest for African American (AA) (57.5%) and Medicaid patients pre-hiatus (57.2%), and this disparity was reduced post-hiatus (65.3% for AA and 63.2% for Medicaid). **CONCLUSIONS:** The return to baseline levels of screen-detected cancer, particularly among AA and Medicaid patients suggest that large-scale breast health education campaigns may be effective in resuming screening practices and in mitigating disparities.

Surgery

Giorgakis E, **Ivanics T**, Khorsandi SE, Wallace D, Burdine L, Jassem W, Mathur AK, and Heaton N. Disparities in the Use of Older Donation After Circulatory Death Liver Allografts in the United States Versus the United Kingdom. *Transplantation* 2022; Epub ahead of print. PMID: 35642976. [Full Text](#)

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BACKGROUND: This study aimed to assess the differences between the United States and the United Kingdom in the characteristics and posttransplant survival of patients who received donation after circulatory death (DCD) liver allografts from donors aged >60 y. **METHODS:** Data were collected from the UK Transplant Registry and the United Network for Organ Sharing databases. Cohorts were dichotomized into donor age subgroups (donor >60 y [D >60]; donor ≤60 y [D ≤60]). Study period: January 1, 2001, to December 31, 2015. **RESULTS:** 1157 DCD LTs were performed in the United Kingdom versus 3394 in the United States. Only 13.8% of US DCD donors were aged >50 y, contrary to 44.3% in the United Kingdom. D >60 were 22.6% in the United Kingdom versus 2.4% in the United States. In the United Kingdom, 64.2% of D >60 clustered in 2 metropolitan centers. In the United States, there was marked inter-regional variation. A total of 78.3% of the US DCD allografts were used locally. One- and 5-y unadjusted DCD graft survival was higher in the United Kingdom versus the United States (87.3% versus 81.4%, and 78.0% versus 71.3%, respectively; P < 0.001). One- and 5-y D >60 graft survival was higher in the United Kingdom (87.3% versus 68.1%, and 77.9% versus 51.4%, United Kingdom versus United States, respectively; P < 0.001). In both groups, grafts from donors ≤30 y had the best survival. Survival was similar for donors aged 41 to 50 versus 51 to 60 in both cohorts. **CONCLUSIONS:** Compared with the United Kingdom, older DCD LT utilization remained low in the United States, with worse D >60 survival. Nonetheless, present data indicate similar survivals for older donors aged ≤60, supporting an extension to the current US DCD age cutoff.

Surgery

Ivanics T, Rajendran L, Abreu PA, Claasen M, Shwaartz C, Patel MS, Choi WJ, Doyle A, Muaddi H, McGilvray ID, Selzner M, Beecroft R, Kachura J, Bhat M, Selzner N, Ghanekar A, Catral M, Sayed B, Reichman T, Lilly L, and Sapisochin G. Long-term outcomes of ablation, liver resection, and liver

transplant as first-line treatment for solitary HCC of 3 cm or less using an intention-to-treat analysis: A retrospective cohort study. *Ann Med Surg (Lond)* 2022; 77:103645. PMID: 35637985. [Full Text](#)

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BACKGROUND: Curative-intent therapies for hepatocellular carcinoma (HCC) include radiofrequency ablation (RFA), liver resection (LR), and liver transplantation (LT). Controversy exists in treatment selection for early-stage tumours. We sought to evaluate the oncologic outcomes of patients who received either RFA, LR, or LT as first-line treatment for solitary HCC ≤ 3 cm in an intention-to-treat analysis. **MATERIALS AND METHODS:** All patients with solitary HCC ≤ 3 cm who underwent RFA, LR, or were listed for LT between Feb-2000 and Nov-2018 were analyzed. Cox regression analysis was then performed to compare intention-to-treat (ITT) survival by initial treatment allocation and disease-free survival (DFS) by treatment received in patients eligible for all three treatments. **RESULTS:** A total of 119 patients were identified (RFA n = 83; LR n = 25; LT n = 11). The overall intention-to-treat survival was similar between the three groups. The overall DFS was highest for the LT group. This was significantly higher than RFA (p = 0.02), but not statistically significantly different from LR (p = 0.14). After multivariable adjustment, ITT survival was similar in the LR and LT groups relative to RFA (LR HR:1.13, 95%CI 0.33-3.82; p = 0.80; LT HR:1.39, 95%CI 0.35-5.44; p = 0.60). On multivariable DFS analysis, only LT was better relative to RFA (LR HR:0.52, 95%CI 0.26-1.02; p = 0.06; LT HR:0.15, 95%CI 0.03-0.67; p = 0.01). Compared to LR, LT was associated with a numerically lower hazard on multivariable DFS analysis, though this did not reach statistical significance (HR 0.30, 95%CI 0.06-1.43; p = 0.13). **CONCLUSION:** For treatment-naïve patients with solitary HCC ≤ 3 cm who are eligible for RFA, LR, and LT, adjusted ITT survival is equivalent amongst the treatment modalities, however, DFS is better with LR and LT, compared with RFA. Differences in recurrence between treatment modalities and equipoise in ITT survival provides support for a future prospective trial in this setting.

Surgery

Lehman HS, Diaz S, Dandalides A, and Carlin AM. Feasibility of an Opioid Sparing Discharge Protocol Following Laparoscopic Bariatric Surgery. *Obes Surg* 2022; Epub ahead of print. PMID: 35507273. [Full Text](#)

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BACKGROUND: Opioids are commonly prescribed after laparoscopic bariatric surgery but have untoward effects including dependence and diversion. Prior investigation revealed that over three-fourths of discharge opioids prescribed to our patients went unused. **OBJECTIVES:** To determine the feasibility of an opioid sparing discharge protocol following laparoscopic bariatric surgery. **METHODS:** A total of 212

opioid-naïve patients undergoing laparoscopic bariatric surgery were examined and divided into two groups; 106 prior to (Cohort A) and 106 after implementation of an opioid sparing discharge protocol (Cohort B). Opioids were converted to morphine milligram equivalents (MME) and post-operative consumption was examined. Data was described as mean \pm standard deviation. RESULTS: No patients in Cohort B and 54.7% (58) in Cohort A received an opioid discharge prescription (37.5 MME). Of the 154 patients that remained, only 1.3% (2) received one after discharge. Cohort A took greater amounts of opioids than Cohort B after discharge (4.74 ± 11 vs. 0.21 ± 2 MME; $p < 0.001$). During hospitalization, Cohort A took greater amounts of opioids (6.92 ± 11 vs. 2.74 ± 5 MME; $p < 0.001$) but lower amounts of methocarbamol (759 ± 590 vs. 966 ± 585 mg; $p = 0.011$). No patient requested an opioid prescription refill or presented to the emergency room secondary to pain. CONCLUSION: Following laparoscopic bariatric surgery, an opioid sparing discharge protocol is feasible with $< 2\%$ of patients receiving opioids after discharge and no increase in emergency room visits. Education regarding these protocols may impact the amount of opioids taken during hospitalization.

Surgery

Miller-Matero LR, Hecht LM, Patel S, Martens KM, Hamann A, and Carlin AM. Exploring gender, psychiatric symptoms, and eating behaviors as predictors of attrition to bariatric surgery. *Am J Surg* 2022; Epub ahead of print. PMID: 35570060. [Full Text](#)

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BACKGROUND: Only a small proportion of eligible individuals undergo bariatric surgery. The purpose was to examine attrition to surgery and whether psychiatric symptoms and eating behaviors differentially predicted attrition among men and women. METHOD: Data was collected from a retrospective chart review of 313 patients who underwent a pre-surgical psychosocial evaluation. RESULTS: The overall attrition rate was 33.5%; 42.6% of men and 31.7% of women experienced attrition. In the multivariate analysis of the entire sample, White patients (OR = 2.33, CI: 1.33, 4.08) and those without a history of binge eating (OR = 2.71, CI: 1.23, 5.97) were more likely to undergo surgery. In a multivariate analysis of women only, race and binge eating independently predicted attrition; however, no factors significantly predicted attrition among men. CONCLUSIONS: Factors identified at the pre-surgical psychosocial evaluation can identify patients at risk for attrition, and these factors may differ for men and women.

Surgery

Natour AK, Rteil A, Shepard A, Weaver M, Nypaver T, Nemeh H, Tanaka D, and Kabbani L. Outcomes of patients with acute type A aortic dissections and concomitant lower extremity malperfusion. *J Vasc Surg* 2022; Epub ahead of print. PMID: 35598820. [Full Text](#)

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OBJECTIVE: Acute lower limb ischemia (ALLI) is a serious risk within the context of aortic dissection repair. The aim of this study was to examine the outcomes of patients with acute type A aortic dissection (ATAD) and concomitant lower extremity malperfusion. METHODS: We performed a retrospective medical record review at our tertiary referral center of patients who underwent ATAD repair between January 2002 and June 2018. Univariate and multivariate analyses compared outcomes of patients with and without lower extremity malperfusion. Primary outcomes were 30-day and 1-year mortality. RESULTS: A total of 378 patients underwent ATAD repair during the study period. The mean age was 57 years, 68% were male, and 51% were White. There were 62 patients (16%) who presented with concomitant ALLI, including 35 (9%) who presented with isolated ALLI and 27 (7%) who had ALLI with

concomitant malperfusion of at least 1 other organ. Of the 62 patients with ALLI, 46 underwent only proximal aortic repair. Six patients died within the first 24 hours, and their limb perfusion were not assessed. Among the 40 patients who underwent isolated proximal repair and survived over 24 hours, 34 (85%) had resolution of their ALLI. Of the 16 patients who underwent concomitant lower extremity peripheral vascular procedures, 10 underwent bypass procedures, and 1 patient died within 24 hours due to refractory coagulopathy and hypotension. All 6 patients with adequate follow-up imaging had asymptomatic occlusion of the bypass graft with recanalization of the occluded native arteries. Patients who presented with any organ malperfusion had increased 30-day (odds ratio, 1.8; $P = .04$) and 1-year mortality (odds ratio, 1.8, $P = .04$) and decreased overall survival ($P = .0026$). In patients who had isolated ALLI, there was no significant difference in 30-day or 1-year mortality or overall survival ($P = .57$). CONCLUSIONS: Proximal repair of ATAD may resolve most associated ALLI, and isolated ALLI may not affect short-term or long-term survival. All patients with follow-up in our study who underwent extra-anatomical bypass developed asymptomatic graft occlusion, which could be attributed to competitive flow from the remodeled native arterial system. We believe that rapid and aggressive restoration of flow to the lower extremity is the best way to treat ALLI malperfusion syndrome. Close monitoring for the development of compartment syndrome is recommended.

Surgery

Shen MR, Jiang S, Millis MA, Bonner SN, Bonham AJ, Finks JF, Ghaferi A, **Carlin A**, and Varban OA. Racial variation in baseline characteristics and wait times among patients undergoing bariatric surgery. *Surg Endosc* 2022; Epub ahead of print. PMID: 35508664. [Full Text](#)

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BACKGROUND: Although bariatric surgery is the most effective treatment for obesity and weight-related comorbid diseases, utilization rates are disproportionately low among non-white patients. We sought to understand if variation in baseline characteristics or access to care exists between white and non-white patients. METHODS: Using a statewide bariatric-specific data registry, we evaluated all patients who underwent bariatric surgery between 2006 and 2020 and completed a preoperative baseline questionnaire, which included a question about self-identification of race. Patient characteristics, comorbidities, and time from initial preoperative clinic evaluation to date of surgery were compared among racial groups. RESULTS: A total of 73,141 patients met inclusion criteria with 18,741 (25.5%) self-identified as non-white. These included Black/African American ($n = 11,904$), Hispanic ($n = 3448$), Asian ($n = 121$), Native Hawaiian/Pacific Islander ($n = 41$), Middle Eastern ($n = 164$), Multiple ($n = 2047$) and other ($n = 608$). Non-white males were the least represented group, accounting for only 4% of all bariatric cases performed. Non-white patients were more likely to be younger (43.0 years vs. 46.6 years, $p < 0.0001$), disabled (16% vs. 11.4%, $p < 0.0001$) and have Medicaid (8.4% vs. 3.8%, $p < 0.0001$) when compared to white patients, despite having higher rates of college education (78.0% vs. 76.6, $p < 0.0001$). In addition, median time from initial evaluation to surgery was also longer among non-white patients (157 days vs. 127 days, $p < 0.0001$), despite having higher rates of patients with a body mass index above 50 kg/m² (39.0% vs. 33.2%, $p < 0.0001$). CONCLUSIONS: Non-white patients undergoing bariatric surgery represent an extremely diverse group of patients with more socioeconomic disadvantages and longer wait times when compared to white patients despite presenting with higher rates of severe obesity. Current guidelines and referral patterns for bariatric surgery may not be equitable and need further examination when considering the management of obesity within diverse populations to reduce disparities in care-of which non-white males are particularly at risk.

Urology

Agochukwu-Mmonu N, Murali A, Wittmann D, Denton B, Dunn RL, Montie J, **Peabody J**, Miller D, and Singh K. Development and Validation of Dynamic Multivariate Prediction Models of Sexual Function Recovery in Patients with Prostate Cancer Undergoing Radical Prostatectomy: Results from the MUSIC Statewide Collaborative. *Eur Urol Open Sci* 2022; 40:1-8. PMID: 35638089. [Full Text](#)

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BACKGROUND: Radical prostatectomy (RP) is the most common definitive treatment for men with intermediate-risk prostate cancer and is frequently complicated by erectile dysfunction. **OBJECTIVE:** To develop and validate models to predict 12- and 24-month post-RP sexual function. **DESIGN SETTING AND PARTICIPANTS:** Using Michigan Urological Surgery Improvement Collaborative (MUSIC) registry data from 2016 to 2021, we developed dynamic, multivariate, random-forest models to predict sexual function recovery following RP. Model factors (established a priori) included baseline patient characteristics and repeated assessments of sexual satisfaction, and Expanded Prostate Cancer Index Composite 26 (EPIC-26) overall scores and sexual domain questions. **OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS:** We evaluated three outcomes related to sexual function: (1) the EPIC-26 sexual domain score (range 0-100); (2) the EPIC-26 sexual domain score dichotomized at ≥ 73 for "good" function; and (3) a dichotomized variable for erection quality at 12 and 24 months after RP. A gradient-boosting decision tree was used for the prediction models, which combines many decision trees into a single model. We evaluated the performance of our model using the root mean squared error (RMSE) and mean absolute error (MAE) for the EPIC-26 score as a continuous variable, and the area under the receiver operating characteristic curve (AUC) for the dichotomized EPIC-26 sexual domain score (SDS) and erection quality. All analyses were conducted using R v3.6.3. **RESULTS AND LIMITATIONS:** We identified 3983 patients at 12 months and 2494 patients at 24 months who were randomized to the derivation cohort at 12 and 24 months, respectively. Using baseline information only, our model predicted the 12-month EPIC-26 SDS with RMSE of 24 and MAE of 20. The AUC for predicting EPIC-26 SDS ≥ 73 (a previously published threshold) was 0.82. Our model predicted 24-month EPIC-26 SDS with RMSE of 26 and MAE of 21, and AUC for SDS ≥ 73 of 0.81. Inclusion of post-RP data improved the AUC to 0.91 and 0.94 at 12 and 24 months, respectively. A web tool has also been developed and is available at https://ml4lhs.shinyapps.io/askmusic_prostate_pro/. **CONCLUSIONS:** Our model provides a valid way to predict sexual function recovery at 12 and 24 months after RP. With this dynamic, multivariate (multiple outcomes) model, accurate predictions can be made for decision-making and during survivorship, which may reduce decision regret. **PATIENT SUMMARY:** Our prediction model allows patients considering prostate cancer surgery to understand their probability before and after surgery of recovering their erectile function and may reduce decision regret.

Urology

Hiller SC, Daignault-Newton S, Rakic I, Linsell S, Conrado B, Jafri SM, Rubenstein R, Abdelhady M, Fischer CP, Gimenez E, Sarle R, Roberts WW, Maitland C, Yousif R, Elgin R, Galejs L, Konheim J, **Leavitt D**, Stockall E, Fontera JR, Wolf JS, Hollingsworth JM, Dauw CA, and Ghani KR. Appropriateness Criteria for Ureteral Stent Omission following Ureteroscopy for Urinary Stone Disease. *Urol Pract* 2022; 9(3):253-263. PMID: Not assigned. [Full Text](#)

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Introduction:To bridge the gap between evidence and clinical judgment, we defined scenarios appropriate for ureteral stent omission after uncomplicated ureteroscopy (URS) using the RAND/UCLA Appropriateness Method. We retrospectively assessed rates of appropriate stent omission, with the goal to implement these criteria in clinical practice. **Methods:**A panel of 15 urologists from the MUSIC (Michigan Urological Surgery Improvement Collaborative) met to define uncomplicated URS and the variables that influence stent omission decision making. Over 2 rounds, they scored clinical scenarios for appropriateness criteria (AC) for stent omission based on a combination of variables. AC were defined by median scores of 1 to 3 (inappropriate), 4 to 6 (uncertain) and 7 to 9 (appropriate). Multivariable analysis determined the association of each variable with AC scores. Uncomplicated URS cases in the MUSIC

registry were assigned AC scores and stenting rates assessed. Results: Seven variables affecting stent decision making were identified. Of the 144 scenarios, 26 (18%) were appropriate, 88 (61%) inappropriate and 30 (21%) uncertain for stent omission. Most scenarios appropriate for omission were pre-stented (81%). Scenarios with ureteral access sheath or stones >10 mm were only appropriate if pre-stented. Stenting rates of 5,181 URS cases correlated with AC scores. Stents were placed in 61% of cases appropriate for omission (practice range, 25% to 98%). Conclusions: We defined objective variables and AC for stent omission following uncomplicated URS. AC scores correlated with stenting rates but there was substantial practice variation. Our findings demonstrate that the appropriate use of stent omission is underutilized.

Urology

Jaiswal A, Baliu-Souza T, Turner K, Nadiminty N, **Rambhatla A**, Agarwal A, Krawetz SA, Dupree JM, Saltzman B, Schon SB, and Avidor-Reiss T. Sperm centriole assessment identifies male factor infertility in couples with unexplained infertility - a pilot study. *Eur J Cell Biol* 2022; 101(3):151243. PMID: 35640396.

[Full Text](#)

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Unexplained infertility affects about one-third of infertile couples and is defined as the failure to identify the cause of infertility despite extensive evaluation of the male and female partners. Therefore, there is a need for a multiparametric approach to study sperm function. Recently, we developed a Fluorescence-Based Ratiometric Analysis of Sperm Centrioles (FRAC) assay to determine sperm centriole quality. Here, we perform a pilot study of sperm from 10 fertile men and 10 men in couples with unexplained infertility, using three centriolar biomarkers measured at three sperm locations from two sperm fractions, representing high and low sperm quality. We found that FRAC can identify men from couples with unexplained infertility as the likely source of infertility. Higher quality fractions from 10 fertile individuals were the reference population. All 180 studied FRAC values in the 10 fertile individuals fell within the reference population range. Eleven of the 180 studied FRAC values in the 10 infertile patients were outliers beyond the 95% confidence intervals ($P = 0.0008$). Three men with unexplained infertility had outlier FRAC values in their higher quality sperm fraction, while four had outlier FRAC values in their lower quality sperm fraction (3/10 and 4/10, $P = 0.060$ and $P = 0.025$, respectively), suggesting that these four individuals are infertile due, in part, to centriolar defects. We propose that a larger scale study should

be performed to determine the ability of FRAC to identify male factor infertility and its potential contribution to sperm multiparametric analysis.

Urology

Piontkowski AJ, Corsi N, Morisetty S, Majdalany S, Rakic I, Li P, Arora S, Jamil M, Rogers C, Autorino R, and Abdollah F. Benefit of lymph node dissection in cN+ patients in the treatment of upper tract urothelial carcinoma: Analysis of NCDB registry. *Urol Oncol* 2022; Epub ahead of print. PMID: 35623996. [Full Text](#)

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OBJECTIVES: The benefits of lymph node dissection (LND) in surgically treated upper tract urothelial carcinoma (UTUC) patients who present with clinically positive nodes at diagnosis remain unclear. The aim of this study was to assess survival differences in cN+ patients who underwent radical nephroureterectomy (RNU) with LND vs. without LND. **METHODS:** The National Cancer Database was used to identify a total number of 423 cN+ patients from 2004 to 2016 with UTUC that underwent RNU. Of the 423 patients, 310 received LND. Kaplan-Meier (KM) plots were used to estimate survival in cN+ patients who received RNU with LND vs. without. Cox proportional hazards regression tested the impact of LND status on overall survival (OS) after adjusting for all available covariates. **RESULTS:** Median age of the patient population was 68 years (IQR 61-76), and 56.74% were male. Median follow-up was 1.8 years (IQR 0.9-3.5). For the entire cohort, the 2-year OS rate was 51.8%, and it was 52.1% vs. 51.1% in patients who underwent LND vs. not (log-rank p-value=0.2). On multivariable analysis, performing LND had no statistically significant impact on OS (HR 0.93 95%CI 0.696-1.235, P = 0.9). Repeating the analysis in patients who had exclusively cN1 (HR 0.76 95%CI 0.469-1.223, P = 0.26) or cN2/3 (HR 0.844 95%CI 0.556-1.28, P = 0.43) disease also failed to demonstrate a significant impact of LND on survival. **CONCLUSION:** In cN+ patients with UTUC, performing LND in addition to RNU at any clinical stage does not seem to have a significant impact on OS.

Urology

Sood A, Grauer R, Jeong W, Butaney M, Mukkamala A, Borchert A, Baumgarten L, Hensley PJ, Abdollah F, and Menon M. Evaluating post radical prostatectomy mechanisms of early continence. *Prostate* 2022; Epub ahead of print. PMID: 35579026. [Full Text](#)

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BACKGROUND: To identify the periprostatic structures associated with early return of urinary continence after radical prostatectomy (RP). **METHODS:** We compared total continence results between four different techniques of robot-assisted radical prostatectomy (RARP). Specifically, we studied 1-week and 1-month zero-pad continence rates of anterior (n = 60), posterior (n = 59), a novel hybrid posterior-anterior (n = 12), and transvesical (n = 12) approaches of RARP. Each technique preserved a unique set of periprostatic anatomic structures, thereby, allowing evaluation of the individual impact of preservation of nerves, bladder neck, and space of Retzius with associated anterior support structures on early continence. Urethral length was preserved in all approaches. The space of Retzius was preserved in posterior and transvesical approaches, while the bladder neck was preserved in posterior and hybrid

approaches. Nerve sparing was done per preoperative oncological risk. For all patients, 24-h pad usage rates and 24-h pad weights were noted at 1 week and 1 month after catheter removal. Multivariable logistic regression analysis was performed to identify predictors of early continence. Data were obtained from prospective studies conducted between 2015 and 2021. RESULTS: At 1 week, 15%, 42%, 45%, and 8% of patients undergoing anterior, posterior, hybrid, and transvesical RARP approaches, respectively, were totally continent ($p = 0.003$). These rates at 1 month were 35%, 66%, 64%, and 25% ($p = 0.002$), respectively. The transvesical approach, which preserved the space of Retzius but not the bladder neck, was associated with the poorest continence rates, while the posterior and hybrid approaches in which the bladder neck was preserved with or without space of Retzius preservation were associated with quickest urinary continence recovery. Bladder neck preservation was the only significant predictor of 1-week and 1-month total continence recovery in adjusted analysis, Odds ratios 9.06 ($p = 0.001$) and 5.18 ($p = 0.004$), respectively. CONCLUSIONS: The beneficial effect of the Retzius-sparing approach on early continence recovery maybe associated with bladder neck preservation rather than space of Retzius preservation.

Urology

Sood A, Keeley J, Palma-Zamora I, Chien M, Corsi N, Jeong W, Rogers CG, Trinh QD, Peabody JO, Menon M, and Abdollah F. Anti-Androgen Therapy Overcomes the Time Delay in Initiation of Salvage Radiation Therapy and Rescues the Oncological Outcomes in Men with Recurrent Prostate Cancer After Radical Prostatectomy: A Post Hoc Analysis of the RTOG-9601 Trial Data. *Ann Surg Oncol* 2022;1-10; Epub ahead of print. PMID: 35608801. [Full Text](#)

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BACKGROUND: It is unknown whether the addition of anti-androgen therapy (AAT) to late salvage radiation therapy (sRT) can lead to oncological outcomes equivalent to that of early sRT in men with recurrent prostate cancer (CaP) after surgery. METHODS: Data on 670 men who participated in the Radiation Therapy Oncology Group (RTOG)-9601 trial and who experienced biochemical recurrence were extracted using the National Clinical Trials Network (NCTN) data archive platform. Patients were stratified into four treatment groups: early sRT (pre-sRT prostate-specific antigen [PSA] < 0.7 ng/mL) and late sRT (pre-sRT PSA ≥ 0.7 ng/mL) with/without concomitant AAT, based on cut-offs reported in the original trial. Time-varying Cox proportional hazards and Fine-Gray competing-risk regression analyses assessed the adjusted hazards of overall mortality, CaP-specific mortality, and metastasis among the four treatment groups. RESULTS: At 15-years (median follow-up of 14.7 years), for patients treated with early sRT, early sRT with AAT, late sRT, and late sRT with AAT, the overall mortality, CaP-specific mortality, and metastasis rates were 22.9, 22.8, 40.1, and 22.9% (log-rank $p = 0.0039$), 12.1, 3.9, 22.7, and 8.0% (Gray's $p = 0.0004$), and 18.8, 14.6, 35.9, and 19.5% (Gray's $p = 0.0004$), respectively. Time-varying multivariable adjusted analysis demonstrated increased hazards of overall mortality in patients receiving delayed sRT versus early sRT (hazards ratio [HR] 1.49, 95% confidence interval [CI] 1.02-2.17); however, no difference remained after the addition of concomitant AAT to late sRT (HR 0.85, 95% CI 0.55-1.32, referent early sRT). Likewise, the hazards of cancer-specific mortality and metastatic progression were worse for late sRT when compared with early sRT, but were no different after the addition of AAT to late sRT. CONCLUSIONS: Poorer outcomes associated with late sRT in men with recurrent CaP may be rescued by delivery of concomitant AAT.

Urology

Sood A, Keeley J, Palma-Zamora I, Chien M, Corsi N, Jeong W, Rogers CG, Trinh QD, Peabody JO, Menon M, and Abdollah F. ASO Visual Abstract: Anti-androgen Therapy Overcomes the Time Delay in Initiation of Salvage Radiation Therapy and Rescues the Oncological Outcomes in Men with Recurrent Prostate Cancer After Radical Prostatectomy-A Post Hoc Analysis of the RTOG 9601 Trial Data. *Ann Surg Oncol* 2022; Epub ahead of print. PMID: 35637326. [Full Text](#)

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Conference Abstracts

Emergency Medicine

Kim R, McKibben L, Lin T, Pang G, Tungate AS, Hendry PL, Kurz MC, Peak DA, Jones J, Rathlev NK, Swor RA, Domeier RM, Velilla MA, **Lewandowski C**, Datner E, Pearson C, Lee DC, Mitchell P, McLean SA, and Linnstaedt SD. P624. Risk Prediction for Posttraumatic Stress Symptoms Following Trauma Exposure. *Biol Psychiatry* 2022; 91(9):S341-S342. PMID: Not assigned. [Full Text](#)

Background: Posttraumatic stress symptoms (PTSS) are common following trauma exposure. Identification of individuals with PTSS at the time of emergency care is important to enable preventive interventions. In this study, we used baseline survey data from two large prospective cohort studies to identify the most influential predictors of PTSS at the time of presentation for emergency care and to develop a clinical decision support tool to identify individuals who develop substantial PTSS. **Methods:** Self-identifying white and black American men and women (n=1,546) presenting to one of sixteen emergency departments (EDs) within 24 hours of motor vehicle collision (MVC) trauma were enrolled. Individuals with substantial PTSS (≥ 33 , IES-R) six months after MVC were identified via follow-up questionnaire. Sociodemographic, pain, general health, event, and psychological/cognitive characteristics collected in the ED and used in prediction modeling. Ensemble learning methods and Monte Carlo cross-validation were used for feature selection and to determine prediction accuracy. External validation was performed on a hold-out sample (30% of total sample). **Results:** 25% (n=394) of individuals reported PTSS six months following MVC. Regularized linear regression was the top performing ensemble learning method. The top thirty factors together showed good reliability in predicting PTSS in the external sample (AUC=0.79+/-0.0017). Top predictors included acute pain severity, expectations of recovery, socioeconomic status, self-reported "race/ethnicity", and psychological symptoms. **Conclusions:** These analyses add to a growing literature indicating that influential predictors of PTSS can be identified and risk for future PTSS estimated from characteristics easily available/assessable at the time of ED presentation following trauma. **Supported By:** NIAMS R01AR060852 (McLean), R01AR056328 (McLean), K01AR071504 (Linnstaedt); NINDS R01NS118563 (Linnstaedt and McLean), and the Rita Allen Foundation (Linnstaedt) **Keywords:** Post-Traumatic Stress Disorder (PTSD), Posttraumatic Stress Symptoms, Symptom Prediction, Machine Learning, Motor Vehicle Collision Trauma

Endocrinology and Metabolism

Yaseen A, and Levy S. Abstract #1182615: Panhypopituitarism Induced by COVID-19 Infection. *Endocr Pract* 2022; 28(5):S115. PMID: Not assigned. [Full Text](#)

Introduction: Coronavirus disease 2019 (COVID-19) infection has led to multiple endocrinopathies. We present a case of panhypopituitarism induced by COVID -19 infection. **Case Description:** 76 yo male with history of type 2 diabetes, hypertension, and 1.5 cm stable, nonfunctioning, pituitary macroadenoma diagnosed in 2017 had multiple admissions for altered mental status and hyponatremia following COVID-19 infection in April 2020. Workup revealed low free T4 0.60 ng/dL (0.8-1.8), low random cortisol 1.8 mcg/dL(2.9-19.4), high prolactin 33.5 ng/mL (2-18), low total testosterone < 10 ng/dl (175-781), SHBG 32.7 nmol/L (13.3-89.5), and low gonadotropins. While hospitalized, he was diagnosed with panhypopituitarism and started on glucocorticoids and levothyroxine. Repeat MRI pituitary done after discharge, documented stability of the macroadenoma without hemorrhage. To date, the patient remains on glucocorticoid replacement and thyroid hormone replacement in stable state. **Discussion:** Hypopituitarism from any etiology has an incidence of 4.2 per 100,000. Hormone replacement therapy remains the mainstay of treatment. This case represents a patient who had unexplained recurrent hyponatremia after COVID-19 infection and later diagnosed with pan-hypopituitarism. Given the continued pandemic, more endocrinopathies related to the COVID-19 infection have been reported. We have data for other viral infections, such as SARS and Dengue, documenting pituitary dysfunction. Review of literature documents SARS infection leading to post infectious hypophysitis with resulting secondary hypocortisolism and hypothyroidism. The cause was thought to be virus binding to pituitary angiotensin-converting enzyme 2 (ACE2) receptors. There is also data supporting COVID-19 infection leading to pituitary apoplexy and hypophysitis, though the number of cases reported is limited. The pathophysiology is thought to be the COVID 19 virus binding to pituitary ACE2 receptors for which it has a 10-20-fold higher affinity. Furthermore, the hypothalamus also expresses ACE2 receptors making it a

target for the virus. The binding leads to cellular destruction and autoimmune collateral damage. Hypothalamic pituitary dysfunction could be due to direct effect of virus. The virus can also lead to reversible hypophysitis.

Hematology-Oncology

Qutob O, Bensenhaver J, Susick L, Petersen L, Lehrberg A, Dimaano F, and Schwartz T. Sentinel Lymph Node Positivity in Clinically Node Negative Breast Cancer Patients After Neoadjuvant Chemotherapy: Opportunities to Defer Intraoperative Frozen Section Analysis. *Ann Surg Oncol* 2022; 29(SUPPL 2):421-421. PMID: Not assigned. [Full Text](#)

INTRODUCTION: Neoadjuvant chemotherapy (NACT) is frequently implemented in a breast cancer treatment plan. In clinically node negative (cN0) patients following NACT, it is routine to perform sentinel lymph node (SLN) biopsy with intraoperative frozen section analysis with subsequent axillary lymph node dissection (ALND) if metastatic disease were detected. We aim to define the rate of sentinel node positivity (ypN1 (sn)) at our institution in patients who presented as cN0 and received NACT. **METHODS:** Using our IRB approved breast cancer database a retrospective chart review was performed for all T1-T3, cN0 primary breast cancer cases who underwent NACT from 2016 to 2021 and have undergone a subsequent definitive operation at our institution. Demographics, clinical characteristics, tumor biology and staging were recorded. We stratified by hormone receptor (HR) and HER2 status defined as: HR negative (0%), HR weakly positive (1-10%), HR positive (>11%), HER2 negative (0, 1+, 2+ negative by FISH), HER2 positive (3+, 2+ positive by FISH) **RESULTS:** We identified 139 cN0 cases undergoing NACT from 2016 to 2021. Forty were excluded, leaving 99 for analysis. Of these, 8 (8 %) were found to be ypN1(sn). Of the 71 HER2 negative cases, we found 32 HR negative (triple negative) and 11 HR weakly positive, none of which (0%) were found to be ypN1(sn), and 28 HR positive of which 7 (25%) were found to be ypN1(sn). Of the 28 HER2 positive cases, we found 11 HR negative and 3 HR weakly positive cases, none of which (0%) were found to be ypN1, and 14 HR positive of which 1 (7%) was found to be a micrometastasis (ypN1mic(sn)) **CONCLUSIONS:** Our results show that for the more aggressive tumor subtypes, including HR negative and HR weakly positive, the rate of ypN1(sn) after NACT in cN0 patients was 0%. These results suggest that frozen section could be avoided at the time of surgery for these patients in lieu of permanent pathology, due to the negligible likelihood of finding ypN1(sn) and thus needing ALND.

Hematology-Oncology

Saad MA, Clark JM, Shah RA, Siddiqui F, Parikh PJ, Gartrelle KJ, Natour AKK, Khan GN, and Kwon DS. A single-center Analysis of 30-and 90-Day Post-pancreatectomy Complications in Patients Undergoing Neoadjuvant Radiation with EBRT vs. MRI-guided SBRT. *Ann Surg Oncol* 2022; 29(SUPPL 2):439-440. PMID: Not assigned. [Full Text](#)

INTRODUCTION: Stereotactic MRI -guided adaptive radiation therapy (SMART) is being investigated for enhanced efficacy in locally advanced, borderline resectable and medically inoperable pancreatic cancer. Traditionally, conventionally fractionated chemoradiation (EBRT) has been used for operable patients. We sought to evaluate whether there would be differences in surgical complications and outcomes in the 30- and 90- day postoperative period in patients who received either neoadjuvant EBRT or SMART followed by definitive surgery. **METHODS:** A retrospective single-center analysis of patients with either resectable, borderline resectable or locally advanced tumors of the pancreas or duodenum, treated with neoadjuvant radiation and surgical management between 2014 and 2021 was performed. Patient demographics and post-surgical complications were collected and stratified according to both treatment arms. The International Study Group of Pancreatic Surgery (ISGPS) classifications were used to define and grade postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE) and postpancreatectomy hemorrhage (PPH). A univariate analysis was done followed by a multivariate analysis. **RESULTS:** Among the 65 patients (mean age 62.6 years, 46% female) who underwent definitive surgical intervention, 44 (67.7%) received EBRT, and 21 (32.3%) received SMART. Baseline characteristics including age, sex, race, ASA, and Charlson comorbidity index (CCI) scores were found to be similar. On univariate analysis, PPH was significantly higher in SMART (OR, 6.6; 95% CI, 1.2 to 37.3; p = 0.034). After adjusting for confounders on multivariate analysis, it appears there is a trend towards higher PPH in the SMART cohort (p = 0.052). **CONCLUSIONS:** Neoadjuvant SMART followed by definitive surgery is

not associated with worse outcomes in the 30- and 90- day postoperative period vs. neoadjuvant EBRT. Although there was a trend towards PPH on multivariate analysis, further discussion is warranted involving vascular resection, vascular stents and anticoagulation.

Hematology-Oncology

Saad MA, Gartelle KJ, Shah RA, Clark JM, Langley KA, Field EA, Steffes CP, and Kwon DS.

Disparity Outcomes in Patients Undergoing Pancreas Surgery at an Urban Tertiary Care Center. *Ann Surg Oncol* 2022; 29(SUPPL 2):443-443. PMID: Not assigned. [Full Text](#)

INTRODUCTION: Previous studies have shown significant disparities in pancreas cancer outcomes in African American (AA) compared to non-AA patients. Pancreas surgery continues to be associated with significant morbidity, however, there is little reported data on pancreas surgical outcomes by race. We sought to evaluate how race would affect surgical outcomes in an urban tertiary care center for patients undergoing pancreas surgery. **METHODS:** A retrospective single-center analysis of patients undergoing pancreas surgery between January 2013 and September 2021 was performed. Patient demographics and post-surgical complications were collected and stratified by race. Area Deprivation Index (ADI) was used to determine patient socioeconomic status. Charlson Comorbidity Index (CCI) was calculated for comorbidities. Clavien-Dindo (CD) complications, as well as postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE) and postpancreatectomy hemorrhage (PPH) were evaluated. Patient reoperation, readmission, and mortality in the 30- and 90- day period were collected and univariate and multivariate analyses were performed. **RESULTS:** Among 461 patients, 82% (N = 378) were nonAA and 18% (N = 83) were AA. Age and sex were found to be significantly different between the two groups, while ADI and CCI were not. Length of stay (LOS), POPF, PPH, PPH grade C and intra-abdominal abscess (IAA) were found to be significant on univariate analysis in the AA cohort. On multivariate analysis, LOS (OR 4.0; 95% CI 2.0-5.7; p < 0.001), POPF (OR 0.6; 95% CI 0.4-1.0; p = 0.043), PPH (OR 0.5; 95% CI 0.2-0.9; p = 0.022), PPH grade C (OR 0.2; 95% CI 0.1-0.7; p = 0.017) and IAA (OR 0.4; 95% CI 0.2-0.9; p = 0.017) were still significantly higher in the AA cohort. **CONCLUSIONS:** AA patients undergoing pancreas surgery were noted to have a longer LOS, higher incidence of POPF, PPH and IAA compared to non-AA patients. However, no significant difference was seen in reoperation rates, major CD complications, or 30- and 90-day readmission. Elucidating patient selection, tumor biology, and preoperative treatment algorithms may shed additional insight on the differences in surgical outcomes in this particular patient cohort.

Hypertension and Vascular Research

Ares G. Regulation of NKCC2 ubiquitination by Neddylation of Cullin-Ring Ligases in Thick Ascending Limb. *FASEB J* 2022; 36. PMID: Not assigned. [Full Text](#)

Hypertension and Vascular Research Division, Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan. Wayne State University, Physiology department, Detroit, Michigan. The Na/K/2Cl cotransporter (NKCC2) reabsorbs ~30% of the filtered NaCl by the glomeruli. Nitric Oxide and atrial natriuretic peptide decrease NaCl reabsorption in thick ascending limbs (TALs) by increasing the second messenger cyclic guanosine monophosphate (cGMP). cGMP decreases surface NKCC2 levels by increasing NKCC2 ubiquitination and proteasomal degradation. The Cullin-RING Ligases (CRLs) are the largest family of E3 ubiquitin ligases, responsible for ~20% of protein ubiquitination in mammals. Since the CRLs requires neddylation for its activation, we hypothesized that neddylation of CRLs is required for the cGMP-dependent increase on NKCC2 ubiquitination in TALs. To test our hypothesis, we pulled down ubiquitinated proteins and biotinylated surface proteins from Sprague-Dawley (SD) rats and blotted for NKCC2. First, we look at the expression of members of the cullin family and found expression of cullin-1, -2, -3, -4 and -5 in TALs from SD rats. Since activity of CRLs is dynamically regulated by neddylation, we blocked cullin neddylation using (MLN4924, 1 μ M) and studied whether cGMP increases NKCC2 ubiquitination. To measure ubiquitination of NKCC2, TALs suspensions were treated with proteasomal inhibitor (MG132, 20 μ M). TALs was divided in 4 aliquots and incubated at 37°C with vehicle or MLN4924 for 10 minutes and treated with vehicle or db-cGMP 500 μ M at 37°C for an extra 50 minutes. We found that blockade of cullin neddylation, inhibits the cGMP-dependent increase in ubiquitinated NKCC2 (baseline: 100%; db-cGMP 500 μ M: 162.5 \pm 10.3%; MLN4924: 75.1 \pm 20.2%; MLN4924 + db-cGMP 500 μ M: 96.8 \pm 19.6 %, p<0.05). As expected, neddylation of cullins was blunted in MLN4924 treated samples

(baseline: 100%; db-cGMP: 120.3 ± 24.4%; MLN4924: 11.0 ± 3.5%; MLN4924 + db-cGMP: 11.4 ± 5.8 %, p<0.05). These data indicate that neddylation of the CRLs mediates the cGMP-dependent increase in NKCC2 neddylation. NKCC2 activity is directly related to surface NKCC2 expression. Therefore, we study whether blockade of cullin neddylation prevents the cGMP-dependent decrease in surface NKCC2 expression. TALs suspensions were divided in 4 aliquots. TALs were incubated at 37°C with vehicle or MLN4924 for 10 minutes and then treated with vehicle or db-cGMP 500 µM at 37°C for an extra 20 minutes. We found that blockade of cullin neddylation, inhibits the cGMP-dependent decrease in surface NKCC2 expression. (baseline: 100%; db-cGMP: 81.0 ± 3.4%; MLN4924: 96.4 ± 2.2%; MLN4924 + db-cGMP: 99.8 ± 9.3 %, p<0.04). These data indicate that cullin neddylation is required for the cGMP-dependent decrease in surface NKCC2 expression. To our knowledge, this is the first evidence pointing to the E3 ubiquitin ligase complex involved in the ubiquitination of NKCC2 in native TALs. Identifying the E3 ubiquitin ligases that regulates NKCC2 activity may provide new targets for the development of specific loops diuretics.

Hypertension and Vascular Research

Arkhipov SN, Liao TDS, Potter DL, Bobbitt KR, Ortiz PA, and Pavlov TS. Dissociation of hypertension and renal damage after cessation of high salt diet in Dahl rats. *FASEB J* 2022; 36. PMID: Not assigned.

[Full Text](#)

BACKGROUND: Every year, thousands of hypertensive patients reduce salt consumption in the efforts to control blood pressure. Most of the studies agreed that about one-third of the patients had an excellent response, one-third had only a modest response, and one-third had little or no response. Irreversibility of high blood pressure is associated with various mechanisms underlying the self-sustaining character of hypertension. We hypothesize that chronic hypertension leads to sustained renal damage and excessive sodium reabsorption, staying even after removing the trigger, caused the initial blood pressure raise. **METHODS:** We used Dahl salt-sensitive rats for chronic continuous observation of blood pressure with radiotelemetry in conscious free moving animals. Rats were fed a 4%NaCl diet to induce hypertension, and then the diet was switched back to normal (0.4%NaCl). Patch-clamp analysis was performed in freshly isolated, split-open cortical collecting ducts to characterize activity of epithelial sodium channel (ENaC), responsible for sodium reabsorption in aldosterone-sensitive distal nephron. Flow cytometry, trichrome staining and FITC-inulin clearance estimated immune cell infiltration, renal damage and renal function. **RESULTS:** We found that blood pressure increase is reversible if induced by a short 3-day long feeding with 4%NaCl diet. A 3-week long high salt diet develops a sustaining hypertension (MAP ~150 mmHg): switching back to 0.4%NaCl diet slightly reduces blood pressure (to 145 mmHg) next day, but later hypertension progresses, reaching ~158 mmHg. Notably, the self-sustaining phase of hypertension was sensitive to benzamil treatment, which lowered BP to ~136 mmHg. Patch clamp analysis revealed that development of hypertension was accompanied with elevated ENaC activity which also stayed high, despite withdrawal of 4%NaCl diet. A separate subset of experiments demonstrated that dietary salt reduction in hypertensive animals decreases the number of total CD45+CD3+CD4+ and CD45+CD3+CD8+ cells in renal tissues. Also, we found a reduced area of protein casts abundance in the post-salt hypertensive group in comparison with age-matched rats kept on a high salt diet, and improving a glomerular filtration rate in the post-salt period. **CONCLUSION:** Based on our earlier publications and current data, we conclude that ENaC activity contributes to both development of salt-sensitive hypertension and its continuation in the absence of high salt challenge. However, dietary salt restriction reduces renal inflammation and damage in hypertensive animals.

Hypertension and Vascular Research

Caceres P. Endothelial Cell-Secreted Semaphorin 3F Promotes Proximal Tubule Cell Maturation and Polarization. *FASEB J* 2022; 36. PMID: Not assigned. [Full Text](#)

Endothelial cells secrete trophic factors that contribute to the maturation of surrounding tissues. The notion of the microvasculature as niche for local differentiation and homeostasis has implication in diseases like diabetic kidney disease, in which the microvasculature is lost at early stages. Endothelial cells are known to produce semaphorins (Sema) as signal molecules that target cells in proximity. The isoform Sema3F is secreted by endothelial cells throughout the body, and it is known to regulate angiogenesis in an autocrine fashion. However, Sema3F can potentially reach other neighboring cell

types, in particular kidney proximal tubule, since this epithelium is closely associated with peritubular capillaries. It is not known whether Sema3F influences proximal tubule homeostasis. We hypothesize that endothelial cells secrete Sema3F, which in turn promotes proximal tubule epithelial maturation and polarization. We utilized the human proximal tubule cell line RPTEC/hTERT since these cells polarize in trans-well permeable support by 2 weeks, and they retain expression and apical-basolateral polarization of proximal tubule proteins. To study the role of endothelial cells in RPTEC/hTERT maturation, we co-culture them with the human endothelial cell line HUVEC. First, we measured Sema3F release from HUVEC endothelial cells by ELISA and observed that they secrete 206 ± 3 pg Sema3F/cm² /day. Next, to determine whether HUVEC endothelial cells promote proximal tubule maturation, we monitored the progressive acquisition of trans-epithelial resistance as a measure of tight junction maturation. We observed that in co-culture with HUVEC endothelial cells, RPTEC/hTERT cells developed a trans-epithelial resistance that was $11 \pm 3\%$ higher at 1 week, and $27 \pm 5\%$ higher at 2 weeks compared to monoculture ($p < 0.05$). To test whether Sema3F stimulates RPTEC/hTERT trans-epithelial resistance, we added 200ng/mL of recombinant human Sema3F to cell cultures. We observed that Sema3F increased RPTEC/hTERT trans-epithelial resistance at 1 week (vehicle= 152 ± 5 Ω /cm² vs. Sema3F= 171 ± 3 Ω /cm² ; $p < 0.05$) and 2 weeks (vehicle= 150 ± 2 Ω /cm² vs. Sema3F= 182 ± 4 Ω /cm² ; $p < 0.05$). Also, Sema3F accelerated polarization of the basolateral protein E-cadherin measured by surface biotinylation over 2 weeks. Finally, to determine whether Sema3F produced by endothelial cells stimulate RPTEC/hTERT maturation, we silenced Sema3F in HUVEC endothelial cells via lentivirus-transduction of silencing shRNAs. We observed that silencing Sema3F in HUVEC cells prevented the stimulation of RPTEC/hTERT trans-epithelial resistance, while control shRNA transduction showed the expected stimulation at 7 days (monoculture= 222 ± 4 Ω /cm² vs. coculture-shSema3F= 218 ± 7 Ω /cm² ; $p = \text{NS}$ vs. coculture-shControl= 231 ± 8 Ω /cm² ; $p < 0.05$). We conclude that HUVEC endothelial cells secrete Sema3F, which reaches RPTEC/hTERT proximal tubule cells in co-culture and stimulates tight junction maturation and polarization. These findings have relevance as a possible mechanism of disease in pathologies like diabetic kidney disease where the microvasculature is compromised.

Hypertension and Vascular Research

Granados Pineda J, Haque M, Ares-Sarmiento G, and Ortiz PA. SPAK-Independent NKCC2 Phosphorylation in Dahl SS Rats: A Role for TNIK in NKCC2 Hyperphosphorylation. *FASEB J* 2022; 36. PMID: Not assigned. [Full Text](#)

Increased NaCl reabsorption in the Thick Ascending Limb (TAL) is implicated in salt sensitive hypertension. NaCl reabsorption by the TAL is mediated by the apical Na/K/2Cl cotransporter NKCC2. We reported that NKCC2 phosphorylation at Thr 96,101 and surface expression are enhanced in Dahl Salt sensitive rats (Dahl SS) on normal or high salt diets. The phosphorylation of SPAK-related proline/alanine-rich kinase (SPAK), an upstream kinase for Thr 96,101 in NKCC2, was found to be higher in Dahl SS TALs. Deletion of SPAK in Dahl SS, lowers NKCC2 phosphorylation and expression and blunts salt-sensitive hypertension, but does not completely prevent this. Other kinases may be involved in NKCC2 phosphorylation. Using a targeted proteomics approach, we identified TNIK (Traf2 and NCK interacting kinase) as a kinase that binds and phosphorylates Thr 96,101 in NKCC2. We hypothesize that TNIK is in part responsible for enhanced NKCC2 phosphorylation in Dahl SS rats. We first measured total expression of SPAK, OSR1 and TNIK by Western blot in TALs isolated from Dahl SS and control rats. SPAK and OSR1 expression (normalized to GAPDH) was similar between strains whereas TNIK expression was 3-fold higher in Dahl SS TALs (control: 100, Dahl SS: $396 \pm 80\%$, $n = 5$, $p < .025$). We then tested whether a novel TNIK inhibitor (KY-05009) decreased NKCC2 phosphorylation in Dahl SS rats. Treating TALs from Dahl SS with KY-05009 (1 μM) for 25 min decreased NKCC2 Thr 96,101 phosphorylation by $40 \pm 4\%$ ($p < 0.05$, $n = 5$). To study whether NKCC2 phosphorylation can be stimulated in the absence of SPAK, we used SPAK knockout Dahl SS rats. Baseline NKCC2 expression and phosphorylation in TALs was 50% lower in Dahl SS-SPAK KO TALs, however, stimulation of Beta-adrenergic receptors with Isoproterenol increased NKCC2 phosphorylation by $192 \pm 49\%$ ($p < 0.01$, $n = 4$) in SPAK-KO. Similarly, the cAMP analogue db-cAMP (500 μM) increased NKCC2 phosphorylation by $939 \pm 183\%$ in SPAK KO ($p < 0.01$ $n = 4$) and by $497 \pm 105\%$ ($p < 0.01$ $n = 4$) in control rat TALs, indicating that a kinase other than SPAK is essential for baseline and cAMP-stimulated NKCC2 phosphorylation in Dahl SS rats. We conclude that enhanced NKCC2 phosphorylation at baseline in Dahl SS TALs is in part caused by TNIK, which show 3-fold higher expression in this strain. SPAK also contributes to higher

baseline NKCC2 phosphorylation, whereas a kinase other than SPAK (either TNIK or OSR1) is involved in cAMP-stimulated NKCC2 Thr 96,101 phosphorylation in Dahl SS TALs.

Hypertension and Vascular Research

Haque MZ, Rey F, and **Ortiz PA**. Gut microbiota depletion with antibiotics enhances fructose induced salt-sensitive hypertension in normal rats. *FASEB J* 2022; 36. PMID: Not assigned. [Full Text](#)

INTRODUCTION- We reported that 20% fructose in drinking water induced salt-sensitive hypertension in normal rats. High fructose (HF) or high salt (HS) intake reportedly alter the gut microbiota, which influences a variety of microbial-regulated bioactive metabolites that can affect blood pressure and renal function. The contribution of the gut microbiota to fructose induced salt-sensitive hypertension or renal function has not been studied. **Aim-** We hypothesized that gut microbiota depletion with antibiotics (ABX) would change fructose induced salt-sensitive hypertension, renal excretory function and plasma levels of bacterial metabolites (lactate, β -hydroxy-butyrate). **METHODS-** Sprague Dawley rats were treated with a cocktail of antibiotics (ABX group, in g/L 1.0 ampicillin, 1.0 neomycin sulphate, 1.0 metronidazole, and 0.5 vancomycin in drinking water) for 4 weeks followed by a 0.33 fractional maintenance dose for up to 12 weeks) or control diet (no-ABX). On week 5, all rats were given 20% fructose (HF) in drinking water and fed a diet with normal salt (NS, 0.4% Na) or high salt content (HS, 4% Na). Rats were divided as: Group 1 (HF + NS, no-ABX, n= 6), Group 2 (HF + NS + ABX, n=6), Group 3 (HF + HS, no-ABX, n= 8), Group 4 (HF + HS + ABX, n= 8). We trained rats and measured systolic blood pressure (SBP) for 12 weeks by tail-cuff and collected feces before and after ABX, to measure gut c-DNA content. On the 12th week, we collected 24- hour urine and plasma before the end of the protocol. **RESULTS:** - Antibiotics induced microbiome depletion (ABX) decreased fecal DNA content by 83%. Baseline SBP (in mmHg) or urine albumin excretion was not affected by ABX. Fructose with normal salt diet did not change SBP with (125 \pm 4) or without ABX (124 \pm 3). HS significantly increased SBP in rats fed fructose without ABX (from 123 \pm 3 to 141 \pm 4, p<.05) but the increase was greater in ABX rats (from 124 \pm 4 to 155 \pm 3, p<.05). Average increase on SBP was 26 \pm 2 in HF+HS with ABX, but only 15 \pm 2 without ABX (p<.001). In HF + HS groups, ABX decreased plasma lactate from 1657 \pm 259 to 905 \pm 144 μ M (p<.01), and β -hydroxy-butyrate from 861 \pm 144 vs 220 \pm 53 μ M (p<.001). Non-fasted plasma insulin was also decreased by ABX in HF+HS rats (0.77 \pm 0.13 to 0.36 \pm 0.06 ng/mL, p<.03). The increase in body weight was similar in HF+HS rats with or without ABX. **CONCLUSION:** - Chronic antibiotic treatment induced gut microbiota depletion and enhanced fructose induced salt-sensitive hypertension in normal rats, an effect that was associated with decreased plasma beta-hydroxy-butyrate, lactate and insulin. Additional studies should focus on direct renal effects of ABX on salt handling.

Hypertension and Vascular Research

Maskey D, Jayakumar A, **Monu SR**, and **Ortiz PA**. Expression of ALMS1 in podocytes: possible role in filtration function. *FASEB J* 2022; 36. PMID: Not assigned. [Full Text](#)

Previously, we identified Alstrom Syndrome 1 (ALMS1) as an interacting partner of NKCC2 in the Thick Ascending limb of the loop of Henle (TAL). Mutations in the ALMS1 gene in humans cause Alström syndrome, characterized by progressive metabolic alterations that include obesity, hypertension, and chronic kidney disease (CKD). SNPs in ALMS1 are associated with lower GFR in GWAS. However, role of ALMS1 in glomerular filtration has not been studied. We hypothesized that ALMS1 is expressed in glomerular podocytes where it may play a role in podocyte filtration function. To begin studying this, we localized ALMS1 expression to podocytes by immunofluorescence labeling of Actinin-4, abundantly expressed in podocytes, and ALMS1. Confocal imaging showed that ALMS1 is co-localized with Actinin-4 in rat podocytes. In addition, ALMS1 was also expressed in an immortalized mouse podocyte cell line, as was Actinin-4 and nephrin, as measured by Western blot and immunofluorescence microscopy. To determine if ALMS1 plays a role in podocyte pathology we measured nephrin expression in ALMS1 KO rats. These rats were generated in the Dahl SS genetic background and are hypertensive on a normal salt diet. We found that nephrin expression in renal cortical lysates was decreased by 61 \pm 08% (p<0.05, n=7) in ALMS1 KO rats. To study if ALMS1 deletion could play a role in filtration barrier function we measured albumin/creatinine ratio in urine samples from 14-16 weeks old wild type (WT) and ALMS1 KO rats. In ALMS1 KO rats, urinary albumin excretion was higher than control rats (WT: 4 \pm 2; ALMS1 KO:

26±6, n=6, p<0.05). Taken together, our data show that ALMS1 is expressed in rat and mouse podocytes where it may play a role in filtration barrier function by maintaining podocyte biology.

Internal Medicine

Yaseen A, and Levy S. Abstract #1182615: Panhypopituitarism Induced by COVID-19 Infection. *Endocr Pract* 2022; 28(5):S115. PMID: Not assigned. [Full Text](#)

Introduction: Coronavirus disease 2019 (COVID-19) infection has led to multiple endocrinopathies. We present a case of panhypopituitarism induced by COVID -19 infection. Case Description: 76 yo male with history of type 2 diabetes, hypertension, and 1.5 cm stable, nonfunctioning, pituitary macroadenoma diagnosed in 2017 had multiple admissions for altered mental status and hyponatremia following COVID-19 infection in April 2020. Workup revealed low free T4 0.60 ng/dL (0.8-1.8), low random cortisol 1.8 mcg/dL(2.9-19.4), high prolactin 33.5 ng/mL (2-18), low total testosterone < 10 ng/dl (175-781), SHBG 32.7 nmol/L (13.3-89.5), and low gonadotropins. While hospitalized, he was diagnosed with panhypopituitarism and started on glucocorticoids and levothyroxine. Repeat MRI pituitary done after discharge, documented stability of the macroadenoma without hemorrhage. To date, the patient remains on glucocorticoid replacement and thyroid hormone replacement in stable state. Discussion: Hypopituitarism from any etiology has an incidence of 4.2 per 100,000. Hormone replacement therapy remains the mainstay of treatment. This case represents a patient who had unexplained recurrent hyponatremia after COVID-19 infection and later diagnosed with pan-hypopituitarism. Given the continued pandemic, more endocrinopathies related to the COVID-19 infection have been reported. We have data for other viral infections, such as SARS and Dengue, documenting pituitary dysfunction. Review of literature documents SARS infection leading to post infectious hypophysitis with resulting secondary hypocortisolism and hypothyroidism. The cause was thought to be virus binding to pituitary angiotensin-converting enzyme 2 (ACE2) receptors. There is also data supporting COVID-19 infection leading to pituitary apoplexy and hypophysitis, though the number of cases reported is limited. The pathophysiology is thought to be the COVID 19 virus binding to pituitary ACE2 receptors for which it has a 10-20-fold higher affinity. Furthermore, the hypothalamus also expresses ACE2 receptors making it a target for the virus. The binding leads to cellular destruction and autoimmune collateral damage. Hypothalamic pituitary dysfunction could be due to direct effect of virus. The virus can also lead to reversible hypophysitis.

Neurology

Zahoor I, Waters J, Datta I, Cerghet M, Poisson L, Rattan R, and Giri S. Predicting Disease Progression in Multiple Sclerosis by using a Combination of Highly Sensitive Single Molecule Array Technology (SIMOA) and Untargeted Metabolomics. *Mult Scler* 2022; 28(1_SUPPL):43-43. PMID: Not assigned. [Full Text](#)

Obstetrics, Gynecology and Women's Health Services

Zahoor I, Waters J, Datta I, Cerghet M, Poisson L, Rattan R, and Giri S. Predicting Disease Progression in Multiple Sclerosis by using a Combination of Highly Sensitive Single Molecule Array Technology (SIMOA) and Untargeted Metabolomics. *Mult Scler* 2022; 28(1_SUPPL):43-43. PMID: Not assigned. [Full Text](#)

Pathology and Laboratory Medicine

Vijayanarayanan A, **Chitale D**, Keller C, and **Mukherjee A.** Neuroepithelial tumor with EWSR1-BEND2 fusion: Case report and review of literature. *J Neuropathol Exp Neurol* 2022; 81(6):493-493. PMID: Not assigned. [Full Text](#)

Public Health Sciences

Arkhipov SN, Liao TDS, Potter DL, Bobbitt KR, Ortiz PA, and Pavlov TS. Dissociation of hypertension and renal damage after cessation of high salt diet in Dahl rats. *FASEB J* 2022; 36. PMID: Not assigned. [Full Text](#)

BACKGROUND: Every year, thousands of hypertensive patients reduce salt consumption in the efforts to control blood pressure. Most of the studies agreed that about one-third of the patients had an excellent

response, one-third had only a modest response, and one-third had little or no response. Irreversibility of high blood pressure is associated with various mechanisms underlying the self-sustaining character of hypertension. We hypothesize that chronic hypertension leads to sustained renal damage and excessive sodium reabsorption, staying even after removing the trigger, caused the initial blood pressure raise. METHODS: We used Dahl salt-sensitive rats for chronic continuous observation of blood pressure with radiotelemetry in conscious free moving animals. Rats were fed a 4%NaCl diet to induce hypertension, and then the diet was switched back to normal (0.4%NaCl). Patch-clamp analysis was performed in freshly isolated, split-open cortical collecting ducts to characterize activity of epithelial sodium channel (ENaC), responsible for sodium reabsorption in aldosterone-sensitive distal nephron. Flow cytometry, trichrome staining and FITC-inulin clearance estimated immune cell infiltration, renal damage and renal function. RESULTS: We found that blood pressure increase is reversible if induced by a short 3-day long feeding with 4%NaCl diet. A 3-week long high salt diet develops a sustaining hypertension (MAP ~150 mmHg): switching back to 0.4%NaCl diet slightly reduces blood pressure (to 145 mmHg) next day, but later hypertension progresses, reaching ~158 mmHg. Notably, the self-sustaining phase of hypertension was sensitive to benzamil treatment, which lowered BP to ~136 mmHg. Patch clamp analysis revealed that development of hypertension was accompanied with elevated ENaC activity which also stayed high, despite withdrawal of 4%NaCl diet. A separate subset of experiments demonstrated that dietary salt reduction in hypertensive animals decreases the number of total CD45+CD3+CD4+ and CD45+CD3+CD8+ cells in renal tissues. Also, we found a reduced area of protein casts abundance in the post-salt hypertensive group in comparison with age-matched rats kept on a high salt diet, and improving a glomerular filtration rate in the post-salt period. CONCLUSION: Based on our earlier publications and current data, we conclude that ENaC activity contributes to both development of salt-sensitive hypertension and its continuation in the absence of high salt challenge. However, dietary salt restriction reduces renal inflammation and damage in hypertensive animals.

Public Health Sciences

Cheng P, Santarossa S, Kalmbach D, and Drake C. P689. Improving Treatment Effectiveness in Marginalized Individuals: Facilitators and Barriers to Digital Cognitive Behavioral Therapy for Insomnia. *Biol Psychiatry* 2022; 91(9):S369. PMID: Not assigned. [Full Text](#)

Background: Digital Cognitive Behavioral Therapy for Insomnia (dCBT-I) is a highly effective treatment self-guided mHealth treatment for insomnia; however, completion and adherence rates are poor, especially among marginalized individuals. The present study aimed to explore facilitators and barriers to dCBT-I. Methods: Thematic analysis was conducted on qualitative data collected in those who engaged with dCBT-I. A total of 151 written feedback, 34 individual interviews, and 1 focus group of six racial minorities with low socioeconomic status (SES) was used. Results: Five themes emerged: digital person to person component, type and extent of information, users' sense of autonomy, app functionality, and importance of tailored content. The majority of participants across demographic groups rated the virtual therapist positive. Users felt that the app was engaging and that the information was understandable and well-paced. Users liked the flexibility of the self-guided program; however a subset of participants were not able to benefit from this feature, likely due to lower health literacy in those with lower SES, this subset comprised those with lower health literacy and SES. This population also reported lower self-efficacy and was significantly in favor of wanting more personalized support. Conclusions: Although dCBT-I has high accessibility and scalability, low health literacy may be a barrier treatment completion, especially for individuals with low SES. This suggests that enhanced support, such as providing more personalized support and tailored content, can improve treatment adherence and completion. Supported By: R01HL159180 Keywords: Insomnia, Cognitive Behavioral Therapy, mHealth

Public Health Sciences

Qutob O, Bensenhaver J, Susick L, Petersen L, Lehrberg A, Dimaano F, and Schwartz T. Sentinel Lymph Node Positivity in Clinically Node Negative Breast Cancer Patients After Neoadjuvant Chemotherapy: Opportunities to Defer Intraoperative Frozen Section Analysis. *Ann Surg Oncol* 2022; 29(SUPPL 2):421-421. PMID: Not assigned. [Full Text](#)

INTRODUCTION: Neoadjuvant chemotherapy (NACT) is frequently implemented in a breast cancer treatment plan. In clinically node negative (cN0) patients following NACT, it is routine to perform sentinel

lymph node (SLN) biopsy with intraoperative frozen section analysis with subsequent axillary lymph node dissection (ALND) if metastatic disease were detected. We aim to define the rate of sentinel node positivity (ypN1 (sn)) at our institution in patients who presented as cN0 and received NACT. METHODS: Using our IRB approved breast cancer database a retrospective chart review was performed for all T1-T3, cN0 primary breast cancer cases who underwent NACT from 2016 to 2021 and have undergone a subsequent definitive operation at our institution. Demographics, clinical characteristics, tumor biology and staging were recorded. We stratified by hormone receptor (HR) and HER2 status defined as: HR negative (0%), HR weakly positive (1-10%), HR positive (>11%), HER2 negative (0, 1+, 2+ negative by FISH), HER2 positive (3+, 2+ positive by FISH) RESULTS: We identified 139 cN0 cases undergoing NACT from 2016 to 2021. Forty were excluded, leaving 99 for analysis. Of these, 8 (8 %) were found to be ypN1(sn). Of the 71 HER2 negative cases, we found 32 HR negative (triple negative) and 11 HR weakly positive, none of which (0%) were found to be ypN1(sn), and 28 HR positive of which 7 (25%) were found to be ypN1(sn). Of the 28 HER2 positive cases, we found 11 HR negative and 3 HR weakly positive cases, none of which (0%) were found to be ypN1, and 14 HR positive of which 1 (7%) was found to be a micrometastasis (ypN1mic(sn)) CONCLUSIONS: Our results show that for the more aggressive tumor subtypes, including HR negative and HR weakly positive, the rate of ypN1(sn) after NACT in cN0 patients was 0%. These results suggest that frozen section could be avoided at the time of surgery for these patients in lieu of permanent pathology, due to the negligible likelihood of finding ypN1(sn) and thus needing ALND.

Public Health Sciences

Zahoor I, Waters J, Datta I, Cerghet M, Poisson L, Rattan R, and Giri S. Predicting Disease Progression in Multiple Sclerosis by using a Combination of Highly Sensitive Single Molecule Array Technology (SIMOA) and Untargeted Metabolomics. *Mult Scler* 2022; 28(1_SUPPL):43-43. PMID: Not assigned. [Full Text](#)

Radiation Oncology

Saad MA, Clark JM, Shah RA, Siddiqui F, Parikh PJ, Gartrelle KJ, Natour AKK, Khan GN, and Kwon DS. A single-center Analysis of 30-and 90-Day Post-pancreatectomy Complications in Patients Undergoing Neoadjuvant Radiation with EBRT vs. MRI-guided SBRT. *Ann Surg Oncol* 2022; 29(SUPPL 2):439-440. PMID: Not assigned. [Full Text](#)

INTRODUCTION: Stereotactic MRI -guided adaptive radiation therapy (SMART) is being investigated for enhanced efficacy in locally advanced, borderline resectable and medically inoperable pancreatic cancer. Traditionally, conventionally fractionated chemoradiation (EBRT) has been used for operable patients. We sought to evaluate whether there would be differences in surgical complications and outcomes in the 30- and 90- day postoperative period in patients who received either neoadjuvant EBRT or SMART followed by definitive surgery. METHODS: A retrospective single-center analysis of patients with either resectable, borderline resectable or locally advanced tumors of the pancreas or duodenum, treated with neoadjuvant radiation and surgical management between 2014 and 2021 was performed. Patient demographics and post-surgical complications were collected and stratified according to both treatment arms. The International Study Group of Pancreatic Surgery (ISGPS) classifications were used to define and grade postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE) and postpancreatectomy hemorrhage (PPH). A univariate analysis was done followed by a multivariate analysis. RESULTS: Among the 65 patients (mean age 62.6 years, 46% female) who underwent definitive surgical intervention, 44 (67.7%) received EBRT, and 21 (32.3%) received SMART. Baseline characteristics including age, sex, race, ASA, and Charlson comorbidity index (CCI) scores were found to be similar. On univariate analysis, PPH was significantly higher in SMART (OR, 6.6; 95% CI, 1.2 to 37.3; p = 0.034). After adjusting for confounders on multivariate analysis, it appears there is a trend towards higher PPH in the SMART cohort (p = 0.052). CONCLUSIONS: Neoadjuvant SMART followed by definitive surgery is not associated with worse outcomes in the 30- and 90- day postoperative period vs. neoadjuvant EBRT. Although there was a trend towards PPH on multivariate analysis, further discussion is warranted involving vascular resection, vascular stents and anticoagulation.

Sleep Medicine

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Background: Digital Cognitive Behavioral Therapy for Insomnia (dCBT-I) is a highly effective treatment self-guided mHealth treatment for insomnia; however, completion and adherence rates are poor, especially among marginalized individuals. The present study aimed to explore facilitators and barriers to dCBT-I. Methods: Thematic analysis was conducted on qualitative data collected in those who engaged with dCBT-I. A total of 151 written feedback, 34 individual interviews, and 1 focus group of six racial minorities with low socioeconomic status (SES) was used. Results: Five themes emerged: digital person to person component, type and extent of information, users' sense of autonomy, app functionality, and importance of tailored content. The majority of participants across demographic groups rated the virtual therapist positive. Users felt that the app was engaging and that the information was understandable and well-paced. Users liked the flexibility of the self-guided program; however a subset of participants were not able to benefit from this feature, likely due to lower health literacy in those with lower SES, this subset comprised those with lower health literacy and SES. This population also reported lower self-efficacy and was significantly in favor of wanting more personalized support. Conclusions: Although dCBT-I has high accessibility and scalability, low health literacy may be a barrier treatment completion, especially for individuals with low SES. This suggests that enhanced support, such as providing more personalized support and tailored content, can improve treatment adherence and completion. Supported By: R01HL159180 Keywords: Insomnia, Cognitive Behavioral Therapy, mHealth

Surgery

Lytle JR, Macias BR, Lee SM, Martin D, Ebert DJ, Hargens AR, **Dulchavsky SA**, Alferova IV, Stenger MB, and Laurie SS. Cardiovascular Responses to Mild Lower Body Negative Pressure during Spaceflight. *FASEB J* 2022; 36. PMID: Not assigned. [Full Text](#)

INTRODUCTION: Weightlessness during spaceflight causes a chronic cephalad fluid shift that has been hypothesized to underlie numerous risks associated with spaceflight, including the development of ocular structural and functional changes and in rare cases venous thrombosis. Acute use of 25 mmHg lower body negative pressure (LBNP) during spaceflight can partially reverse this headward fluid shift and thus, may represent a promising countermeasure. However, there are limited data on how the cardiovascular system responds to sustained use of mild LBNP during spaceflight when cardiovascular deconditioning and adaptation may cause crewmembers to be more susceptible to orthostatic stressors than they would have been on Earth. PURPOSE: The purpose of this study was to quantify the heart rate (HR) and blood pressure response throughout ~60 minutes of exposure to 25 mmHg LBNP during spaceflight and determine if this response was augmented at later time points during 6-month spaceflight missions. HYPOTHESIS: We hypothesized that crewmembers would experience an increase in HR during LBNP that would be sufficient to maintain mean arterial pressure (MAP) and this would not be augmented later in spaceflight. METHODS: Brachial arterial pressure and HR were measured before and throughout ~60 min of 25 mmHg LBNP after ~45 days (FD45) and ~150 days (FD150) of spaceflight in 12 crewmembers. Total LBNP session times varied slightly due to logistical constraints. MAP and HR changes from baseline with LBNP exposure were analyzed with splines models. Marginal means were used for estimation and statistical comparisons across time and between flight days. RESULTS: Before LBNP use, HR was 59 beats per min (BPM 95% CI: 56 - 62) and MAP was 93 mmHg (95% CI: 90 - 96). During LBNP exposure on FD45, HR increased by 9 BPM (95% CI: +7 - +10) at 15 min of exposure, and increased further to +10 BPM (95% CI: +8 - +12) at 30 min, and +11 BPM (95% CI: +9 - +14) at 45 min. On FD150, HR increased by 8 BPM (95% CI: +5 - +11) at 15 min of exposure but plateaued thereafter. MAP decreased by 5 mmHg (95% CI: -8 - -2) at 15 min and remained lower thereafter. MAP responses during ~60 min of LBNP exposure were not statistically different between FD45 and FD150. A total of 46 sessions of LBNP were successfully completed, and only a single case of mild hypotensive symptoms was reported, and this session was completed. CONCLUSION: These data suggest that the cardiovascular system can accommodate up to 60 min of sustained use of mild levels of LBNP during long-duration spaceflight. There was a single report of mild hypotensive symptoms during use of LBNP by an individual who had low blood pressure prior to the start of the LBNP session. Thus, the absolute arterial blood pressure

should be taken into consideration when determining if an LBNP session will be a potential challenge to the cardiovascular system during spaceflight.

Surgery

Qutob O, Bensenhaver J, Susick L, Petersen L, Lehrberg A, Dimaano F, and Schwartz T. Sentinel Lymph Node Positivity in Clinically Node Negative Breast Cancer Patients After Neoadjuvant Chemotherapy: Opportunities to Defer Intraoperative Frozen Section Analysis. *Ann Surg Oncol* 2022; 29(SUPPL 2):421-421. PMID: Not assigned. [Full Text](#)

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Surgery

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Surgery

Saad MA, Gartelle KJ, Shah RA, Clark JM, Langley KA, Field EA, Steffes CP, and Kwon DS. Disparity Outcomes in Patients Undergoing Pancreas Surgery at an Urban Tertiary Care Center. *Ann Surg Oncol* 2022; 29(SUPPL 2):443-443. PMID: Not assigned. [Full Text](#)

INTRODUCTION: Previous studies have shown significant disparities in pancreas cancer outcomes in African American (AA) compared to non-AA patients. Pancreas surgery continues to be associated with significant morbidity, however, there is little reported data on pancreas surgical outcomes by race. We sought to evaluate how race would affect surgical outcomes in an urban tertiary care center for patients undergoing pancreas surgery. **METHODS:** A retrospective single-center analysis of patients undergoing pancreas surgery between January 2013 and September 2021 was performed. Patient demographics and post-surgical complications were collected and stratified by race. Area Deprivation Index (ADI) was used to determine patient socioeconomic status. Charlson Comorbidity Index (CCI) was calculated for comorbidities. Clavien-Dindo (CD) complications, as well as postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE) and postpancreatectomy hemorrhage (PPH) were evaluated. Patient reoperation, readmission, and mortality in the 30- and 90- day period were collected and univariate and multivariate analyses were performed. **RESULTS:** Among 461 patients, 82% (N = 378) were nonAA and 18% (N = 83) were AA. Age and sex were found to be significantly different between the two groups, while ADI and CCI were not. Length of stay (LOS), POPF, PPH, PPH grade C and intra-abdominal abscess (IAA) were found to be significant on univariate analysis in the AA cohort. On multivariate analysis, LOS (OR 4.0; 95% CI 2.0-5.7; p < 0.001), POPF (OR 0.6; 95% CI 0.4-1.0; p = 0.043), PPH (OR 0.5; 95% CI 0.2-0.9; p = 0.022), PPH grade C (OR 0.2; 95% CI 0.1-0.7; p = 0.017) and IAA (OR 0.4; 95% CI 0.2-0.9; p = 0.017) were still significantly higher in the AA cohort. **CONCLUSIONS:** AA patients undergoing pancreas surgery were noted to have a longer LOS, higher incidence of POPF, PPH and IAA compared to non-AA patients. However, no significant difference was seen in reoperation rates, major CD complications, or 30- and 90-day readmission. Elucidating patient selection, tumor biology, and preoperative treatment algorithms may shed additional insight on the differences in surgical outcomes in this particular patient cohort.

Books and Book Chapters

Nephrology

Jalota Sahota R, and Anjum F. Pulmonary Interstitial Emphysema. StatPearls Publishing. 2022. PMID: 32809319. [Full Text](#)

Henry Ford Hospital
Hofstra University, Zucker School of Medicine

Pulmonary interstitial emphysema (PIE) is a rare, abnormal pathology that occurs more commonly in neonates but can be seen in adults as well. The increased air pressure within the alveoli and alveolar airspaces can disrupt the adjacent lung interstitial tissue, damaging the lung structure and causing linear and cystic spaces that can be complicated with air leaks. The leaked air is collected outside normal air passages and inside the interstitium or bronchovascular complexes. Premature infants with pulmonary interstitial emphysema can develop respiratory distress syndrome. The critical goal is to be able to maintain sufficient gas exchange. Without adequate gas exchange, lungs will be damaged, resulting in prolonged hypoxia, respiratory acidosis, and pulmonary hypoperfusion. PIE is a diagnosis based on imaging and histopathology. Administration of surfactant and high-frequency ventilation has been shown to decrease the incidence of PIE in premature infants. The latest management of infants with respiratory distress syndrome is prophylaxis with synthetic surfactant and continuous positive airway pressure, possibly without mechanical ventilation.

Nephrology

Jalota Sahota R, and Anjum F. Lung Torsion. StatPearls Publishing. 2022. PMID: 32809737. [Full Text](#)

Henry Ford Hospital
Hofstra University, Zucker School of Medicine

Lung torsion is a rare pathology that is classically seen when there is a disruption in the thoracic cavity. Disruptions can include thoracotomy, lung transplantation, and trauma. Lung torsion is a life-threatening disease that requires a timely diagnosis because lung rotation can cause vascular compromise and airway obstruction, which can result in necrosis of the lung tissue. With immediate management, the affected lung or pulmonary lobe can be salvaged. Overall, lung torsion has a poor prognosis due to misdiagnosis and delay in treatment. If detorsion occurs and the lung is fixed in place, then it can recover to full function.

Nephrology

Jalota Sahota R, and Sayad E. Tension Pneumothorax. StatPearls Publishing. 2022. PMID: 32644516. [Full Text](#)

Henry Ford Hospital
Baylor College of Medicine/ Texas Children's Hospital

Pneumothorax is the collapse of the lung when air accumulates between the parietal and visceral pleura inside the chest. The air is outside the lung but inside the thoracic cavity. This places pressure on the lung and can lead to its collapse and a shift of the surrounding structures. Pneumothoraces can be traumatic or atraumatic. Traumatic pneumothoraces occur secondary to penetrating or blunt trauma or iatrogenic. Iatrogenic pneumothorax is a traumatic pneumothorax that results from injury to the pleura, with air introduced into the pleural cavity secondary to diagnostic or therapeutic medical intervention. Atraumatic pneumothoraces are further divided into primary (unknown etiology) and secondary (patient with an underlying pulmonary disease). Pneumothoraces are classified as simple (no shift of mediastinal structures), tension (shift in mediastinal structures present), or open (air passing through an open chest wound). A tension pneumothorax is a severe condition that results when air is trapped in the pleural space under positive pressure, displacing mediastinal structures, and compromising cardiopulmonary function. Early recognition of this condition is life-saving both outside the hospital and in modern ICU. Knowledge of necessary emergency thoracic decompression procedures are essential for all healthcare

professionals. Traumatic and tension pneumothoraces are life-threatening and require immediate treatment.

Nephrology

Jalota Sahota R, and Soos MP. Subclavian Vein Thrombosis. StatPearls Publishing. 2022. PMID: 32644695. [Full Text](#)

Henry Ford Hospital
McLaren Greater Lansing

Subclavian vein thrombosis (SCVT) is a condition where a blood clot forms in the subclavian vein. SCVT can occur from multiple etiologies and is a potentially life-threatening pathology if not treated in a timely manner. SCVT occurs due to either a primary etiology or a secondary etiology. Primary thrombosis is further delineated as effort induced (Paget-Schroetter syndrome) or idiopathic (frequently associated with undiagnosed malignancy). Secondary subclavian vein thrombosis is associated with catheters or lines in the vein. While primary thrombosis is rare, the incidence of secondary thrombosis continues to rise as a consequence of complex cardiac devices and long term central venous catheters (CVC) placement in cancer patients. SCVT has high rates of acute mortality and long term disability without proper and timely treatment. Early diagnosis and treatment are essential in preventing fatal acute complications, such as pulmonary embolism and long term morbidity related to venous inflow restriction.

Henry Ford Health Publications on COVID-19

Anesthesiology

Zador L, Nowak K, Sitarik A, MacLean L, Han X, Kalsi M, Yeldo N, Sibai N, Penning D, and Lewis M. The Burnout Epidemic Within A Viral Pandemic: Impact of a Wellness Initiative. *Perioper Care Oper Room Manag* 2022; 27:100251. PMID: 35382030. [Full Text](#)

Behavioral Health Services/Psychiatry/Neuropsychology

Reffi AN, Kalmbach DA, Cheng P, Jovanovic T, Norrholm SD, Sexton MB, Mahr G, Arnett L, Seymour G, and Drake CL. Sleep reactivity as a potential pathway from childhood abuse to adult insomnia. *Sleep Med* 2022; 94:70-75. PMID: 35504109. [Full Text](#)

Behavioral Health Services/Psychiatry/Neuropsychology

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Emergency Medicine

Bunch CM, Moore EE, Moore HB, Neal MD, Thomas AV, Zackariya N, Zhao J, Zackariya S, Brenner TJ, Berquist M, Buckner H, Wiarda G, Fulkerson D, Huff W, Kwaan HC, Lankowicz G, Laubscher GJ, Lourens PJ, Pretorius E, Kotze MJ, Moolla MS, Sithole S, Maponga TG, Kell DB, Fox MD, Gillespie L, Khan RZ, Mamczak CN, March R, Macias R, Bull BS, and Walsh MM. Immuno-Thrombotic Complications of COVID-19: Implications for Timing of Surgery and Anticoagulation. *Front Surg* 2022; 9:889999. PMID: 35599794. [Full Text](#)

Emergency Medicine

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